# Cardiovascular Disease Burden and Cost-effectiveness of Cardiovascular Risk Screening in Sri Lanka.

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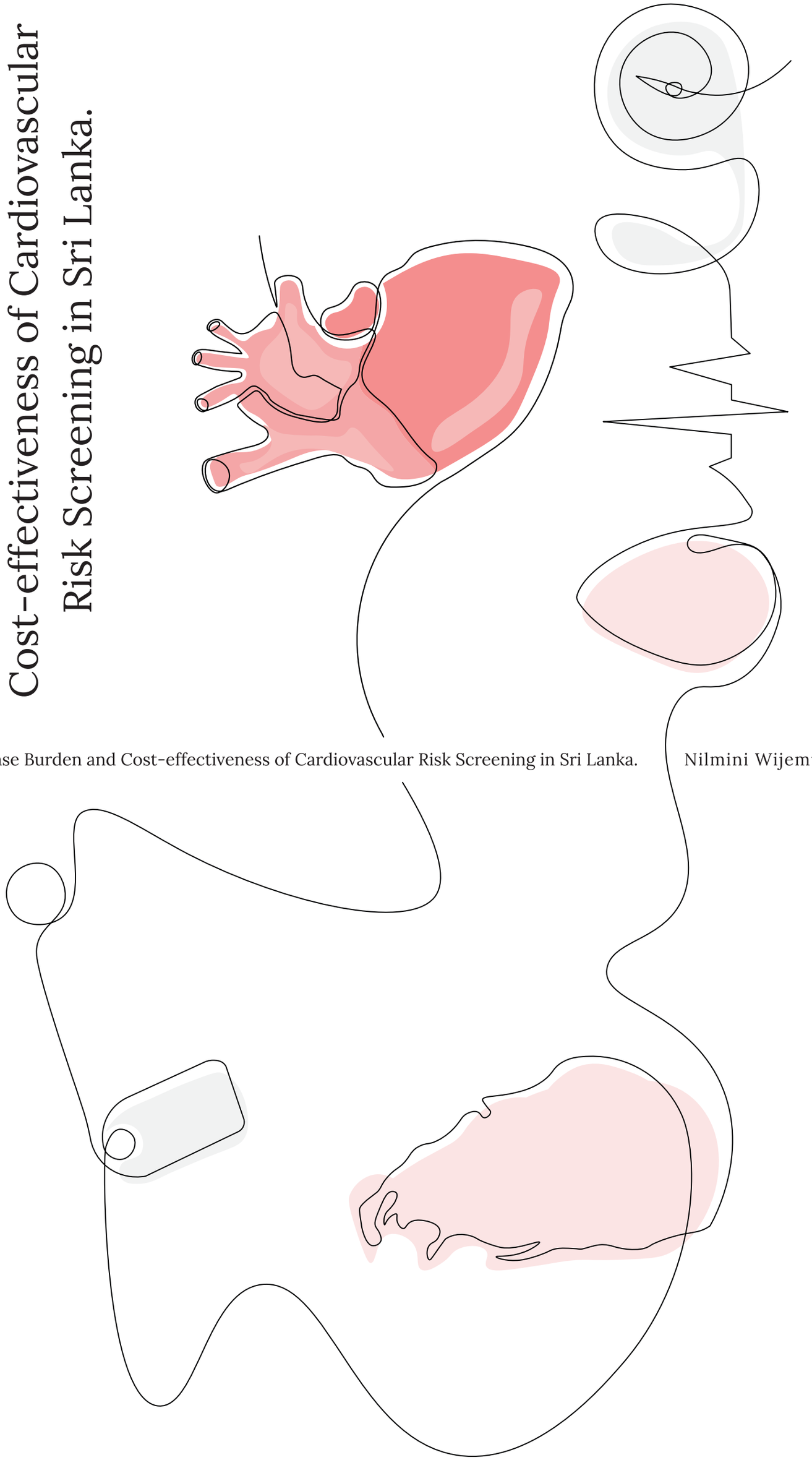

# Cardiovascular Disease Burden and Cost-effectiveness of Cardiovascular Risk Screening in Sri Lanka.

**De ziektelast als gevolg van hart- en vaatziekten en de kosteneffectiviteit van screening op cardiovasculaire aandoeningen in Sri Lanka.**

Thesis

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## DOCTORAL COMMITTEE

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# CONTENTS

# Chapter

# Introduction

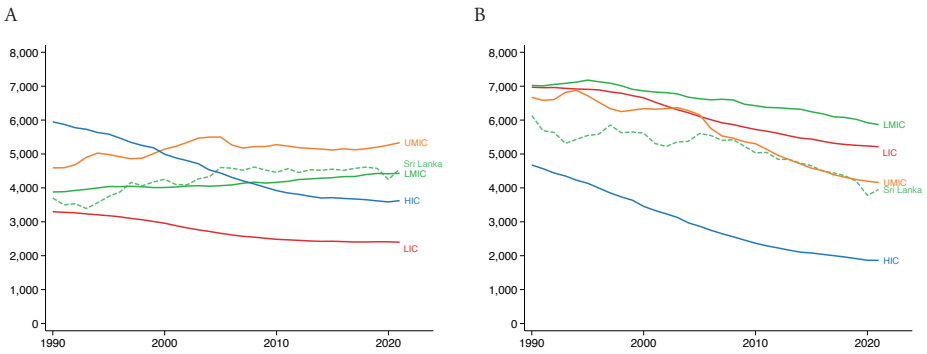
# INTRODUCTION

For the last three decades, there has been a rapid decline in the global burden of disease, largely driven by falling prevalence of communicable, maternal, neonatal and nutritional disease in low-income countries (LICs) and lower-middle-income countries (LMICs). However, at the age of 30 years, the risk of dying prematurely (before 70) from one of the four most common non-communicable diseases (NCDs)—cardiovascular disease (CVD), respiratory disease, diabetes and cancer—is 1.5 times higher in low- and middle-income countries than in high-income countries (HICs) (1).

One of the single largest groups of conditions that contribute to the burden of NCDs globally is atherosclerotic cardiovascular disease: a chronic disease of the circulatory system that includes ischaemic heart disease (IHD) and stroke. Atherosclerotic CVD (henceforth, CVD) accounts for one-third of deaths globally, and is the leading cause of mortality (2). It is also estimated to have accounted for 38% of premature mortality between the ages of 30 and 70 years in 2015 (2), which is significant given the social and economic ramifications of mortality in the working-age population.

Whilst HICs have seen a steady decline in the burden of CVD, falling by 27% between 1990 and 2021 to reach 3,624 disability-adjusted life years (DALYs) per 100,000, over the same period, the burden increased by 14% in LMICs, to reach 4,431 DALYs per 100,000 population, and by 16% in upper-middle income countries (UMIC), to reach 5,335 DALYs per 100,000 popu-

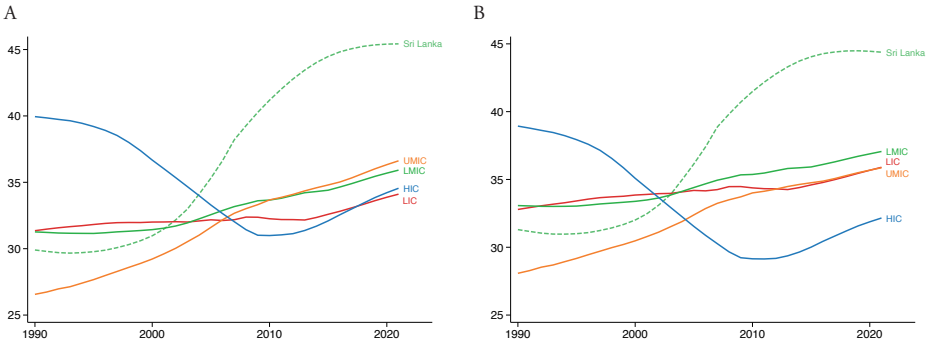
***Figure 1 Burden of cardiovascular disease (DALYs per 100,000)***




**Notes:** A. Unstandardized DALYs per 100,000 B. Age-standardized DALYS per 100,000. Cardiovascular disease defined as ischaemic heart disease and stroke. Countries categorised using World Bank country classifications by income level: 2022-2023. HIC = High-income, UMIC = Upper-middle income, LMIC = Lower-middle income, LIC = Low-income countries.

Source: Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2021 (GBD 2021) Results. Seattle: Institute for Health Metrics and Evaluation (IHME), 2022. Available from http://vizhub.healthdata.org/gbd-results. (9 July 2024).

***Figure 2 Summary exposure value for high blood pressure (0 to 100 scale)***




**Notes:** A. Age unstandardized B. Age-standardized. Summary Exposure Value (SEV) for high blood pressure indicates the population's overall exposure to different levels of hypertension, accounting for both the prevalence and associated health risk of each level on a scale from 0 (no exposure) to 100 (entire population at highest risk). Countries categorised using World Bank country classifications by income level: 2022-2023. HIC = High-income, UMIC = Upper-middle income, LMIC = Lower-middle income, LIC = Low-income countries

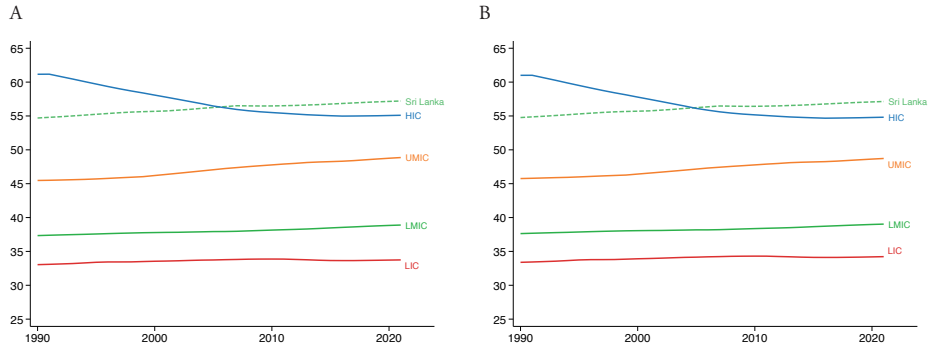
Source: Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2021 (GBD 2021) Results. Seattle: Institute for Health Metrics and Evaluation (IHME), 2022. Available from http://vizhub.healthdata.org/gbd-results. (9 July 2024).

lation (Figure 1A). Similarly, cardiovascular deaths declined in HICs but increased in LMICs and UMICs and in 2021 accounted for 22% and 31% of all deaths, respectively. Adjusting for differences in the age composition of populations between countries and over time, the disparities remain (Figure 1B): the age-standardized CVD burden decreased by 60% between 1990 to 2021 in HICs, compared to 40% in UMICs, and only 14-16% in LMICs and LICs, and in 2021 this burden was 2-3 times larger in low- and middle-income countries than in HICs.

There are several independent risk factors for CVD. The main one is hypertension, which decreased in age-standardized prevalence in most high-income countries from 1990–2019, but has remained at similar or increased levels in most LICs and many LMICs and UMICs (3, 4). The unstandardized rates, and the absolute number of people with hypertension, in low- and middle-income countries have increased over time as these populations age and increase in size (5). The age-standardized summary exposure value of high blood pressure, a parameter that accounts for different levels of blood pressure and the associated risk at each level, is higher for low- and middle-income countries than for HICs and has steadily increased for these countries since 1991 (Figure 2).

Another key risk factor for CVD, high low-density lipoprotein (LDL) cholesterol, saw declines in age-standardized prevalence in HICs between the 1970s and 2010 concordant with increased statin use and reduced saturated-fat intake (6). Age-standardized and non-standardized

*Figure 3 Summary exposure value for high LDL cholesterol (0 to 100 scale)*




**Notes:** A. Age unstandardized B. Age-standardized. Summary Exposure Value (SEV) for high LDL cholesterol indicates the population's overall exposure to different levels of hypertension, accounting for both the prevalence and associated health risk of each level on a scale from 0 (no exposure) to 100 (entire population at highest risk). Countries categorised using World Bank country classifications by income level: 2022-2023. LDL = low-density lipoprotein, HIC = High-income, UMIC = Upper-middle income, LMIC = Lower-middle income, LIC = Low-income countries
Source: Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2021 (GBD 2021) Results. Seattle: Institute for Health Metrics and Evaluation (IHME), 2022. Available from http://vizhub.healthdata.org/gbd-results. (9 July 2024).

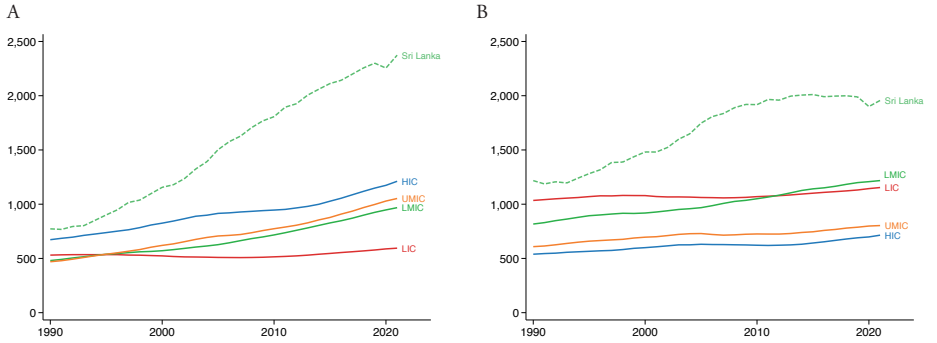
summary exposure values due to high LDL cholesterol also declined in HICs, but they have steadily increased in low- and middle-income countries (Figure 3).

Another independent CVD risk factor, and a condition with significant morbidity itself, is diabetes mellitus. The absolute and age-standardized prevalence of diabetes has doubled to tripled in low-, middle- and high-income countries, whilst the DALY burden has increased as well. With age-standardization, the prevalence of diabetes has increased faster in LICs, LMICs and UMICs, than in HICs (7). Whilst the unstandardized DALY burden remains higher in HICs, the age-standardized DALY burden per 100,000 population is higher in low- and middle-income countries (Figure 4).

## The role of primary prevention in reducing the CVD burden

Reasons for the rapid decline in the age-standardized CVD disease burden and mortality in HICs from the 1970s to the early 2000s have been studied extensively. Multiple studies in HICs have found that a reduction in risk factors was likely to have accounted for approximately 45%–60% of the decline in coronary heart disease events and deaths, while the remaining decline can be attributed to improvements in acute care and secondary prevention after coronary heart disease events (8-11). Of these risk factors, reductions in systolic blood pressure, total cholesterol, and increases in HDL cholesterol are each estimated to account for 10–15% of the total reductions in ischaemic heart disease events (10). Some studies found higher impacts: a Norwegian study attributed 31% of the reduction in incident coronary heart disease to the reduction in total cholesterol (11), and a US study estimated that reductions in

*Figure 4 DALYs from diabetes (per 100,000 population)*




**Notes:** A. Unstandardized DALYs per 100,000 B. Age-standardized DALYS per 100,000. Diabetes disease defined as diabetes mellitus type 1 and type 2. Countries categorised using World Bank country classifications by income level: 2022-2023. HIC = High-income, UMIC = Upper-middle income, LMIC = Lower-middle income, LIC = Low-income countries Source: Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2021 (GBD 2021) Results. Seattle: Institute for Health Metrics and Evaluation (IHME), 2022. Available from http://vizhub.healthdata.org/gbd-results. (9 July 2024).

total cholesterol and systolic blood pressure contributed to 28% and 31% of the reduction in coronary heart disease deaths respectively (9). The study in the US also estimated that hypertension management and statins for primary prevention accounted respectively for 20% and 10% of declines seen in coronary heart disease deaths attributed to all medical and surgical treatments available for the prevention and management of coronary heart disease.

Low- and middle-income countries have also seen a decline in the age-standardized CVD burden, yet overall rates remain far higher, and the rate of decline, particularly in LMICs and LICs, is sluggish (2). In low- and middle-income countries, high systolic blood pressure and high low-density lipoprotein cholesterol are estimated to be the modifiable risk factors with the highest attributable fractions for ischaemic heart disease (12).

## The role of primary prevention in low- and middle-income countries

Recognizing the importance of screening and treating risk factors for CVD, the World Health Organization (WHO) produced the Package of Essential Noncommunicable Disease (PEN) Interventions for Primary Health Care in Low Resource Settings guidelines (13, 14). This has been supplemented by the WHO HEARTS technical packages that set out guidelines to screen and manage high CVD risk, hypertension, diabetes and hypercholesterolemia (15, 16). The total CVD risk approach is used, where typically the ten-year risk of having a CVD event or death is calculated using a risk screening tool utilizing risk factors (depending on the risk tool) such as age, hypertension, body mass index, diabetes and smoking status. Management is initiated depending on the CVD risk, alongside management for hypertension, diabetes and hypercholesterolemia.

Whilst there is some evidence that the introduction of these CVD screening and management programs results in clinical improvements (17), and modelling studies have suggested that PEN-based screening programs can be cost-effective (18, 19), a systematic review of programs in LMICs found that international guidelines for these programs need to be tailored to local settings for maximum impact (20).

## Sri Lanka as a special case to study for NCD care

Sri Lanka is an LMIC that is advanced amongst its peers in its demographic transition. Sri Lanka made substantial gains in reducing the burden from maternal, child health and communicable diseases in the 20th century, and outperformed UMICs in key indicators such as life expectancy alongside neonatal, infant, under-five and maternal mortality by 2013 (21). Furthermore, the rate of decline in the age-standardized CVD burden is similar to the decline seen in UMICs since 2010 (Figure 1). Many of the health-related achievements are accredited to a highly efficient publicly funded health system with high rates of equitable access, alongside efficient procurement of medications that ensures Sri Lankans have access to essential medicines free at publicly funded outpatient clinics, or at affordable, regulated prices through community pharmacies (22).

Nevertheless, Sri Lanka faces several key health challenges. With increasing life expectancy, the population is ageing, resulting in an age structure closer to that of UMICs, with 12% of the population aged 65 years and above, compared to the LMIC mean of 6% (23). Ageing populations experience a higher burden of NCD. Even though the life expectancy in Sri Lanka is higher than the mean for UMICs, the healthy life expectancy at birth is slightly lower, reflecting a higher burden of disease (21). There is also stagnation in the improvement of male life expectancy: whereas all-cause mortality declined by 67% between 1950–2006 in females, it only declined by 19% in males, with circulatory disease burden being the major cause of this slow decline (24). Relatedly, male life expectancy is also slightly lower than the mean male life expectancy in UMICs (25). Furthermore, Sri Lanka has one of the highest prevalences of diabetes in the world, affecting 23% of adults aged 18 years and over (26).

Although it is known that CVD is the leading cause of death in Sri Lanka, there is little detailed research available on the burden, distribution and impact of CVD on the Sri Lankan population, and the impact of undiagnosed CVD and its risk factors. One unpublished study gives an estimate of IHD in a subnational sample from 2006 (27), whilst other studies are smaller and over two decades old. Another subnational study of 736 adults showed that out of scale of 0 to 1, where 1 is full health, and 0 is death, Sri Lankans with a cardiac condition rated their QOL at 0.64. However, this does not disentangle the impact of age, gender, sociodemographic factors and other conditions, and is difficult to use in modelling studies (28). Furthermore, there is very limited evidence in low- and middle-income countries of the health and healthcare

burden presented by undiagnosed and diagnosed CVD, hypertension and diabetes. This includes whether there are significant differences in health, QOL and healthcare use by condition and diagnosis status, and whether early diagnosis and treatment makes a difference in these parameters. Such findings would further strengthen the value of a CVD-risk screening strategy which not only aims to prevent CVD, but also detect and treat hypertension and diabetes (29).

In 2011, Sri Lanka introduced a PEN-based screening program at Healthy Lifestyle Centres (HLCs) to screen for high-risk of CVD, as well as its risk factors, hypertension and diabetes, and organise appropriate counselling and preventative medical management for high-risk individuals (30). Screening occurs in close to 1,000 HLCs nationally, which have the capacity to screen over 650,000 people annually. However, there are challenges in achieving screening targets. For example, male attendance at HLCs is poor. Only 28% of those screened in 2019 were male (31). The initial national policy was to screen those without existing CVD aged 40–65 years (32), and this was revised in 2018 to screen all those aged 35 years and above (33). Other modifications to the policy have been introduced. However, there are no known or published formal analyses that assess the impacts, cost, cost-effectiveness or distributional impacts of either the original screening policy, or the more recent modifications. There are frequent changes in recommendations given by global bodies such as the WHO on the exact design of these PEN-based programs, however limited attention has been given to analyse the potential updates and alternative designs, both in Sri Lanka and other low- and middle-income countries. In an initial analysis I carried out in 2014, using subnational data from 2006 (34), I found that the CVD-risk screening strategy that had been initiated in 2011 was likely to have minimal impact, preventing a mere 400 deaths over 10 years, and that critical modifications to the screening protocol could increase its impact by 10-fold (35).

Prior to 2018, there were only limited national data available on CVD and its risk factors. The data available included STEPs surveys from 2006 and 2014–2015, which lacked data such as standard screening questionnaires for ischaemic heart disease, a detailed past medical history and medications history, an inventory of household assets to estimate socioeconomic status accurately, detailed healthcare use, medications use, and questionnaires to determine health-related quality of life (QOL) (36, 37).

Recognizing the gap in data to perform a comprehensive health economic analysis to analyse chronic disease screening programs in Sri Lanka, colleagues and I established the Sri Lankan Health and Ageing Study (SLHAS), with the first wave of data collected on a nationally representative cohort of 6,665 Sri Lankan adults in 2018–9. We collected data that would allow us to quantify the burden of the diseases targeted by the NCD screening program in Sri Lanka, including the prevalence of these conditions, and the impact of these conditions on health, health-related QOL and healthcare use. We also ensured that enough data were

collected for modelling and economic analyses. Before the SLHAS was conducted, we did not have data in Sri Lanka, or even South Asia, to estimate the loss in QOL (disutility) of having chronic diseases such as CVD, hypertension and diabetes after controlling for age, gender and sociodemographic characteristics. This thesis extensively uses the data we collected from the SLHAS to quantify the burden of disease from CVD and model the potential cost and impact on QOL of alternative CVD-risk programs, including modifications to the current screening program, introducing opportunistic screening in existing healthcare visits, and the distributional impact of such programs by socioeconomic groups. The analyses in this thesis could be useful for policymakers in Sri Lanka to justify the need for an extensive CVD-risk program, and to optimize it to maximise impact while maintaining equitable outcomes.

### Research objectives

In this thesis, I highlight the magnitude of the problem posed by CVD in the Sri Lankan population, based on prevalence, and impacts on health, QOL and healthcare use. I then explore how CVD risk screening could be better tailored to maximise equitable impact in a finite health budget. The background for this study motivates the following research questions.

1. What is the impact of CVD and its associated risk-factors—hypertension, diabetes and hypercholesterolemia—on health and healthcare use of the Sri Lankan population?
2. Are there modifications to the screening setting and clinical criteria for CVD risk screening and treatment that could enhance its impact while remaining cost-effective?
3. Would the benefits of key modifications to CVD screening in an opportunistic setting be fairly distributed over different socioeconomic groups?

## OUTLINE OF THE THESIS

### Part 1 – Prevalence and health impact of cardiovascular and other chronic diseases

Clearly defining the burden of CVD, hypertension and diabetes, not only measured by prevalence but also by indicators such as QOL and healthcare use of both undiagnosed and diagnosed conditions, reinforces the value of the national screening program, and can identify potential gaps and burdens faced by specific sociodemographic groups, to better target the screening program.

Chapters 2, 3, and 4 focus on the first research question, quantifying the prevalence and impacts of CVD, and key associated conditions, including hypertension and diabetes in Sri Lanka.

Chapter 2 estimates the prevalence of ischaemic heart disease (IHD) and angina—both coronary heart diseases (CHDs)—in Sri Lanka, and documents the demographic profiles of people

with these conditions. This information is useful to understand the importance of CHD in Sri Lanka, and to determine if there are sociodemographic disparities in the patterns of disease, particularly by ethnicity, sector of residence, level of education, household socioeconomic quintile, and area socioeconomic tertile, which may be informative in targeting CVD-risk screening. It also compares the prevalence by age and gender estimated by local data with prevalence modelled using the Global Burden of Diseases (GBD) study data.

Chapter 3 provides a Sri Lanka-specific disutility catalogue showing the mean reduction in QOL of conditions such as IHD, angina, stroke, hypertension, diabetes, depression and other common NCDs. This study builds on previous work in Sri Lanka, which found the mean utility of people with cardiac conditions, hypertension, and diabetes was far less than people without any of these conditions (28). The current work estimates the loss in QOL associated with each condition after controlling for sociodemographic characteristics, including age and gender, as well as for other comorbidities. It underlines the impact of the chronic diseases studied on QOL, and is also required and used in subsequent chapters to calculate quality-adjusted life years, which is a common parameter utilised in cost-effectiveness analyses.

Chapter 4 focuses on the broader impacts on health and healthcare use of Sri Lankans living with coronary heart disease (CHD), hypertension, diabetes and depression, a condition with a bidirectional relationship with CHD and diabetes. The health outcomes considered are physical and mental functioning, and health-related QOL, and the healthcare outcomes are annual inpatient visits, outpatient visits and out-of-pocket spending. The chapter focuses on whether there are differences in these health and healthcare outcomes for people having either indications of these conditions without a diagnosis, or a diagnosis, compared to people without these conditions, as this has implications for the importance of screening and treating these conditions early.

## Part 2 – The (distributional) impact of CVD screening and treatment programs

Chapter 5 and 6 answer on the second research question, where I analyse potential key modifications to the PEN-based screening program in Sri Lanka, estimating the costs and health gains. Previous studies have shown that while components of the PEN-based screening are considered "best buys," it is imperative that international guidelines for CVD screening be analysed and modified to better fit each country's context and ability to spend (19, 20).

Chapter 5 focuses on modifying the current screening program at HLCs, focusing on the technical parameters of the CVD screening program. It models restricting the age group screened to 40 years and above, using the new WHO CVD risk tool released in 2019, lowering the CVD risk threshold at which statins are prescribed, and implementing newer recommendations for

reducing the blood pressure threshold for individuals with high CVD risk and diabetes, and prescribing statin treatment for all people with diabetes. The disutility catalogue derived in Chapter 3 is used to model incremental QALYs gained from each scenario, and provides a costing for each scenario, to recommend modifications that are likely to be cost-effective in Sri Lanka.

Chapter 6 looks at an alternative way of undertaking CVD, hypertension and diabetes screening, using existing healthcare encounters, rather than at the dedicated healthy lifestyle centres where there are challenges in coverage and poor male attendance. Opportunistic screening could potentially be effective given the frequent use of outpatient care by Sri Lankans, estimated at 7 to 8 visits annually (38). This chapter uses modelling to simulate a 1-month screening program (for which there is more robust data), and a 1-year screening program in the public and private sectors, assessing the distributional impact of these programs by analysing the distribution of new diagnoses by socioeconomic status.

Finally, I look at the last research question in Chapter 7, which combines the recommended modifications to the current CVD screening program in chapter 5 and the concept of opportunistic screening in chapter 6 to assess the cost-effectiveness of several different screening scenarios run in a public-sector opportunistic screening program. It also assesses the distributional impact of each scenario by socioeconomic status to establish whether a scenario may be preferred to another when taking account of the equity impact alongside efficiency in a finite fiscal space, where money diverted to an expanded screening program results in the loss of health in other areas. This is one of the first distributional cost-effectiveness analyses to be undertaken in a LMIC and it is the first such analysis anywhere that uses stochastic dominance to evaluate and compare programme-specific health distributions based on general ethical principles that encapsulate willingness to trade off equity against efficiency (39).

Each chapter in the thesis uses data from the Sri Lankan Health and Ageing Study. The study was established with a huge effort from many people in Sri Lanka and overseas. As a Co-Investigator of the study, I have been involved from the initial stages: in 2015, I attended meetings at the University of Lausanne on behalf of the project director, to discuss and finetune the objectives of the SLHAS, which was part of the multi-centre "Inclusive Social Protection for Chronic Health Problems" project supported by the Swiss Programme for Research on Global Issues for Development (r4d programme). From 2015–2018 I led the development of several questionnaire modules, notably the chronic disease, risk screening and quality of life modules, and researched and worked with a team to establish the Computer-Assisted Personal Interview platform and procure key equipment for the study, including new technologies such as a portable electrocardiograph machine. Immediately prior to and during the study from 2018–2019, I trained data collectors on key modules, visited field sties, and also oversaw

laboratory testing with the laboratory team, individually checking, and compiling over 70,000 laboratory test results for each individual in the study.

All the studies are co-authored; however, I am the lead author of every study, performing the data cleaning and analysis, writing the original drafts and finalising each chapter. All co-authors reviewed and edited these chapters. Chapters 2–6 have been published, and Chapter 7 will be submitted.

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# Chapter 2

# The prevalence and epidemiological features of ischaemic heart disease in Sri Lanka

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# ABSTRACT


## Background

There is limited evidence on the prevalence of ischaemic heart disease (IHD) and its association with risk factors and socioeconomic status (SES) in low- and middle-income countries (LMICs). Given the relatively high levels of access to healthcare in Sri Lanka, the association of IHD with SES may be different from that observed in other LMICs.

## Objectives

To estimate the prevalence of IHD in Sri Lanka, determine its associated risk factors and its association with SES.

## Methods

We analysed data from 6,513 adults aged ≥18 years examined in the 2018/19 Sri Lanka Health and Ageing Study. We used the Rose angina questionnaire to classify participants as having angina (Angina+) and used self-report or medical records to identify participants with a history of IHD (History+). The association of Angina+ and History+ with age, ethnicity, sector of residence, education level, household SES wealth quintile, area SES wealth quintile, hypertension, diabetes, smoking, total cholesterol, cholesterol-to-HDL ratio, waist-to-hip ratio and body mass index were analysed in unadjusted and adjusted models. Additional analyses were performed to investigate sensitivity to correction for missing data and to benchmark estimates against evidence from other studies.

## Conclusions

We estimated prevalence of History+ of 3.9% (95% CI 3.3%–4.4%) and Angina+ of 3.0% (95% CI 2.4%–3.5%) in adults aged 18 years and over. The prevalence of Angina+ was higher in women than men (3.9% vs 1.9%, $p<0.001$) whilst prevalence of History+ was lower (3.8% vs 4.0%, $p=0.8$), which may suggest a higher rate of undiagnosed IHD in women. History of IHD was strongly associated with age, hypertension and diabetes status even after adjusting for sociodemographic factors. Though the prevalence of History+ was higher in the most developed area SES tertile and urban areas, History+ was also associated with less education but not household SES, consistent with patterns emerging from other LMICs.

## 2.1 INTRODUCTION

Low- and -middle income countries (LMICs) are experiencing an increasing burden of cardiovascular disease (CVD) as they move through the epidemiological and demographic transitions (1, 2). In high-income countries (HICs), CVD prevalence first increased in more affluent groups before the burden shifted down groups with lower socioeconomic status (SES). In LMICs, as the burden of CVD increases, it may shift even more rapidly to people of lower SES (1, 3).

Sri Lanka is advanced in its epidemiological transition. The proportion of total disability adjusted life years (DALYs) attributable to maternal and child health (MCH) conditions is one-third of the average in LMICs (4), whilst ischaemic heart disease (IHD) (8.5%), stroke (5.6%) and diabetes (8.6%) account for relatively more DALYs. Sri Lankans have access to free universal healthcare and cheap medicines (5). Process quality of care is high for indicators that need low- to moderate-resources (6). However, it is not known whether this translates to a different epidemiological pattern of IHD prevalence and its associations with risk factors and with SES.

Like many LMICs, Sri Lanka lacks reliable estimates of IHD prevalence. Using models, the Global Burden of Disease (GBD) project estimates that IHD prevalence in Sri Lanka is 2.2% (males 2.7%, females 1.7%) (4). Both the crude (2.2%) and age-standardized (2.0%) GBD estimates of IHD prevalence in Sri Lanka are below the average for the South Asia World Bank region (2.6% and 3.6%) and all other World Bank regions, except for Latin America and Caribbean (1.9% and 1.9%), and Sub-Saharan Africa (0.1% and 2.1%).

The available local surveybased estimates cover a variety of age groups and populations, and are almost more than two decades old. A study of 975 middle-aged males (35–59 years) in the Central Province in 1994 found that 5.4% of participants satisfied the criteria for angina or possible myocardial infarction using the Rose angina questionnaire (RAQ), and a further 3.2% of people satisfied ECG criteria of IHD (7). In a study of 4,484 people in 7 of the 9 provinces in Sri Lanka in 2005, the estimated age-sex standardized IHD prevalence in Sri Lanka was 9.3% based on RAQ, ECG criteria and treatment for IHD (8). The prevalence was higher in women (11.3%) than men (7.2%). Another study of 30–65-year-olds in four provinces in Sri Lanka in 2003 found that 4.9% of women and 4.5% of men had angina using RAQ (9, 10).

Estimates of IHD prevalence for HICs are typically based on patient databases (11) and self-reported history of IHD or responses on RAQ in population-based surveys (12-14). Most LMICs lack comprehensive patient databases or registries and few have nationally representative surveys that collect data that can be used to estimate IHD prevalence. The aim of this paper was to estimate the prevalence of IHD, and its association with risk factors and SES, in Sri Lanka, using nationally representative survey data.

## 2.2 MATERIALS AND METHODS

### 2.2.1 Sample design and selection

We used data from the first wave of the SLHAS, a nationally representative survey of adults aged 18 years and over, conducted from November 2018 to November 2019. Stratified, multi-stage cluster sampling randomly selected one adult from randomly sampled households from 298 primary sampling units defined by Grama Niladhari Divisions (GND) (the smallest administrative unit) located in all 25 districts of Sri Lanka (15). Interviews were conducted at field clinics. Participants were asked about a history of IHD, hypertension, and diabetes. They were asked to bring their medical records with them to the field clinic. If available, these were also checked for a history of IHD, hypertension or diabetes. Data on age, gender, education level, household assets, housing materials, and water and sanitation facilities were collected through self-reports. Medication history from the previous two weeks was recorded. Weight, height, waist and hip circumference were measured, and body mass index and waist-to-hip ratio was calculated. Participants were instructed to fast. Fasting blood samples were taken by nurses and were tested for blood glucose and lipid profile. People who were fasting and did not report diabetes had oral glucose tolerance tests, and those who had not fasted had random blood glucose and non-fasting lipid profiles.

### 2.2.2 Outcomes

The London School of Hygiene Chest Pain Questionnaire—the RAQ—was used to identify people with Rose angina (16, 17). The RAQ has previously been validated for use in Sri Lanka (7). A person satisfied the criteria for Rose angina (Angina+) if they reported ever having chest pain which appeared upon exertion, was situated at any level of the sternum or left anterolateral chest and arm, which caused the respondent to slow down or stop, and was relieved within ten minutes of rest. A person satisfied the criteria for Rose plus possible infarction if they satisfied the criteria for Rose+ or reported ever having severe chest pain across the front of the chest for thirty minutes or more (Infarction+). We used this outcome in a supplementary analysis.

Participants were defined as having a history of IHD (History+) if either they self-reported when questioned that a doctor had ever told them that they have IHD or that they had experienced a myocardial infarction, or their medical records, if brought to the interview, showed a history of IHD. Of the participants with a history of IHD, 88.5% both self-reported and had medical records of this condition, 8.1% self-reported but did not have medical records confirming this and 3.4% had medical records but did not self-report.

We analysed two main outcomes: a) Rose angina (Angina+), and b) history of IHD (History+).

### 2.2.3 Risk factors and covariates

Education level was categorized into four groups: no formal education; primary education which included grades 1 to 5; secondary education which included grades 6 to 12, or O-level or A-level certification; and tertiary education which included undergraduate degrees or post-graduate diplomas and degrees. For comparisons with another study, education was also categorized into low (no formal education or primary education), intermediate (secondary education) or high education (tertiary education).

We created a proxy for household SES through a wealth index equal to the first principal component from analysis of household reported durable assets, housing quality, water and sanitation facilities, and other assets (Appendix Text A1) (18). Similarly, we calculated area SES from the first principal component of social and economic indicators for each GND obtained from the 2012 census (19). We created household SES groups from the tertiles and quintiles of the household wealth index and area SES tertile groups from tertiles of the wealth index by GND.

A participant was classified as hypertensive if they a) reported that a doctor had ever told them that they have hypertension or high blood pressure, or b) they were currently taking antihypertensives based on self-report, medical records or medications they brought to the interview or c) brought their medical records to the interview and these stated a history of hypertension, or d) the mean of two blood pressure measurements, taken 10 minutes apart, was 140/90 mmHg or greater (15). A participant was classified as diabetic if they a) reported that a doctor had ever told them that they have diabetes of high blood sugar, or b) they were currently taking oral or injectable hypoglycaemics based on self-report, medical records or medications they brought to the interview, or c) brought their medical records to the interview and these stated a history of diabetes, or d) gave a blood sample that showed fasting blood glucose ≥ 126 mg/dL, a random glucose ≥ 200 mg/dL, or an oral glucose tolerance test result ≥ 200 mg/dL (19). A participant who had ever smoked 100 cigarettes or other tobacco products was classified as having a history of smoking.

A participant was recorded as taking statins based on self-report, medical records or medications they brought to the interview belonging to WHO Anatomical Therapeutic Classification (ATC) class C10 (lipid modifying agents).

### 2.2.4 Statistical analysis

We estimated IHD prevalence from the sample means of Angina+ and History+. We examined prevalence by gender, age groups, ethnicity, sector of residence (rural, urban, estate, rural/estate), education level, household SES quintile group, and area SES tertile group. We examined variation in prevalence by estimating unadjusted and adjusted odds ratios of each outcome using univariate and multivariate logit models respectively. In the univariate analysis we used the same variables, with age as a continuous variable, and included hypertension status,

diabetes status, smoking status, total cholesterol, cholesterol-to-HDL ratio, BMI and waist-to-hip ratio. In the multivariate analysis, we used the same variables as the univariate analysis, except due to similarities in cholesterol and cholesterol-to-HDL ratio, and BMI and waist-to-hip ratio, we ran one model which included total cholesterol and BMI, and a second model which included cholesterol-to-HDL and waisttohip ratios. Continuous variables—age, total cholesterol, total cholesterol-to-HDL ratio, BMI and waist-to-hip ratio—were standardized to show the odds ratio of one standard deviation change in that variable. A sub analysis was performed to estimate associations between History+ and cholesterol, including statin use and statin intensity in the multivariate regression model using total cholesterol and BMI.

In all analyses, the data were weighted to make them representative of the national population. The original survey design weights were modified using iterative proportional fitting (IPF) to match the district, provincial and national structure along the dimensions of age, sex, sector, and ethnicity (15, 19). When estimating differences in IHD status by diabetes status, the sample weights were further modified to account for possible nonrandom participation in the oral glucose tolerance and fasting blood glucose tests. We multiplied each participant's original weight by their propensity to provide a glucose test and recalibrated the weights to match the age–sex–ethnicity total weights (19).

We tested the significance of odds ratios in unadjusted and adjusted logit models, using a Wald test for both joint significance of categorical variables (that is, testing whether all levels of a categorical variable have an odds ratio (OR) of one) and specific pairwise comparisons within a categorical variable (that is, testing if the OR between two levels of a categorical variable are the same), and a t-test for continuous variables. All models were adjusted for the complex survey design, accounting for clustering with a finite population correction. All analyses were performed using Stata 17.0 (20).

**2.2.5 Sensitivity analysis** Missing data on Rose angina status and risk factors and covariates potentially make the complete case sample used for the analysis unrepresentative of the population, even after the application of weights. In sensitivity analysis, we used multiple imputation to impute missing values for Angina status, education category, diabetes status, smoking status, total cholesterol and BMI. We repeated estimation of the univariate and multivariate logit regression models for each outcome using the resulting sample with imputation.

To make comparisons with estimates of the prevalence of myocardial infarction among men aged 35–59 years from another study Mendis and Ekanayake (7), we conducted an additional analysis with the sample restricted to that demographic group and using the Infarction+ outcome.

## 2.3 RESULTS

We excluded 3 participants who were less than 18 years old, and 152 participants with missing data for history of IHD, leaving 6,513 (97.7%) participants for analysis. Of these, 6,459 (99.2%) had complete data on RAQ.

Table 1 describes the characteristics of the samples used for Angina+ prevalence and History+ prevalence with data on 6,459 and 6,513 participants respectively. The distribution of demographic and risk factors are very similar between Angina and History samples in both the unweighted and weighted samples. With weighting, the mean age of the History sample was

***Table 1 Sociodemographic and risk factor distribution of participants in the Angina sample and History sample***

| | Angina | | | History | | |
|---|---|---|---|---|---|---|
| | **Unweighted *N*** | **Unweighted % / Mean (SD)** | **Weighted % / Mean (SD)** | **Unweighted *N*** | **Unweighted % / Mean (SD)** | **Weighted % / Mean (SD)** |
| Age | 6,459 | 50.0 (17.2) | 43.8 (16.7) | 6,513 | 50.1 (17.2) | 43.9 (16.7) |
| Sex | | | | | | |
| Male | 3,166 | 49.0 | 47.6 | 3,188 | 48.9 | 47.6 |
| Female | 3,293 | 51.0 | 52.4 | 3,325 | 51.1 | 52.4 |
| Ethnic group | | | | | | |
| Sinhala | 4,552 | 70.5 | 74.9 | 4,594 | 70.5 | 74.9 |
| SL Tamil | 1,266 | 19.6 | 12.5 | 1,273 | 19.5 | 12.5 |
| Indian Tamil | 203 | 3.1 | 2.8 | 205 | 3.1 | 2.8 |
| Muslim | 412 | 6.4 | 9.5 | 415 | 6.4 | 9.5 |
| Other | 26 | 0.4 | 0.3 | 26 | 0.4 | 0.3 |
| Sector | | | | | | |
| Rural | 3,566 | 55.2 | 70.6 | 3,590 | 55.1 | 70.6 |
| Urban | 1,939 | 30.0 | 19.6 | 1,960 | 30.1 | 19.6 |
| Estate | 166 | 2.6 | 0.6 | 168 | 2.6 | 0.7 |
| Rural/Estate | 788 | 12.2 | 9.2 | 795 | 12.2 | 9.2 |
| Education | | | | | | |
| No formal schooling | 245 | 3.8 | 2.8 | 252 | 3.9 | 2.8 |
| Primary educated | 903 | 14.0 | 9.9 | 914 | 14.0 | 10.0 |
| Secondary educated | 5,041 | 78.1 | 82.8 | 5,074 | 78.0 | 82.7 |
| Tertiary educated | 263 | 4.1 | 4.5 | 266 | 4.1 | 4.5 |
| Household SES quintile | | | | | | |
| Poorest | 1,535 | 23.8 | 19.6 | 1,547 | 23.8 | 19.6 |
| Poorer | 1,283 | 19.9 | 19.9 | 1,298 | 19.9 | 19.9 |
| Middle | 1,194 | 18.5 | 19.7 | 1,200 | 18.4 | 19.6 |

*Table 1 Sociodemographic and risk factor distribution of participants in the Angina sample and History sample*

| | Angina | | | History | | |
|---|---|---|---|---|---|---|
| | Unweighted *N* | Unweighted % / Mean (SD) | Weighted % / Mean (SD) | Unweighted *N* | Unweighted % / Mean (SD) | Weighted % / Mean (SD) |
| Richer | 1,167 | 18.1 | 20.0 | 1,179 | 18.1 | 20.0 |
| Richest | 1,280 | 19.8 | 20.8 | 1,289 | 19.8 | 20.8 |
| Area SES tertile | | | | | | |
| Least developed | 2,349 | 36.4 | 33.2 | 2,367 | 36.3 | 33.2 |
| Middle | 1,851 | 28.7 | 33.6 | 1,862 | 28.6 | 33.6 |
| Most developed | 2,259 | 35.0 | 33.2 | 2,284 | 35.1 | 33.3 |
| Hypertension status | | | | | | |
| No | 4,216 | 65.3 | 73.0 | 4,246 | 65.2 | 72.9 |
| Yes | 2,243 | 34.7 | 27.0 | 2,267 | 34.8 | 27.1 |
| Diabetes status | | | | | | |
| No | 3,206 | 67.8 | 77.1 | 3,226 | 67.7 | 77.1 |
| Yes | 1,524 | 32.2 | 22.9 | 1,538 | 32.3 | 22.9 |
| Smoking status | | | | | | |
| Non-smoker | 4,872 | 77.2 | 79.2 | 4,911 | 77.2 | 79.2 |
| Ex- or current smoker | 1,439 | 22.8 | 20.8 | 1,450 | 22.8 | 20.8 |
| Total cholesterol (mean) | 6,386 | 206.2 (47.5) | 208.6 (46.9) | 6,440 | 206.1 (47.5) | 208.5 (46.9) |
| Cholesterol-to-HDL ratio (mean) | 6,384 | 4.3 (1.3) | 4.4 (1.3) | 6,438 | 4.3 (1.3) | 4.4 (1.3) |
| BMI | 6,412 | 23.8 (4.6) | 23.9 (4.6) | 6,465 | 23.8 (4.6) | 23.9 (4.6) |
| Waist-to-hip ratio (mean) | 6,429 | 0.9 (0.1) | 0.9 (0.1) | 6,483 | 0.9 (0.1) | 0.9 (0.1) |

43.9 years (standard deviation 16.7 years), 23% were diabetic, 27% were hypertensive and 21% had a history of smoking.

The estimated prevalence of Angina+ was 3.0% (95% CI 2.4%–3.5%) and the prevalence of History+ was 3.9% (95% CI 3.3%–4.4%) in adults aged 18 years and over (Table 2). The prevalence of Angina+ was higher in women than men (3.9% vs 1.9%, p<0.001) but was similar to men for History+ (3.8% vs 4.0%, p=0.8). The prevalence of Angina+ was higher in the poorest household SES quintile (4.4% vs 2.0%, p=0.04), but the prevalence of History+ was similar (3.8% vs 4.0%, p=0.9). The prevalence of History+ was higher in the urban sector than rural sector (6.1% vs 3.3%, p<0.001), and in the most developed area SES tertile than least developed (5.1% vs 2.8%, p<0.001).

*Table 2 Prevalence of Angina+ and History+ by sociodemographic category*

| | Angina+, % (95% CI) | | | | History+, % (95% CI) | | | |
|---|---|---|---|---|---|---|---|---|
| | Male (n = 3,166) | Female (n = 3,293) | All (n = 6,459) | | Male (n = 3,188) | Female (n = 3,325) | All (n = 6,513) | |
| All | 1.9 (1.4 – 2.5) | 3.9 (3.0 – 4.8) | 3.0 (2.4 – 3.5) | *** | 4.0 (3.2 – 4.8) | 3.8 (2.9 – 4.6) | 3.9 (3.3 – 4.4) | |
| Age category | | | | | | | | |
| <35 | 1.2 (0.1 – 2.2) | 1.9 (0.7 – 3.1) | 1.5 (0.7 – 2.3) | | 0.5 (0.1 – 0.9) | 0.2 † | 0.4 (0.1 – 0.6) | |
| 35-44 | 1.3 (0.2 – 2.3) | 3.7 (1.9 – 5.6) | 2.5 (1.4 – 3.7) | * | 1.5 (0.4 – 2.7) | 1.3 (0.2 – 2.4) | 1.4 (0.5 – 2.4) | |
| 45-54 | 2.1 (0.4 – 3.8) | 4.7 (2.2 – 7.2) | 3.5 (2.0 – 4.9) | | 3.1 (1.3 – 4.8) | 2.6 (1.0 – 4.2) | 2.8 (1.8 – 3.8) | |
| 55-64 | 2.8 (0.9 – 4.7) | 6.0 (3.6 – 8.4) | 4.5 (3.0 – 5.9) | * | 7.8 (4.9 – 10.7) | 8.4 (5.4 – 11.4) | 8.1 (6.2 – 10.1) | |
| 65-74 | 3.5 (1.4 – 5.5) | 6.7 (4.1 – 9.3) | 5.3 (3.7 – 7.0) | * | 14.5 (10.4 – 18.7) | 11.3 (8.0 – 14.6) | 12.6 (10.1 – 15.2) | |
| 75-84 | 5.4 (1.9 – 9.0) | 2.2 † | 3.7 (1.5 – 5.8) | | 15.7 (9.7 – 21.7) | 13.8 (6.0 – 21.6) | 14.7 (10.5 – 18.8) | |
| 85+ | 3.4 (1.0 – 5.8) | 5.0 † | 4.5 † | | 12.1 † | 4.9 (0.4 – 9.4) | 7.2 (1.3 – 13.1) | |
| Ethnicity | | | | | | | | |
| Sinhala | 2.1 (1.4 – 2.9) | 4.2 (3.1 – 5.3) | 3.2 (2.5 – 3.9) | *** | 4.2 (3.2 – 5.2) | 3.6 (2.7 – 4.5) | 3.9 (3.3 – 4.5) | |
| Sri Lankan Tamil | 1.6 (0.8 – 2.4) | 1.1 (0.6 – 1.7) | 1.3 (0.8 – 1.9) | | 3.8 (2.1 – 5.6) | 2.2 (1.0 – 3.5) | 3.0 (1.9 – 4.1) | |
| Indian Tamil | 2.9 † | 11.6 (1.7 – 21.5) | 7.2 (2.2 – 12.2) | | 0.8 † | 6.1 † | 3.4 † | |
| Muslim | 0.7 (0.1 – 1.2) | 2.8 (0.2 – 5.5) | 1.8 (0.3 – 3.3) | | 3.5 † | 6.5 (1.5 – 11.5) | 5.1 (2.4 – 7.8) | |
| Other | 0.0 (0.0 – 0.0) | 13.2 (9.8 – 16.6) | 5.1 † | ** | 0.0 (0.0 – 0.0) | 13.2 (9.8 – 16.6) | 5.1 † | |
| Sector | | | | | | | | |
| Rural | 2.0 (1.3 – 2.7) | 3.9 (2.9 – 5.0) | 3.0 (2.3 – 3.7) | ** | 3.5 (2.5 – 4.5) | 3.2 (2.3 – 4.1) | 3.3 (2.7 – 4.0) | |
| Urban | 1.4 (0.5 – 2.3) | 3.3 (1.6 – 4.9) | 2.4 (1.4 – 3.4) | | 5.8 (4.0 – 7.5) | 6.3 (3.7 – 9.0) | 6.1 (4.6 – 7.5) | |
| Estate | 4.3 † | 7.9 (2.7 – 13.2) | 5.8 (2.4 – 9.1) | *** | 1.9 † | 5.6 † | 3.4 (1.3 – 5.5) | |
| Rural/Estate | 2.3 † | 4.8 (0.9 – 8.6) | 3.4 (1.6 – 5.2) | | 3.9 (1.9 – 5.9) | 2.8 † | 3.4 (2.0 – 4.8) | |
| Education | | | | | | | | |
| No formal schooling | 4.5 (2.7 – 6.2) | 4.7 (2.7 – 6.6) | 4.6 (1.3 – 7.9) | | 3.1 † | 7.8 (0.7 – 15.0) | 6.3 (2.5 – 10.1) | |
| Primary educated | 4.6 (1.7 – 7.5) | 7.9 (4.8 – 10.9) | 6.4 (4.6 – 8.1) | | 6.4 (3.9 – 8.9) | 9.6 (5.7 – 13.6) | 8.1 (5.7 – 10.6) | |
| Secondary educated | 1.5 (0.9 – 2.1) | 3.4 (2.4 – 4.3) | 2.5 (1.9 – 3.1) | *** | 3.9 (3.0 – 4.8) | 3.0 (2.3 – 3.8) | 3.4 (3.0 – 3.9) | |
| Tertiary educated | 3.4 (0.2 – 6.7) | 3.1 † | 3.3 (0.6 – 6.0) | | 1.3 † | 0.8 † | 1.0 (0.1 – 2.0) | |
| Household SES quintile | | | | | | | | |
| Poorest | 2.8 (1.0 – 4.7) | 5.4 (3.0 – 7.7) | 4.4 (2.7 – 6.0) | | 4.8 (2.9 – 6.8) | 3.2 (1.2 – 5.1) | 3.8 (2.6 – 5.1) | |
| Poorer | 2.1 (0.8 – 3.3) | 4.1 (2.0 – 6.2) | 3.2 (2.0 – 4.5) | | 2.6 (1.4 – 3.8) | 6.0 (3.3 – 8.7) | 4.5 (3.0 – 6.1) | |
| Middle | 1.9 (0.6 – 3.2) | 2.6 (0.9 – 4.3) | 2.3 (1.0 – 3.5) | | 3.4 (1.4 – 5.4) | 3.0 (1.3 – 4.6) | 3.2 (1.9 – 4.4) | |
| Richer | 1.9 (0.5 – 3.2) | 4.2 (1.6 – 6.8) | 2.9 (1.7 – 4.2) | | 4.0 (2.3 – 5.6) | 3.8 (2.3 – 5.3) | 3.9 (2.9 – 4.8) | |
| Richest | 1.3 (0.5 – 2.1) | 2.9 (0.8 – 5.0) | 2.0 (1.0 – 3.1) | | 4.9 (2.9 – 7.0) | 2.9 (1.1 – 4.7) | 4.0 (2.8 – 5.2) | |
| Area SES tertile | | | | | | | | |
| Least developed | 2.8 (1.6 – 4.0) | 3.9 (2.8 – 5.1) | 3.4 (2.6 – 4.2) | | 2.3 (1.5 – 3.2) | 3.2 (2.1 – 4.3) | 2.8 (1.9 – 3.7) | |
| Middle | 1.4 (0.6 – 2.2) | 4.4 (2.0 – 6.7) | 3.0 (1.8 – 4.1) | ** | 4.2 (2.4 – 6.0) | 3.4 (1.9 – 4.9) | 3.8 (2.8 – 4.8) | |
| Most developed | 1.6 (0.8 – 2.3) | 3.4 (1.7 – 5.0) | 2.5 (1.5 – 3.5) | * | 5.5 (3.6 – 7.4) | 4.8 (3.0 – 6.5) | 5.1 (4.1 – 6.1) | |

**Notes:** Data are weighted. Significance levels shown for difference between males and females (*** $p \leq 0.001$, ** $0.001 < p \leq 0.01$, * $0.01 < p \leq 0.05$). CI Confidence Interval. †Confidence intervals not shown as lower bounds of CIs were below zero.

***Table 3 Unadjusted and adjusted odds ratios for risk factors of Angina+ and History+ cases***

| | Angina+ | | History+ | |
|---|---|---|---|---|
| | **Unadjusted odds ratio (95% CI)** | **Adjusted odds ratio (95% CI)** | **Unadjusted odds ratio (95% CI)** | **Adjusted odds ratio (95% CI)** |
| Age (years) | 1.49 (1.28 - 1.74) *** | 1.28 (0.97 - 1.68) | 3.02 (2.60 - 3.51) *** | 2.46 (1.92 - 3.15) *** |
| Gender | | | | |
| Male | (Ref) *** | (Ref) *** | (Ref) | (Ref) |
| Female | 2.05 (1.44 - 2.90) | 3.07 (1.64 - 5.75) | 0.95 (0.69 - 1.32) | 0.89 (0.59 - 1.33) |
| Ethnicity | | | | |
| Sinhala | (Ref) *** | (Ref) ** | (Ref) | (Ref) |
| Sri Lankan Tamil | 0.40 (0.25 - 0.64) | 0.34 (0.20 - 0.60) | 0.76 (0.50 - 1.15) | 0.73 (0.43 - 1.25) |
| Indian Tamil | 2.33 (1.08 - 5.04) | 1.29 (0.40 - 4.11) | 0.86 (0.24 - 3.08) | 0.70 (0.18 - 2.80) |
| Muslim | 0.55 (0.23 - 1.34) | 0.43 (0.14 - 1.34) | 1.32 (0.73 - 2.39) | 0.95 (0.48 - 1.89) |
| Other | 1.62 (0.21 - 12.83) | 2.28 (0.37 - 13.93) | 1.33 (0.17 - 10.62) | 0.81 (0.14 - 4.62) |
| Sector | | | | |
| Rural | (Ref) | (Ref) | (Ref) ** | (Ref) |
| Urban | 0.79 (0.49 - 1.29) | 1.27 (0.56 - 2.88) | 1.87 (1.35 - 2.58) | 1.43 (0.82 - 2.48) |
| Estate | 1.97 (1.02 - 3.80) | 2.33 (0.90 - 6.02) | 1.02 (0.52 - 1.99) | 1.28 (0.56 - 2.92) |
| Rural/Estate | 1.14 (0.63 - 2.06) | 0.86 (0.34 - 2.13) | 1.02 (0.64 - 1.62) | 1.57 (0.80 - 3.11) |
| Education level | | | | |
| No formal education | (Ref) *** | (Ref) | (Ref) *** | (Ref) |
| Primary education | 1.41 (0.68 - 2.91) | 1.37 (0.56 - 3.37) | 1.33 (0.70 - 2.51) | 1.48 (0.58 - 3.77) |
| Secondary education | 0.53 (0.24 - 1.18) | 0.94 (0.36 - 2.42) | 0.53 (0.28 - 1.03) | 1.17 (0.43 - 3.18) |
| Tertiary education | 0.71 (0.23 - 2.19) | 1.23 (0.34 - 4.42) | 0.16 (0.06 - 0.43) | 0.32 (0.07 - 1.37) |
| Household SES quintile | | | | |
| Poorest | (Ref) | (Ref) | (Ref) | (Ref) |
| Poorer | 0.73 (0.40 - 1.34) | 1.06 (0.46 - 2.45) | 1.19 (0.71 - 1.99) | 1.41 (0.76 - 2.64) |
| Middle | 0.51 (0.25 - 1.05) | 0.59 (0.24 - 1.48) | 0.82 (0.50 - 1.34) | 0.99 (0.50 - 1.95) |
| Richer | 0.66 (0.38 - 1.16) | 1.18 (0.51 - 2.72) | 1.02 (0.67 - 1.55) | 0.89 (0.49 - 1.63) |
| Richest | 0.45 (0.21 - 0.97) | 0.44 (0.16 - 1.22) | 1.05 (0.65 - 1.71) | 0.94 (0.47 - 1.90) |
| Area SES tertile | | | | |
| Least developed | (Ref) | (Ref) | (Ref) ** | (Ref) |
| Middle | 0.87 (0.53 - 1.43) | 0.99 (0.53 - 1.84) | 1.38 (0.89 - 2.13) | 0.99 (0.57 - 1.70) |
| Most developed | 0.74 (0.46 - 1.19) | 0.71 (0.31 - 1.62) | 1.90 (1.28 - 2.82) | 1.30 (0.67 - 2.52) |
| Hypertension status | | | | |
| No hypertension | (Ref) *** | (Ref) | (Ref) *** | (Ref) * |
| Hypertensive | 2.11 (1.51 - 2.95) | 1.58 (0.95 - 2.61) | 5.90 (4.34 - 8.04) | 1.94 (1.17 - 3.22) |
| Diabetes status | | | | |
| No diabetes | (Ref) * | (Ref) | (Ref) *** | (Ref) *** |
| Diabetes | 1.66 (1.10 - 2.52) | 1.27 (0.81 - 1.98) | 3.82 (2.66 - 5.47) | 2.14 (1.46 - 3.13) |

| | | | | |
|---|---|---|---|---|
| Smoking status | | | | |
| Non-smoker | (Ref) | (Ref) * | (Ref) | (Ref) |
| Ex- or current smoker | 0.81 (0.55 - 1.17) | 2.09 (1.04 - 4.21) | 1.32 (0.95 - 1.84) | 1.20 (0.72 - 2.00) |
| Total cholesterol | 0.89 (0.77 - 1.03) | 0.88 (0.74 - 1.05) | 0.59 (0.48 - 0.73) *** | 0.58 (0.46 - 0.74) *** |
| Cholesterol-to-HDL ratio | 0.76 (0.63 - 0.91) ** | - | 0.66 (0.56 - 0.78) *** | - |
| BMI | 0.97 (0.82 - 1.15) | 0.92 (0.71 - 1.18) | 1.13 (0.98 - 1.31) | 1.06 (0.89 - 1.27) |
| Waist-to-hip ratio | 1.17 (0.97 - 1.41) | - | 1.51 (1.29 - 1.76) *** | - |

**Notes:** *** $p \leq 0.001$, ** $0.001 < p \leq 0.01$, * $0.01 < p \leq 0.05$. CI Confidence Interval. Joint significance shown for categorical variables. Odds ratios for continuous variables age, total cholesterol, cholesterol-to-HDL ratio, BMI and waist-to-hip ratio shown for one standard deviation increase in that variable. Cholesterol-to-HDL ratio and waist-to-hip ratio are dropped from the adjusted model.

Table 3 shows unadjusted and adjusted odds ratios of Angina+ and History+ for each risk factor and covariate. There were significant associations between Angina+ status and age, gender, ethnicity, education level, hypertension, diabetes, and cholesterol-to-HDL ratio, while there were significant associations with History+ status and age, sector of residence, education level, area SES, hypertension, diabetes, total cholesterol, cholesterol-to-HDL ratio and waist-to-hip ratio in unadjusted models.

In adjusted models, people who were older by one standard deviation of age had higher odds of Angina+ (adjusted OR 1.28, 95% CI 0.97–1.68, p=0.08) and History+ (adjusted OR 2.46, 95% CI 1.92–3.15, p<0.001). Females had higher odds than males of Angina+ (adjusted OR 3.07, 95% CI 1.64–5.75, p=0.001) but not of History+ (adjusted OR 0.89, 95% CI 0.59–1.33, p=0.6). People of Sri Lankan Tamil ethnicity had lower odds of Angina+ compared to people of Sinhala ethnicity (adjusted OR 0.34, 95% CI 0.20–0.60, joint significance: p=0.002), though the lower odds were not significant for History+. In adjusted models, education level, household and area SES quintiles were not significant. However, a separate analysis (Appendix Table A1) found that people with low education (no education or primary education) or intermediate level of education (secondary education) had higher adjusted odds (adjusted OR 4.2, 95% CI 1.2–14.4, p=0.02; adjusted OR 3.4, 95% CI 1.1–10.8, p=0.04 respectively) of History+ compared to people with high education (tertiary or above).

Hypertensive people had higher odds than normotensive people of History+ (adjusted OR 1.94, 95% CI 1.17–3.22, p=0.01) though the association with Angina+ was not significant (adjusted OR 1.58, 95% CI 0.95–2.61, p=0.08). Previous or current smoking was associated with Angina+ (adjusted OR 2.09, 95% CI 1.04–4.21, p=0.04), but the association with

History+ was not significant (adjusted OR 1.20, 95% CI 0.72–2.00, p=0.5). A one standard deviation increase in total cholesterol and cholesterol-to-HDL ratio was associated with lower odds of History+ (adjusted OR 0.58, 95% CI 0.46–0.74, p<0.001; 0.72, 95% CI 0.58–0.90, p=0.004 respectively) (Appendix Table A2). However, the association with total cholesterol was weaker after controlling for statin use (adjusted OR 0.79, 95% CI 0.62–1.01, p=0.06) and intensity of statin use (adjusted OR 0.81, 95% CI 0.64–1.02, p=0.07) (Appendix Table A3). BMI and waist-to-hip ratio was not significant in the adjusted models.

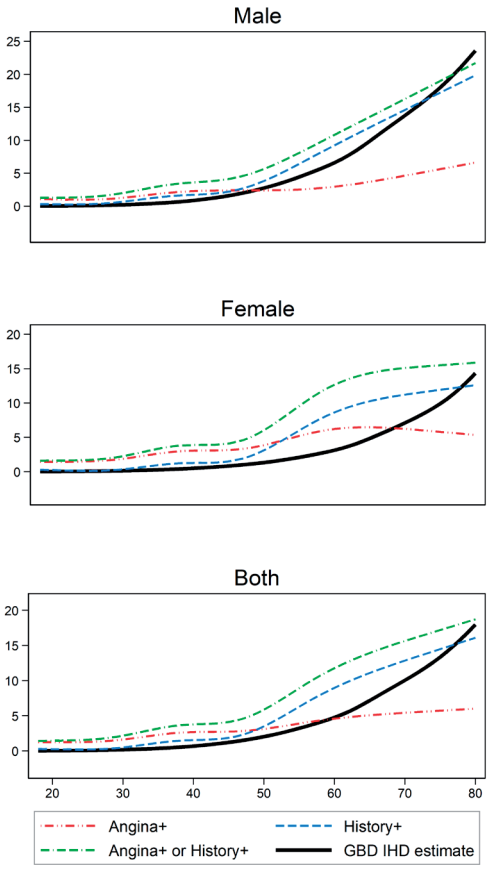
Sensitivity analysis with imputed values for angina status and covariates with missing data gave similar results to the complete-cases sample analysis, with a stronger association of hypertension with Angina+ and History+, and education level with Angina+ (Appendix Table A4).
When restricted to the population aged 40 years and over, the prevalence of Angina+ was 3.7% (95% CI 3.0%–4.5%) and History+ was 6.7% (95% CI 5.7%–7.6%). Assuming no IHD in the population younger than 18 years of age, the prevalence of Angina+ or History+ in the total population is 3.8% (95% CI 3.4%–4.3%) whilst the prevalence of Angina+ is 1.9% (95 CI 1.5%–2.2%) and History+ is 2.5% (95% CI 2.1%–2.8%). Analysis of males aged 35 years and 59 years, combining both angina and possible myocardial infarction on RAQ gave a prevalence of Infarction+ of 8.9% (95% CI 7.7%–10.2%). Restriction to the population aged 30-65 years gave an estimated prevalence of Angina+ in males as 2.2% (95% CI 1.4%–2.9%) and females as 4.3% (95% CI 3.2%–5.4%). The prevalence of History+ is somewhat higher than the prevalence of IHD estimated by the GBD study when analysed by age and gender, particularly between the ages of 50–70, with the difference more pronounced for women (Figure 1).

## 2.4 DISCUSSION

Estimating IHD prevalence in LMICs is challenging given the lack of adequate data, especially representative population surveys with measurements that allow identification of IHD. The RAQ has been used in a wide-range of population surveys in both HICs and some LMICs to estimate prevalence of angina, which has usually been found to be associated with a higher risk of future coronary artery events (21, 22). Our study presents the first known estimates of IHD prevalence in Sri Lanka using nationally representative data, with analysis of the correlation of IHD with known risk factors and sociodemographic features.

The prevalence of IHD in Sri Lanka using RAQ or IHD history, appears to be high at 3.8%, with the estimated prevalence higher than estimates produced by the GBD study (2.2%). Estimates of IHD for females in this study are higher than GBD estimates, and females have higher–almost double the odds–of being Angina+ than males, confirming a pattern of female preponderance for angina symptoms globally. People in urban areas and the most developed

***Figure 1 Comparison of smoothed IHD prevalence by age and gender, using Angina+ and History+ criteria with IHD prevalence estimates from Global Burden of Disease***




**Notes:** Smoothed prevalence by age are shown for Angina+, History+, and Angina+ or History+, fitting cubic splines with six knots to allow for non-linear relationships using weighted data for participants aged 18–80 years. Shaded regions represent 95% confidence intervals. GBD = Global Burden of Disease study, IHD = Ischaemic Heart Disease.

SES tertile had higher odds of History+. People with hypertension and diabetes also had higher odds of History+ even after adjustment.

Compared to data collected from four Sri Lankan provinces two decades ago, which used the Angina+ definition and a sample aged 30–65 years, our study found a lower prevalence for men (2.2% vs 4.5% of men and 4.3% vs 4.9% of women) (9, 10). Meanwhile our study prevalence was higher compared to estimates from one province more than three decades ago using the Ischaemia+ definition in people aged 35–59 years (8.9% vs 5.4%) (7). The estimated prevalence of angina (3.0%) is within the bounds of angina on RAQ in a metanalysis of 74

studies of 31 LMIC and highincome countries which found the prevalence of angina on RAQ ranged from 0.73% to 14.4% (9).

The overall prevalence of Angina+ or History+, 3.8% (95% CI 3.4%–4.3%), is higher than GBD study estimates for IHD (2.2%, 95% CI 1.9%–2.5%) for Sri Lanka. A prevalence of 3.8% is similar to the crude prevalence of IHD estimated by GBD for the Middle East and North Africa region (3.6%, 95% CI 3.4%–3.9%), which GBD reports as the World Bank region with the second highest prevalence of IHD (4). The GBD uses similar definitions for IHD prevalence, including angina based on the RAQ and myocardial infarction, performing modelling on data from 61 countries to generate countryspecific estimates (23). Similar to our study, the GBD definition does not include estimates based on electrocardiograph (ECG) evidence for prior MI citing limited specificity and sensitivity. The GBD uses modelling of incident myocardial infarction, and scales angina prevalence based on RAQ, to angina prevalence using claims data from the United States, which may account for the lower prevalence of IHD in the GBD study. Nevertheless, restricting prevalence estimates to History+, the prevalence is still somewhat higher in this study than GBD estimates, particularly for Sri Lankan women aged 50–70 years. Recent findings in diabetes prevalence using the same survey data also found far higher rates in Sri Lanka than what was estimated by the NCD Risk Factor Collaboration (NCD-RisC) (19, 24), suggesting that current global estimates for metabolic syndrome-related conditions may be systematically underestimated for Sri Lanka.

Our study found a higher prevalence and odds ratio of Angina+, which focuses on angina symptoms, in women than men. Globally, the prevalence of angina is typically reported to be higher in females than in males, although males were more often diagnosed with IHD in most populations in the world (9). Research suggests that there could be differences in the symptoms women with IHD report compared to men, and that they are more likely to have non-obstructive coronary artery disease than obstructive disease, which, amongst other factors, can lead to underdiagnosis of IHD (25, 26). Whilst this study focused on typical and not atypical symptoms, is not clear if even women with typical symptoms of angina are as likely to seek medical care as men, and if they do, whether physicians diagnose them with IHD (9). Furthermore, women with typical symptoms are less likely than men to have obstructive disease on angiogram (27, 28) or can also have normal coronary arteries (29). However, these women still have higher rates of cardiovascular events than women with no symptoms (28-31). Importantly, there is evidence that women with typical symptoms may receive less medical intervention than men (27), possibly because women with symptoms and a normal or nonobstructive angiogram would be likely to receive little medical treatment for IHD (28, 29). Given that our study is in line with global findings that women have a higher prevalence of angina symptoms, but a similar prevalence of diagnosed IHD as men, it is also possible then that women in Sri Lanka with IHD are underdiagnosed, and that these underdiagnosed

symptomatic women could have a poorer prognosis than those without symptoms. Therefore, it is important to ensure there is an equal focus on diagnosing IHD in women, particularly those who present with symptoms of angina.

As expected, increasing age, hypertension and diabetes were strongly associated with History+. Furthermore, the prevalence of History+ was higher in people living in the most developed area SES tertile and urban areas. Though the prevalence of Angina+ was higher in the poorest household quintile, a household wealth gradient was not seen for History+. Though statistically significant ORs were not seen for the household SES gradient for Angina+, there may again be a possibility of underdiagnosis of IHD in the poorest household SES quintile as was seen for women compared to men, and this needs further investigation with longitudinal data.

Typically, CVDs in LMICs are thought to shift from a disease concentrated in the affluent, to one concentrated in the poor: a demographic shift that was seen in highincome countries. However, the speed of this transition from rich to poor may be faster in LMICs than historically seen elsewhere (32). In subnational data collected in 2005/6, the prevalence of CVD risk factors–diabetes, obesity and hypertension–was higher in urban areas (33-35), which were generally higherincome areas (33), with obesity also confirmed to be higher in the rich. The pattern remained largely the same in 2018/9 where the prevalence of diabetes and hypertension was higher in urban areas, the most developed area SES tertile, and richer household quintiles. However, the development of ischaemic heart disease is multifactorial and arises due to a combination of risk factors and medical management of risk factors. Countering the pattern of metabolic conditions concentrating in urban and affluent populations, are CVD risk factors such as smoking which may be higher in the poor (36, 37), and hypertension, which also has a high prevalence in rural areas (15). However, in this study, it appears that IHD, proxied by History+, is still more common in urban and more affluent areas in Sri Lanka.

Similar to a prospective study of CVD conducted in 20 countries, including LMICs, we found that History+ had a stronger association with level of education than household wealth (38). After adjusting for age, gender, ethnicity, sector, household and area SES and CVD risk factors, people with low levels of education had higher odds than people with high levels of education of History+, whilst no such pattern was seen for household SES. While the lack of a gradient of History+ for household SES could hold if there is an element of underdiagnosis of IHD in poorer quintiles, it is unlikely that rates of underdiagnosis apply to household SES but not to lower education levels. It is generally considered that Sri Lankans, including the less affluent, have access to universal healthcare with a focus on primary prevention (5, 39), and access to cheap medicines (40-43), all of which may contribute to better primary prevention of IHD and management of conditions which increase the risk of IHD (42). Therefore, it is important that research in the Sri Lankan context on the development, diagnosis, treatment

and control of IHD and its risk factors such as diabetes and hypertension, not only focus on wealth gradients, but level of education as well.

Some known risk factors for IHD did not appear to be significant for either Angina+ or History+ or both. For example, the odds of History+ reduced for one standard deviation increase of total cholesterol (OR 0.59). However, this could be due to statin treatment of History+ participants, which is part of standard treatment guidelines. In multivariate models including statin treatment, and statin treatment intensity, the odds ratio increased to 0.79 and 0.81 and was no longer statistically significant. The association of History+ with past or current smoking was not strong, and could be due to underreporting of smoking in participants. The odds ratios associated with anthropometric measurements are mixed. Higher odds of History+ were associated with a one standard deviation increase in waist-to-hip ratios and with BMI to a lesser extent in the unadjusted model, but neither were significant in the adjusted models. Meanwhile an increase in BMI was associated with higher odds of History+, but less so for Angina+, similar to findings in India (44). The association of anthropometric measurements with IHD risk in South Asians is not fully understood, and there is debate as to which anthropometric measure is more closely correlated with IHD (45). A separate analysis using various obesity indices, such as BMI, waist circumference, waist-to-hip circumference, waist circumferencetoheight and body fat analysis and their association with IHD and other IHD risk factors would be useful.

Our study may have implications for the CVD risk screening tool which estimates the 10 year risk of developing CVD, produced by the WHO in 2019 (46). Data from the 2017 GBD study, which uses similar techniques to the 2019 study, was used to recalibrate risk models to age-sex-region specific incidences, to create regionspecific CVD risk calculators and charts for use in CVD risk screening programs. Furthermore, the incidence of CVD predicted for the SLHAS cohort using the WHO-2019 risk tool for Sri Lanka closely follows the incidence of IHD estimated by the 2019 GBD study (47). Given the finding of possible underestimation of IHD prevalence in the GBD study, particularly in women, it is important to monitor and validate the performance of the WHO-2019 risk screening tool using longitudinal data as it becomes available in the future.

There are some limitations in this study. The prevalence based on the respondent's recall of a doctor diagnosis of IHD or medical records kept by the respondent, may be misclassified, and possibly underestimates the true prevalence. Prevalence based on RAQ, which is neither specific nor highly sensitive for IHD provides support for the prevalence of IHD. In the absence of registration data to further support these findings, an analysis of the ECG records of study participants using specific criteria for coronary heart disease may provide further insight to the prevalence of IHD.

This is a crosssectional study, and it did not account for survival bias, or changes in risk factors that may occur with aggressive treatment and behavioural changes following the development of IHD. Future follow-up of participants who have not reported IHD will be useful to check whether they developed IHD, and assess the relationship between baseline CVD risk factors and angina status on RAQ in the Sri Lankan population. A population-based cohort study of a population aged 20–54 years in Norway, for example, suggested that the increased risk of IHD of participants with angina based on a shortened RAQ was explained largely by known cardiovascular disease risk factors (13).

## 2.5 CONCLUSIONS

This study provides the first survey-based national estimates of the prevalence of IHD in Sri Lanka. In a setting without comprehensive registration data of IHD, surveys of selfreported IHD and angina using RAQ can provide credible estimates of prevalence. As expected, people who were older, or had hypertension or diabetes had higher odds of having IHD. The strength of the association with age, hypertension, and diabetes in adjusted models and lack of association with wealth quintiles could be consistent with other indicators of equality in access to basic healthcare. Nevertheless, there was an association of IHD with lower education levels, consistent with studies from other LMICs which warrants further attention. The prevalence of angina was higher in women, however selfreported IHD was slightly higher in men, consistent with many international studies, and suggests a possible underdiagnosis of IHD in women. Further studies analysing ECG data to confirm these patterns, follow-up of this current cohort to detect incident IHD, and analysing risk factor distribution amongst various socioeconomic groups will provide a more complete picture of the epidemiology of IHD in Sri Lanka.

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# APPENDIX

***Table A1 Unadjusted and adjusted odds ratio for Angina+ and History+ cases using 3-level categorization of education and SES***

| | Unadjusted | | | Adjusted | | |
|---|---|---|---|---|---|---|
| | **Odds ratio (95% CI)** | **p-value (Group)** | **p-value (Versus reference)** | **Odds ratio (95% CI)** | **p-value (Group)** | **p-value (Versus reference)** |
| **Angina+** | | | | | | |
| Education level | | | | | | |
| High (Ref) | | 0.000 *** | - | | 0.4 | - |
| Low | 1.9 (0.8 - 4.6) | - | 0.2 | 1.1 (0.4 - 3.5) | - | 0.9 |
| Intermediate | 0.7 (0.3 - 1.8) | - | 0.5 | 0.8 (0.3 - 2.2) | - | 0.6 |
| Household SES Tertile | | | | | | |
| High (Ref) | | 0.06 | - | | 0.3 | - |
| Low | 1.9 (1.1 - 3.3) | - | 0.03 * | 1.7 (0.8 - 3.9) | - | 0.2 |
| Medium | 1.2 (0.7 - 2.0) | - | 0.6 | 1.3 (0.6 - 2.7) | - | 0.6 |
| **History+** | | | | | | |
| Education level | | | | | | |
| High (Ref) | | 0.000 *** | - | | 0.1 | - |
| Low | 7.9 (3.1 - 20.1) | - | 0.000 *** | 4.2 (1.2 - 14.4) | - | 0.02 * |
| Intermediate | 3.4 (1.3 - 8.4) | - | 0.010 ** | 3.4 (1.1 - 10.8) | - | 0.04 * |
| Household SES Tertile | | | | | | |
| High (Ref) | | 0.91 | - | | 0.8 | - |
| Low | 0.9 (0.7 - 1.3) | - | 0.7 | 1.0 (0.6 - 1.7) | - | 0.8 |
| Medium | 0.9 (0.6 - 1.4) | - | 0.7 | 1.2 (0.7 - 2.2) | - | 0.5 |

**Notes:** *** $p \leq 0.001$, ** $0.001 < p \leq 0.01$, * $0.01 < p \leq 0.05$. CI Confidence Interval. Joint significance shown for p-value (Group). Significance tested against reference group for p-value (Versus reference). Adjusted estimates used multivariate regressions with the same covariates as shown in Table 2, with modifications for education level and household SES tertile as specified in this table.

***Table A2 Adjusted odds ratio of Angina+ and History+ by sociodemographic category, using cholesterol-to-HDL ratio and waist-to-hip ratio***

| | Angina+ | | History+ | |
|---|---|---|---|---|
| | **Unadjusted odds ratio (95% CI)** | **Adjusted odds ratio (95% CI)** | **Unadjusted odds ratio (95% CI)** | **Adjusted odds ratio (95% CI)** |
| Age (years) | 1.49 (1.28 - 1.74) *** | 1.22 (0.94 - 1.58) | 3.02 (2.60 - 3.51) *** | 2.32 (1.83 - 2.94) *** |
| Gender | | | | |
| Male | (Ref) *** | (Ref) *** | (Ref) | (Ref) |
| Female | 2.05 (1.44 - 2.90) | 2.84 (1.54 - 5.23) | 0.95 (0.69 - 1.32) | 0.78 (0.51 - 1.18) |
| Ethnicity | | | | |

| | | | | |
|---|---|---|---|---|
| Sinhala | (Ref) *** | (Ref) ** | (Ref) | (Ref) |
| Sri Lankan Tamil | 0.40 (0.25 - 0.64) | 0.34 (0.20 - 0.60) | 0.76 (0.50 - 1.15) | 0.82 (0.49 - 1.36) |
| Indian Tamil | 2.33 (1.08 - 5.04) | 1.38 (0.42 - 4.53) | 0.86 (0.24 - 3.08) | 0.74 (0.18 - 3.03) |
| Muslim | 0.55 (0.23 - 1.34) | 0.42 (0.14 - 1.31) | 1.32 (0.73 - 2.39) | 0.92 (0.45 - 1.89) |
| Other | 1.62 (0.21 - 12.83) | 2.50 (0.44 - 14.14) | 1.33 (0.17 - 10.62) | 1.05 (0.19 - 5.66) |
| Sector | | | | |
| Rural | (Ref) | (Ref) | (Ref) ** | (Ref) |
| Urban | 0.79 (0.49 - 1.29) | 1.26 (0.56 - 2.86) | 1.87 (1.35 - 2.58) | 1.50 (0.86 - 2.60) |
| Estate | 1.97 (1.02 - 3.80) | 2.22 (0.85 - 5.86) | 1.02 (0.52 - 1.99) | 1.27 (0.61 - 2.68) |
| Rural/Estate | 1.14 (0.63 - 2.06) | 0.83 (0.33 - 2.09) | 1.02 (0.64 - 1.62) | 1.51 (0.76 - 3.02) |
| Education level | | | | |
| No formal education | (Ref) *** | (Ref) | (Ref) *** | (Ref) |
| Primary education | 1.41 (0.68 - 2.91) | 1.32 (0.53 - 3.30) | 1.33 (0.70 - 2.51) | 1.47 (0.59 - 3.63) |
| Secondary education | 0.53 (0.24 - 1.18) | 0.86 (0.33 - 2.25) | 0.53 (0.28 - 1.03) | 1.13 (0.44 - 2.92) |
| Tertiary education | 0.71 (0.23 - 2.19) | 1.17 (0.32 - 4.25) | 0.16 (0.06 - 0.43) | 0.35 (0.09 - 1.39) |
| Household SES quintile | | | | |
| Poorest | (Ref) | (Ref) | (Ref) | (Ref) |
| Poorer | 0.73 (0.40 - 1.34) | 1.03 (0.44 - 2.38) | 1.19 (0.71 - 1.99) | 1.33 (0.70 - 2.52) |
| Middle | 0.51 (0.25 - 1.05) | 0.57 (0.22 - 1.42) | 0.82 (0.50 - 1.34) | 0.97 (0.50 - 1.88) |
| Richer | 0.66 (0.38 - 1.16) | 1.11 (0.49 - 2.52) | 1.02 (0.67 - 1.55) | 0.88 (0.47 - 1.64) |
| Richest | 0.45 (0.21 - 0.97) | 0.41 (0.15 - 1.17) | 1.05 (0.65 - 1.71) | 0.91 (0.45 - 1.86) |
| Area SES tertile | | | | |
| Least developed | (Ref) | (Ref) | (Ref) ** | (Ref) |
| Middle | 0.87 (0.53 - 1.43) | 0.98 (0.52 - 1.84) | 1.38 (0.89 - 2.13) | 1.07 (0.62 - 1.82) |
| Most developed | 0.74 (0.46 - 1.19) | 0.73 (0.31 - 1.69) | 1.90 (1.28 - 2.82) | 1.31 (0.66 - 2.58) |
| Hypertension status | | | | |
| No hypertension | (Ref) *** | (Ref) | (Ref) *** | (Ref) ** |
| Hypertensive | 2.11 (1.51 - 2.95) | 1.50 (0.92 - 2.47) | 5.90 (4.34 - 8.04) | 2.03 (1.24 - 3.31) |
| Diabetes status | | | | |
| No diabetes | (Ref) * | (Ref) | (Ref) *** | (Ref) *** |
| Diabetes | 1.66 (1.10 - 2.52) | 1.22 (0.77 - 1.93) | 3.82 (2.66 - 5.47) | 2.28 (1.56 - 3.35) |
| Smoking status | | | | |
| Non-smoker | (Ref) | (Ref) * | (Ref) | (Ref) |
| Ex- or current smoker | 0.81 (0.55 - 1.17) | 2.07 (1.02 - 4.20) * | 1.32 (0.95 - 1.84) | 1.12 (0.69 - 1.84) |

| | | | | |
|---|---|---|---|---|
| Total cholesterol | 0.89 (0.77 - 1.03) | - | 0.59 (0.48 - 0.73) *** | - |
| Cholesterol-to-HDL ratio | 0.76 (0.63 - 0.91) ** | 0.78 (0.62 - 0.97) * | 0.66 (0.56 - 0.78) *** | 0.72 (0.58 - 0.90) ** |
| BMI | 0.97 (0.82 - 1.15) | - | 1.13 (0.98 - 1.31) | - |
| Waist-to-hip ratio | 1.17 (0.97 - 1.41) | 1.11 (0.85 - 1.44) | 1.51 (1.29 - 1.76) *** | 1.11 (0.93 - 1.34) |

**Notes:** *** p ≤ 0.001, ** 0.001 < p ≤ 0.01, * 0.01 < p ≤ 0.05. CI Confidence Interval. Joint significance shown for categorical variables. Odds ratios for continuous variables age, cholesterol-to-HDL ratio, waist-to-hip ratio, total cholesterol and BMI shown for one standard deviation increase in that variable. Total cholesterol and BMI are dropped from the adjusted model.

***Table A3 Adjusted odds ratio for History+ cases with and without controlling for statin use and intensity***

| | History + Adjusted odds ratio (95% CI) | | |
|---|---|---|---|
| | **Without controlling for statin use** | **Controlling for statin use** | **Controlling for statin intensity** |
| Total cholesterol | 0.58 (0.46 - 0.74) *** | 0.79 (0.62 - 1.01) | 0.81 (0.64 - 1.02) |
| On statin | | | |
| No | - | (Ref) *** | - |
| Yes | - | 5.01 (2.67 - 9.40) | - |
| Statin intensity | | | |
| No statin | - | - | (Ref) *** |
| Low intensity | - | - | 2.20 (0.68 - 7.09) |
| Moderate intensity | - | - | 4.56 (2.31 - 9.02) |
| High intensity | - | - | 22.09 (9.70 - 50.30) |

**Notes**: *** p ≤ 0.001, ** 0.001 < p ≤ 0.01, * 0.01 < p ≤ 0.05. CI Confidence Interval. Joint significance shown for categorical variables. Odds ratios for total cholesterol shown for one standard deviation increase in that variable. Multivariate regressions used the same covariates as shown in Table 2, with and without controlling for statin use. Statin intensity obtained from Table 3 in the 2018 Ameican Heart Association (1).

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*Table A4 Unadjusted and adjusted odds ratios for Angina+ and History+ cases using imputed data*

| | Angina+ | | History+ | |
|---|---|---|---|---|
| | **Unadjusted odds ratio (95% CI)** | **Adjusted odds ratio (95% CI)** | **Unadjusted odds ratio (95% CI)** | **Adjusted odds ratio (95% CI)** |
| Age (years) | 1.50 (1.29 - 1.76) *** | 1.22 (1.00 - 1.48) * | 3.02 (2.60 - 3.51) *** | 2.29 (1.85 - 2.83) *** |
| Gender | | | | |
| Male | (Ref) *** | (Ref) *** | (Ref) | (Ref) |
| Female | 2.06 (1.45 - 2.92) | 2.33 (1.43 - 3.80) | 0.95 (0.69 - 1.32) | 0.92 (0.63 - 1.34) |
| Ethnicity | | | | |
| Sinhala | (Ref) *** | (Ref) *** | (Ref) | (Ref) |
| Sri Lankan Tamil | 0.41 (0.26 - 0.64) | 0.32 (0.19 - 0.53) | 0.76 (0.50 - 1.15) | 0.65 (0.40 - 1.08) |
| Indian Tamil | 2.28 (1.05 - 4.94) | 1.64 (0.67 - 4.00) | 0.86 (0.24 - 3.08) | 0.73 (0.22 - 2.39) |
| Muslim | 0.54 (0.23 - 1.31) | 0.53 (0.21 - 1.38) | 1.32 (0.73 - 2.39) | 0.86 (0.51 - 1.45) |
| Other | 1.61 (0.20 - 12.68) | 1.12 (0.14 - 8.95) | 1.33 (0.17 - 10.62) | 0.44 (0.06 - 3.39) |
| Sector | | | | |
| Rural | (Ref) | (Ref) | (Ref) ** | (Ref) |
| Urban | 0.79 (0.49 - 1.28) | 0.98 (0.50 - 1.89) | 1.87 (1.35 - 2.58) | 1.46 (1.00 - 2.14) |
| Estate | 1.97 (1.03 - 3.78) | 2.19 (0.90 - 5.35) | 1.02 (0.52 - 1.99) | 1.13 (0.51 - 2.52) |
| Rural/Estate | 1.12 (0.62 - 2.04) | 1.09 (0.53 - 2.26) | 1.02 (0.64 - 1.62) | 1.30 (0.73 - 2.30) |
| Education level | | | | |
| No formal education | (Ref) *** | (Ref) * | (Ref) *** | (Ref) |
| Primary education | 1.44 (0.69 - 2.98) | 1.74 (0.82 - 3.72) | 1.33 (0.70 - 2.51) | 1.75 (0.85 - 3.60) |
| Secondary education | 0.53 (0.24 - 1.18) | 0.99 (0.43 - 2.28) | 0.53 (0.28 - 1.03) | 1.34 (0.63 - 2.85) |
| Tertiary education | 0.71 (0.23 - 2.18) | 1.75 (0.57 - 5.35) | 0.16 (0.06 - 0.43) | 0.45 (0.13 - 1.53) |
| Household SES quintile | | | | |
| Poorest | (Ref) | (Ref) | (Ref) | (Ref) |
| Poorer | 0.75 (0.41 - 1.37) | 0.90 (0.47 - 1.73) | 1.19 (0.71 - 1.99) | 1.33 (0.75 - 2.37) |
| Middle | 0.51 (0.25 - 1.04) | 0.65 (0.32 - 1.33) | 0.82 (0.50 - 1.34) | 0.87 (0.50 - 1.52) |
| Richer | 0.66 (0.38 - 1.16) | 0.90 (0.46 - 1.75) | 1.02 (0.67 - 1.55) | 0.97 (0.57 - 1.64) |
| Richest | 0.45 (0.21 - 0.97) | 0.61 (0.25 - 1.44) | 1.05 (0.65 - 1.71) | 0.99 (0.54 - 1.82) |
| Area SES tertile | | | | |
| Least developed | (Ref) | (Ref) | (Ref) ** | (Ref) |
| Middle | 0.88 (0.54 - 1.44) | 0.88 (0.54 - 1.44) | 1.38 (0.89 - 2.13) | 0.95 (0.56 - 1.62) |
| Most developed | 0.75 (0.47 - 1.20) | 0.81 (0.42 - 1.54) | 1.90 (1.28 - 2.82) | 1.09 (0.62 - 1.91) |
| Hypertension status | | | | |
| No hypertension | (Ref) *** | (Ref) ** | (Ref) *** | (Ref) *** |
| Hypertensive | 2.15 (1.54 - 3.00) | 1.68 (1.16 - 2.43) ** | 5.90 (4.34 - 8.04) | 2.29 (1.55 - 3.39) |
| Diabetes status | | | | |
| No diabetes | (Ref) * | (Ref) | (Ref) *** | (Ref) ** |
| Diabetes | 1.53 (1.06 - 2.22) | 1.16 (0.76 - 1.78) | 4.54 (3.26 - 6.32) | 1.82 (1.25 - 2.67) |

| | | | | |
|---|---|---|---|---|
| Smoking status | | | | |
| Non-smoker | (Ref) | (Ref) | (Ref) | (Ref) |
| Ex- or current smoker | 0.76 (0.53 - 1.11) | 1.31 (0.79 - 2.18) | 1.34 (0.96 - 1.87) | 1.33 (0.92 - 1.91) |
| Total cholesterol | 0.88 (0.76 - 1.02) | 0.85 (0.74 - 0.99) * | 0.59 (0.48 - 0.73) *** | 0.61 (0.49 - 0.76) *** |
| Cholesterol-to-HDL ratio | 0.76 (0.63 - 0.91) ** | - | 0.66 (0.56 - 0.78) *** | - |
| BMI | 0.98 (0.83 - 1.15) | 0.95 (0.79 - 1.13) | 1.13 (0.98 - 1.30) | 1.09 (0.94 - 1.27) |
| Waist-to-hip ratio | 1.16 (0.97 - 1.40) | - | 1.50 (1.29 - 1.75) *** | - |

Notes: *** $p \leq 0.001$, ** $0.001 < p \leq 0.01$, * $0.01 < p \leq 0.05$. CI Confidence Interval. Joint significance shown for categorical variables. Odds ratios for continuous variables age, cholesterol-to-HDL ratio, waist-to-hip ratio, total cholesterol and BMI shown for one standard deviation increase in that variable. Total cholesterol and BMI are dropped from the adjusted model.

## Text A1 Estimation of household socioeconomic status using principal components analysis

The SLHAS Wave 1 uses an asset index approach to generate a proxy measure of each household's living standard. The index was computed by using principal components analysis (PCA) of a set of householdlevel variables relating to asset ownership or household characteristics. Variables were selected from those used in recent Sri Lanka Household Income and Expenditure Surveys conducted by the Department of Census and Statistics, selecting those with most predictive performance, and excluding some assets that are only relevant to agricultural households (e.g., tractor, thresher, fishing equipment). Variables were either dichotomous (e.g., household has a car) or categorical (e.g., type of drinking water source), apart from one ordinal variable (number of bedrooms). Dichotomous variables consisted of whether the household possessed each of the following items: radio/cassette player, television, VCD/DVD player, washing machine, fridge, electric fan, domestic phone, mobile phone, computer, internet access, camera/video camera, bicycle, motorcycle/scooter, three-wheeler, motor car/van, and bus/lorry/tipper.

Categorical variables were transformed into dichotomous indicators by creating separate dummy variables for each category. They consisted of the following (numbers in parentheses indicates number of categories in each): flooring material (5), material of wall (7), type of housing tenure (12), drinking water source (16), type of toilet (4), method of household garbage disposal (6), lighting power source (5), cooking fuel (13), and type of cooking place (3).

There was a small percentage of missing values in each variable (2–3%). These were imputed with either the PSU or stratum level mean of the variable or failing those the district/sector or national means. The principal component factor or index obtained by PCA after combining all these variables was then used to divide the sample into population weighted quantiles of equal size. Separate indices were not estimated for urban or rural sectors, but analysis indicates little difference between sectors in how the national index performs.

# Chapter ٣

# Population norms and disutility catalogue for chronic conditions in Sri Lanka

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# ABSTRACT


## Objectives

To produce Sri Lankan population norms of utility values, EQ-VAS scores, and reported problems in each domain of the EQ-5D-5L, as well as a disutility catalogue, based on a representative set of Sri Lankan preferences.

## Methods

Data from a nationally representative sample of 6,415 adults from the Sri Lanka Health and Ageing Study (SLHAS) in 2018/19 were used. Sri Lankan preferences were applied to EQ-5D-5L scores to produce utility values. Descriptive statistics were produced for responses by EQ-5D-5L dimension, mean utility values, and EQ-VAS scores, disaggregated by demographic and disease group. Multivariable logistic regression assessed associations with problems in each dimension, and demographic and chronic diseases. Robust ordinary least squares and Tobit regressions were performed to estimate the marginal disutility of demographic covariates and disease conditions.

## Results

The mean utility value for the overall population was 0.867. Utility values decreased with age and increased with increasing education and richer socioeconomic quintiles. Males had higher utility values than females (0.89 vs 0.84; $p<0.001$). Utility values declined by 0.007 with each year increase in age ($p<0.001$) and statistically significant ($p<0.05$) differences in utility were found by ethnicity, socioeconomic quintile, and disease conditions such as stroke, diabetes, cancer, depression, and musculoskeletal conditions, using a Tobit regression.

## Conclusions

This study provides the first nationally representative set of population norms based on a local value set for key demographic groups and selected chronic disease conditions for Sri Lanka. It also provides a catalogue that can be easily used to calculate QALYs for cost-utility analysis when modelling public health interventions.

# 3.1 INTRODUCTION

With the increasing burden of chronic diseases, which can lead to prolonged morbidity, measures such as quality-adjusted life-years (QALYs) and disability-adjusted life years (DALYs) are essential to quantify the burden of disease and both can be used in economic evaluations. QALYs rely on Health-Related Quality of Life (HRQoL) weights, which measure the quality of life of people of varying health states, while DALYs use disability weights, which quantify loss of functioning. In contrast to DALYs, weights for QALYs are typically elicited from the general population in the setting of interest. A common way to do this is to use a pre-scored multi-attribute utility instrument (MAUI), such as the EQ-5D-5L. The EQ-5D-5L is a tool developed by EuroQOL to measure health status in five dimensions with five levels of severity (1). Preferences to produce a scoring function for each health state can be elicited using techniques such as time-trade off (TTO) and standard gamble, to produce a utility value set (or weights) for each health state (2).

Until recently, Sri Lanka was the only country in the South Asian region that had a published value set for the EQ-5D-3L and EQ-5D-5L. A value set was derived for the EQ-5D-3L states using a TTO technique (3), and a cross-walk method, developed by the EuroQoL group, was used to produce a value set for the EQ-5D-5L states (4). Data from the same study were used to produce population norms for HRQoL in Sri Lanka, the first of its kind for South Asia. As noted by the authors, the study sample used to produce these population norms was small–736 people from four out of 25 districts, and skewed towards females and Sinhalese participants, owing to logistical constraints at the time of data collection. Furthermore, whilst the mean utility is given for the overall sample and by gender, it is unclear how other factors such as age and sociodemographic factors would impact the HRQoL of chronic conditions.

Catalogues for utilities by chronic disease conditions based on HRQoL have been developed for the United Kingdom (UK) and the United States (US) (5-7). These catalogues present mean utility values by condition, estimates for the marginal disutility for a set of chronic conditions, and the marginal impact of covariates such as age, gender, race, education status, and income. These marginal disutility values can be applied easily to model the impact of interventions using QALYs. With the calculation of QALYs, cost utility analyses can be performed to determine the cost and impact (QALYs gained) of different proposed programs.

Although utility values by demographic features and disease status have been available in high-income countries for nearly two decades, these utility values generally should not be translated to other countries, where social differences can result in people weighting health states differently (3, 8). For example, it was found that problems in mobility lead to a far lower HRQoL in Sri Lanka, Thailand, Indonesia and South Korea than in high-income countries,

with differences also seen within South-East Asian countries (9, 10). These differences may reflect less support, accessibility and healthcare for people with disabilities (3).

Wave 1 of the Sri Lanka Health and Ageing Study (SLHAS) is the first nationally representative survey that collected EQ-5D-5L data, covering 6,665 adults aged 18 and above. We aimed to use these data to provide a comprehensive description of ED-5D-5L responses and utility values by demographic and disease characteristics for Sri Lankans, which can be used in a range of health-economic analyses. We had five specific objectives. The first was to describe mean and median utility values by demographic characteristics and disease conditions. The second was to describe, by age group, the distribution of responses to each EQ-5D domain, as well as mean and median utility values, and EQ-VAS scores. The third was to report and test the odds of reporting a problem in each EQ-5D domain by demographic characteristics and disease conditions. The fourth objective was to produce a nationally representative disutility catalogue using EQ-5D-5L utility values based on Sri Lankan preferences, which could be utilised to calculate QALYs for cost-utility analysis. The final objective was to compare the utility values of SLHAS participants, calculated from the Sri Lankan value set to those calculated using an Indian value set.

## 3.2 METHODS

### 3.2.1 Data

The SLHAS is a longitudinal cohort study that recruited its first participants using a nationally representative survey of 6,665 adults aged 18 years and over (11). In a stratified, multi-stage cluster sampling design, one adult was randomly selected from randomly sampled households in 297 primary sampling units, defined as Grama Niladhari Divisions, located in all 25 districts of Sri Lanka. Consenting participants attended a survey field clinic held nearby, where a questionnaire was completed, blood samples were taken and measurements such as blood pressure were taken. Data were collected from November 2018 to November 2019. The EQ-5D-5L questionnaire was administered, where respondents were asked to grade their health status in five dimensions (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression) from one to five, where one is the best health state and five is the worst. This instrument can define 3,125 health states, where 11111 represents full health and 55555 represents the poorest health state. Additionally, participants were asked to rate their current health on a scale of 0 (worst health you can imagine) to 100 (best health you can imagine) on a visual scale, known as the Visual Analogue Scale (VAS) (1). Data on demographic characteristics including level of education and ethnicity were collected, along with information on durable household assets, housing quality, water and sanitation facilities, and other assets, which were used to construct a proxy for socioeconomic status. To simplify categorization of the diverse

ethnicities in Sri Lanka, we defined Muslim ethnicity as those who identified as "Muslim", "Moor", or "Malay" (12). Participants were categorized into four sectors, based on area of residence: urban, rural, estate, or rural/estate, where rural/estate refers to areas that are a mix or rural and estate sectors.

### 3.2.2 Utility values

We used the value set produced by Kularatna et al. (4) which used a cross-walking method to generate a utility value set for EQ-5D-5L health states. This cross-walks an existing value set for Sri Lankans, produced by a TTO method for all EQ-5D-3L health states (3). Although the Sri Lankan EQ-5D-5L value set has not been validated in Sri Lanka, it is likely more appropriate than using a directly valued EQ-5D-5L value set from another country, as it is derived from a Sri Lankan population. The value sets produced by Kularatna et al. (4) have been used in Sri Lanka and other South Asian countries (13, 14). Recently, a EQ-5D-5L utility value set was published for India (15), and we separately calculated utility values for our sample using the Indian utility value set. The value set from India directly valued the EQ-5D-5L and combined TTO and DCE methods.

### 3.2.3 Identifying and classifying chronic conditions

Participants were explicitly asked whether they have had ischaemic heart disease, including angina, coronary heart disease or a heart attack, stroke, hypertension, diabetes, asthma, chronic obstructive pulmonary disease (COPD), liver disease, cancer, or depression. The Rose Angina questionnaire was used to determine whether the participants had symptoms consistent with angina. Participants were also asked if they had any other additional chronic conditions, and up to three were coded using the International Classification of Disease (ICD) and International Classification of Primary Care (ICPC). They were asked to bring their medications, medication lists and medical records to the clinic. If they were taking medications, they were asked which condition they were using them for. Medical records, when available (19.5% of participants), were also checked for any diagnoses of chronic conditions. A summary of which sources were used to identify conditions, such as selfreport only, or medical reports only, for each condition is shown in Appendix Table A1.

Participants were classified as having "Rose Angina" if they fulfilled the Rose criteria and did not have a diagnosis of ischaemic heart disease, either by self-report or medical records. Participants were classified as having diabetes or hypertension if they fulfilled any of the following criteria: they reported a diagnosis; their medical records stated a diagnosis; or they were taking medications (oral hypoglycemics or insulin for diabetes, or antihypertensives for hypertension). Any additional chronic conditions reported were coded in the field using ICD-10 or ICPC-2 reason-for-encounter (RFE) categories, and subsequently classified into broad leveltwo Global Burden of Disease (GBD) categories during analysis. Only two leveltwo GBD

conditions: musculoskeletal conditions, and "other chronic diseases" were present in more than 50 participants. "Other chronic conditions" included unrelated conditions such as congenital birth defects; gynaecological diseases; and endocrine, metabolic, blood and immune disorders, and were therefore not included as a specific condition in the analysis. The total count of all reported chronic conditions was determined for each participant.

### 3.2.4 Statistical analysis

We created socioeconomic status (SES) quintiles using a wealth index equal to the first principal component from a principal components analysis of household reported durable assets, housing quality, water and sanitation facilities, and other assets. Full details of assets used, and the methodology, is in Appendix Text A1. Sample weights which represent the national population were used, with calibration to address the observed skewed representation of different ethnic groups, as described previously (12). In short, SLHAS provides non-response weights which modelled the propensity of participation based on characteristics collected at recruitment, and produced weights that are adjusted to the age-sex population structure of strata (the primary sampling units were categorized into 57 strata based on district and sector of residence), districts and provinces. These weights were then calibrated to match the strata, age-sex, ethnic and sector population structure at district, province and national levels using iterative proportional fitting, an additional step that was required due to some under-representation of Muslim people in the sample (16).

For the first objective, the mean, median, and 25th and 75th percentiles of EQ-5D-5L utility values for each sociodemographic category and condition of interest were calculated using weighted data. We used Somers' D statistic, a rank-based non-parametric statistic, to test the likelihood that the utility value is higher (or lower) in pair-wise comparisons of utility values between categories of demographic groups and presence versus absence of disease, with sample weights and survey clustering applied. For the second objective, we calculated the number and percentage in each age group giving each response of the five dimensions of the EQ-5D-5L (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). For the third objective, multivariate logistic regressions were performed, with the dependent variable as the presence of any reported problems in each dimension (i.e., slight problems, moderate problems, severe problems, or unable), and covariates of gender, age, sex, ethnicity, education category, sector of residence, SES quintile, and disease categories. In total, 11 diseases were included.

For the fourth objective, multivariate regressions were performed on weighted data, using the utility value as the dependent variable, and the same covariates as in the logistic regressions. Due to the ceiling effect of EQ-5D-based utility values, in samples where 50% or more respondents have a ceiling utility value, regression methods such as Tobit and censored least absolute deviations (CLAD) can produce less biased results (17). Some authors suggest instead, that

robust OLS regression produces less biased estimates than Tobit regressions, however this is under the key assumption that utility values are censored at 1, and values cannot exceed "full health" (18). However, Sullivan argues that utility values could exceed full health, such as a marathon runner who may have a level of health that exceeds the definition of "full health", supporting the use of either CLAD or Tobit regressions (19). Several recent studies performing similar regression analysis used either robust OLS or Tobit regressions (20-22). Therefore, we used both multivariate robust OLS regression using the vce(robust) function on Stata, and Tobit regression. The adjusted R2 was calculated for each model to test model performance. In a supplementary analysis, the number of chronic conditions (0, 1, 2, or 3 or more) was added to the regression models.

For the final objective, the relationship between utility values for the SLHAS participants calculated using the Sri Lankan value set and Indian value sets was explored using a scatter plot and a fitted cubic spline. To assess agreement and identify systematic differences between the two value sets for the SLHAS sample, a Bland Altman plot, with a mean difference line was plotted. Given the non-normal distribution of differences, a non-parametric limit of agreement method described by Bland and Altman was applied, where we determined the upper limit and lower limit of differences between which 98% of values lay (23). Stata version 17 was used to perform all analyses (24).

## 3.3 RESULTS

A total of 6,415 study participants (96%) had answered all EQ-5D-5L questions. The percentage of people reporting full health was 50% (56% in the weighted sample). The mean, median, 25th and 75th percentiles of utility values are shown by demographic characteristics (Table 1) and disease condition (Table 2).

***Table 1 Utility values by demographic covariates***

| | | | | EQ-5D-5L Utility Value | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Number** | **%** | **Mean Age (yrs)** | **Mean** | | **Standard Error** | **25th percentile** | **Median** | **75th percentile** |
| Overall | 6,415 | 100.0 | 43.9 | 0.867 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Gender | | | | | | | | | |
| Male | 3,155 | 49.3 | 43.2 | 0.893 | * | 0.004 | 0.832 | 1.000 | 1.000 |
| Female | 3,260 | 50.7 | 44.6 | 0.844 | * | 0.004 | 0.737 | 1.000 | 1.000 |
| Age category | | | | | | | | | |
| 18-29 | 514 | 4.9 | 20.9 | 0.943 | † | 0.006 | 0.849 | 1.000 | 1.000 |
| 30-39 | 808 | 8.6 | 29.2 | 0.941 | † | 0.005 | 0.849 | 1.000 | 1.000 |
| 40-49 | 1,266 | 16.4 | 39.1 | 0.896 | † | 0.005 | 0.832 | 1.000 | 1.000 |

*Table 1 Utility values by demographic covariates*

| | | | | | | EQ-5D-5L Utility Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number | % | Mean Age (yrs) | Mean | | Standard Error | 25th percentile | Median | 75th percentile |
| 50-59 | 1,100 | 16.9 | 49.3 | 0.853 | † | 0.007 | 0.737 | 1.000 | 1.000 |
| 60-69 | 1,166 | 20.7 | 59.0 | 0.812 | † | 0.008 | 0.667 | 0.832 | 1.000 |
| 70-79 | 1,067 | 21.5 | 68.9 | 0.758 | † | 0.011 | 0.631 | 0.790 | 1.000 |
| 80+ | 494 | 11.0 | 79.8 | 0.649 | † | 0.017 | 0.484 | 0.667 | 0.832 |
| Ethnic group | | | | | | | | | |
| Sinhala | 4,492 | 70.8 | 43.9 | 0.883 | | 0.003 | 0.790 | 1.000 | 1.000 |
| SL Tamil | 1,236 | 19.0 | 42.6 | 0.827 | ‡ | 0.008 | 0.737 | 0.832 | 1.000 |
| Indian Tamil | 196 | 3.1 | 44.6 | 0.815 | ‡ | 0.018 | 0.667 | 0.832 | 1.000 |
| Muslim | 416 | 6.4 | 45.5 | 0.813 | ‡ | 0.014 | 0.684 | 0.849 | 1.000 |
| Other | 43 | 0.7 | 49.2 | 0.913 | | 0.024 | 0.832 | 1.000 | 1.000 |
| Education category | | | | | | | | | |
| No formal schooling | 247 | 4.7 | 60.4 | 0.722 | § | 0.021 | 0.612 | 0.758 | 1.000 |
| Primary | 889 | 16.4 | 57.7 | 0.751 | § | 0.011 | 0.631 | 0.776 | 1.000 |
| Secondary | 4,976 | 75.3 | 41.9 | 0.884 | § | 0.003 | 0.810 | 1.000 | 1.000 |
| Tertiary | 261 | 3.7 | 39.1 | 0.923 | § | 0.009 | 0.832 | 1.000 | 1.000 |
| Sector | | | | | | | | | |
| Urban | 1,931 | 30.8 | 44.5 | 0.858 | | 0.007 | 0.776 | 1.000 | 1.000 |
| Rural | 3,552 | 54.6 | 43.8 | 0.874 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Estate | 168 | 2.6 | 45.4 | 0.824 | | 0.017 | 0.768 | 0.849 | 1.000 |
| Rural/estate | 764 | 12.0 | 43.6 | 0.849 | | 0.009 | 0.75 | 1.000 | 1.000 |
| SES quintile | | | | | | | | | |
| Poorest quintile | 1,578 | 25.5 | 47.2 | 0.810 | | 0.007 | 0.667 | 0.832 | 1.000 |
| 2 | 1,268 | 19.7 | 44.4 | 0.862 | ¶ | 0.007 | 0.762 | 1.000 | 1.000 |
| 3 | 1,195 | 18.4 | 43.6 | 0.879 | ¶ | 0.006 | 0.790 | 1.000 | 1.000 |
| 4 | 1,134 | 17.4 | 42.3 | 0.891 | ¶ | 0.006 | 0.824 | 1.000 | 1.000 |
| Richest quintile | 1,240 | 19.0 | 42.2 | 0.897 | ¶ | 0.006 | 0.832 | 1.000 | 1.000 |

**Notes:** Number and % columns are unweighted. Mean age and EQ-5D-5L data are weighted as described in text.

* Pairwise comparison is statistically significant (p<0.001)

† All pairwise combinations are statistically significant at level p<0.001, except 40-49 vs 50-59 (p=0.014)

‡ Statistically significant vs Sinhala (p<0.001)

§ All pairwise combinations are statistically significant at level p<0.001, except no formal school vs primary educated (p=0.252) and secondary vs tertiary educated (p=0.004)

¶ Statistically significant vs poorest quintile (p<0.001)

Mean utility values were lower for women than men (0.844 vs 0.893; p<0.001), and fell with age (Table 1). Sri Lankan Tamils, Indian Tamils and Muslims had lower mean utility levels than Sinhalese, and people with lower levels of education had lower mean utility values than people with higher levels of education (p<0.001). The poorest quintile had lower utility values than richer quintiles (p<0.001). People with ischaemic heart disease (IHD), angina using Rose criteria, stroke, hypertension, diabetes, asthma, COPD, cancer, depression, and musculoskel-

etal conditions, had lower mean utility values than those without these conditions (Table 2). Mean utility values decreased with an increase in the number of chronic conditions reported.

***Table 2 Utility values by disease conditions***

| | | | | EQ-5D-5L Utility Value | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Number** | **%** | **Mean Age (yrs)** | **Mean** | | **Standard Error** | **25th percentile** | **Median** | **75th percentile** |
| Overall | 6,415 | 100.0 | 43.9 | 0.867 | | 0.003 | 0.776 | 1.000 | 1.000 |
| IHD | | | | | | | | | |
| No | 6,049 | 93.0 | 43.2 | 0.872 | | 0.003 | 0.790 | 1.000 | 1.000 |
| Yes | 366 | 7.0 | 61.7 | 0.748 | *** | 0.017 | 0.599 | 0.776 | 1.000 |
| Rose angina | | | | | | | | | |
| No | 6,179 | 97.5 | 43.8 | 0.869 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 151 | 2.5 | 47.8 | 0.825 | ** | 0.019 | 0.676 | 0.832 | 1.000 |
| Stroke | | | | | | | | | |
| No | 6,314 | 98.1 | 43.8 | 0.870 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 101 | 1.9 | 61.9 | 0.583 | *** | 0.042 | 0.422 | 0.667 | 0.810 |
| Hypertension | | | | | | | | | |
| No | 4,917 | 71.7 | 40.6 | 0.889 | | 0.003 | 0.810 | 1.000 | 1.000 |
| Yes | 1,498 | 28.3 | 60.7 | 0.762 | *** | 0.009 | 0.620 | 0.810 | 1.000 |
| Diabetes | | | | | | | | | |
| No | 5,345 | 80.9 | 42.1 | 0.882 | | 0.003 | 0.790 | 1.000 | 1.000 |
| Yes | 1,070 | 19.1 | 55.6 | 0.779 | *** | 0.010 | 0.650 | 0.832 | 1.000 |
| Asthma | | | | | | | | | |
| No | 5,849 | 90.7 | 43.8 | 0.871 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 566 | 9.3 | 46.1 | 0.831 | ** | 0.012 | 0.694 | 1.000 | 1.000 |
| COPD | | | | | | | | | |
| No | 6,320 | 98.4 | 43.8 | 0.868 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 95 | 1.6 | 54.2 | 0.763 | ** | 0.035 | 0.667 | 0.832 | 1.000 |
| Liver disease | | | | | | | | | |
| No | 6,396 | 99.7 | 43.9 | 0.868 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 19 | 0.3 | 48.0 | 0.800 | | 0.079 | 0.667 | 1.000 | 1.000 |
| Cancer | | | | | | | | | |
| No | 6,370 | 99.2 | 43.9 | 0.869 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 45 | 0.8 | 55.6 | 0.631 | *** | 0.055 | 0.440 | 0.667 | 0.824 |
| Depression | | | | | | | | | |
| No | 6,351 | 99.0 | 43.9 | 0.869 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 64 | 1.0 | 49.9 | 0.703 | *** | 0.034 | 0.522 | 0.688 | 0.849 |

***Table 2 Utility values by disease conditions***

| | | | | EQ-5D-5L Utility Value | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Number** | **%** | **Mean Age (yrs)** | **Mean** | | **Standard Error** | **25th percentile** | **Median** | **75th percentile** |
| Musculoskeletal | | | | | | | | | |
| No | 6,327 | 99.1 | 43.8 | 0.869 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 51 | 0.9 | 53.7 | 0.702 | *** | 0.040 | 0.590 | 0.684 | 0.832 |
| Neurological | | | | | | | | | |
| No | 6,360 | 99.7 | 43.9 | 0.868 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 18 | 0.3 | 52.0 | 0.841 | | 0.061 | 0.640 | 1.000 | 1.000 |
| Chronic kidney disease | | | | | | | | | |
| No | 6,368 | 99.8 | 43.9 | 0.868 | | 0.003 | 0.776 | 1.000 | 1.000 |
| Yes | 10 | 0.2 | 65.5 | 0.729 | | 0.076 | 0.523 | 0.737 | 1.000 |
| Number of chronic conditions | | | | | | | | | |
| 0 | 3,714 | 53.1 | 39.1 | 0.903 | † | 0.003 | 0.832 | 1.000 | 1.000 |
| 1 | 1,550 | 25.9 | 48.9 | 0.839 | † | 0.006 | 0.737 | 0.849 | 1.000 |
| 2 | 763 | 14.2 | 58.5 | 0.764 | † | 0.012 | 0.631 | 0.790 | 1.000 |
| 3+ | 351 | 6.8 | 62.8 | 0.669 | † | 0.020 | 0.518 | 0.667 | 0.849 |

**Notes:** Number and % columns are unweighted. Mean age and EQ-5D-5L data are weighted as described in text. Significance of differences (yes vs no) denoted by *** P-value < 0.001, ** 0.001 ≤ P-value < 0.01, * 0.01 ≤ P-value < 0.05. † Significant for all pair-wise combinations (p<0.001).

***Table 3 Participant responses by EQ-5D-5L dimension, utility values and EQ-VAS by age category***

| | Age groups (years) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Dimensions** | **18-24 n (%)** | **25-34 n (%)** | **35-44 n (%)** | **45-54 n (%)** | **55-64 n (%)** | **65-74 n (%)** | **75+ n (%)** | **Total n (%)** |
| Mobility | | | | | | | | |
| No problems | 488 (93.9) | 758 (94.3) | 1,094 (86.2) | 843 (76.6) | 758 (65.4) | 596 (56.6) | 194 (38.3) | 4,731 (79.3) |
| Slight problems | 21 (4.2) | 39 (4.5) | 125 (10.0) | 188 (16.6) | 270 (22.2) | 288 (26.1) | 140 (28.5) | 1,071 (13.4) |
| Moderate problems | 3 (1.4) | 7 (0.8) | 38 (2.9) | 51 (4.9) | 92 (8.3) | 118 (10.5) | 105 (22.7) | 414 (5.0) |
| Severe problems | 2 (0.5) | 4 (0.4) | 8 (0.8) | 18 (1.9) | 42 (3.9) | 62 (6.3) | 52 (10.0) | 188 (2.3) |
| Unable | 0 (0.0) | 0 (0.0) | 1 (0.0) | 0 (0.0) | 4 (0.2) | 3 (0.6) | 3 (0.5) | 11 (0.1) |
| Selfcare | | | | | | | | |
| No problems | 513 (99.8) | 805 (99.7) | 1,254 (99.2) | 1,069 (96.1) | 1,107 (95.0) | 944 (88.6) | 390 (77.3) | 6,082 (96.3) |
| Slight problems | 1 (0.2) | 2 (0.2) | 8 (0.6) | 22 (3.0) | 37 (2.8) | 78 (6.4) | 63 (12.8) | 211 (2.3) |
| Moderate problems | 0 (0.0) | 0 (0.0) | 3 (0.1) | 7 (0.7) | 13 (1.7) | 29 (3.2) | 16 (4.0) | 68 (0.9) |

The number and percentage of people with each response for the five dimensions are shown in Table 3 by age-category. The dimension where the highest percentage of people reported a problem was pain/discomfort (32.1%), followed by mobility (20.7%) and anxiety/depression

| | Age groups (years) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Dimensions** | **18-24 n (%)** | **25-34 n (%)** | **35-44 n (%)** | **45-54 n (%)** | **55-64 n (%)** | **65-74 n (%)** | **75+ n (%)** | **Total n (%)** |
| Severe problems | 0 (0.0) | 0 (0.0) | 1 (0.0) | 2 (0.1) | 7 (0.4) | 13 (1.2) | 14 (3.7) | 37 (0.4) |
| Unable | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 2 (0.1) | 3 (0.6) | 11 (2.1) | 17 (0.2) |
| Usual activities | | | | | | | | |
| No problems | 505 (98.1) | 792 (98.9) | 1,210 (95.9) | 1,017 (91.9) | 1,016 (87.9) | 863 (82.0) | 320 (63.9) | 5,723 (92.2) |
| Slight problems | 6 (1.4) | 13 (0.8) | 41 (3.0) | 57 (5.4) | 100 (8.5) | 121 (10.4) | 99 (20.3) | 437 (5.0) |
| Moderate problems | 2 (0.2) | 1 (0.1) | 10 (0.8) | 19 (2.1) | 35 (3.1) | 56 (5.2) | 39 (7.6) | 162 (1.8) |
| Severe problems | 1 (0.3) | 0 (0.0) | 5 (0.3) | 5 (0.4) | 12 (0.5) | 19 (1.5) | 18 (4.7) | 60 (0.6) |
| Unable | 0 (0.0) | 2 (0.2) | 0 (0.0) | 2 (0.3) | 3 (0.1) | 8 (1.0) | 18 (3.5) | 33 (0.3) |
| Pain/discomfort | | | | | | | | |
| No problems | 435 (84.5) | 657 (83.1) | 891 (71.0) | 675 (61.3) | 640 (55.7) | 501 (50.3) | 203 (39.0) | 4,002 (67.9) |
| Slight problems | 61 (11.7) | 112 (12.5) | 258 (20.2) | 302 (27.4) | 342 (29.8) | 360 (31.4) | 170 (32.9) | 1,605 (21.8) |
| Moderate problems | 15 (3.1) | 37 (4.2) | 97 (7.3) | 99 (8.7) | 155 (12.7) | 166 (14.5) | 95 (21.9) | 664 (8.5) |
| Severe problems | 3 (0.6) | 2 (0.2) | 19 (1.4) | 22 (2.6) | 24 (1.7) | 36 (3.4) | 23 (5.7) | 129 (1.7) |
| Unable | 0 (0.0) | 0 (0.0) | 1 (0.2) | 2 (0.0) | 5 (0.2) | 4 (0.3) | 03 (0.5) | 15 (0.1) |
| Anxiety/depression | | | | | | | | |
| No problems | 460 (89.6) | 703 (88.3) | 1,047 (83.0) | 893 (82.5) | 885 (78.0) | 778 (74.4) | 347 (69.1) | 5,113 (82.7) |
| Slight problems | 39 (7.6) | 74 (8.1) | 151 (11.2) | 147 (12.3) | 207 (16.6) | 184 (15.6) | 99 (20.8) | 901 (11.9) |
| Moderate problems | 14 (2.6) | 23 (2.5) | 53 (4.8) | 42 (3.6) | 58 (4.1) | 82 (7.8) | 34 (7.9) | 306 (4.2) |
| Severe problems | 0 (0.0) | 6 (0.9) | 14 (0.9) | 14 (1.2) | 14 (1.2) | 19 (2.0) | 9 (1.0) | 76 (1.0) |
| Unable | 1 (0.2) | 2 (0.2) | 1 (0.0) | 4 (0.3) | 2 (0.1) | 4 (0.3) | 5 (1.2) | 19 (0.2) |
| Utility value | | | | | | | | |
| Mean | 0.943 | 0.941 | 0.896 | 0.853 | 0.812 | 0.758 | 0.649 | 0.867 |
| Standard error | 0.006 | 0.005 | 0.005 | 0.007 | 0.008 | 0.011 | 0.017 | 0.003 |
| Median | 1.000 | 1.000 | 1.000 | 1.000 | 0.832 | 0.790 | 0.667 | 1.000 |
| 25th percentile | 0.849 | 0.849 | 0.832 | 0.737 | 0.667 | 0.631 | 0.484 | 0.776 |
| 75th percentile | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.832 | 1.000 |
| EQ-VAS score | | | | | | | | |
| Mean | 83.7 | 84.3 | 81.7 | 78.8 | 77.1 | 72.2 | 72.4 | 80.2 |
| Standard error | 0.8 | 0.7 | 0.6 | 0.7 | 0.7 | 0.8 | 1.4 | 0.3 |
| Median | 89.0 | 90.0 | 80.0 | 80.0 | 80.0 | 75.0 | 75.0 | 80.0 |
| 25th percentile | 75.0 | 75.0 | 75.0 | 70.0 | 70.0 | 60.0 | 60.0 | 70.0 |
| 75th percentile | 99.0 | 100.0 | 99.0 | 95.0 | 90.0 | 90.0 | 90.0 | 98.0 |

**Notes:** Numbers are unweighted. Percentages, utility values and EQ-VAS scores are weighted as described in text.

*Table 4 Multivariate logistic regressions of reported problems in EQ-5D-5L dimensions by demographic covariates*

| | Mobility | | Self-care | |
|---|---|---|---|---|
| | **OR (95% CI)** | ***P*-value** | **OR (95% CI)** | ***P*-value** |
| Gender (Ref: Female) | | | | |
| Male | 0.55 (0.46, 0.66) | <0.001 | 0.55 (0.38, 0.79) | 0.001 |
| Age | 1.05 (1.04, 1.06) | <0.001 | 1.08 (1.06, 1.10) | <0.001 |
| Ethnic group (Ref: Sinhala) | | | | |
| Sri Lankan Tamil | 1.13 (0.88, 1.46) | 0.33 | 3.54 (2.31, 5.44) | <0.001 |
| Indian Tamil | 1.76 (1.02, 3.04) | 0.041 | 2.32 (1.24, 4.33) | 0.008 |
| Muslim | 1.85 (1.36, 2.50) | <0.001 | 4.97 (3.03, 8.16) | <0.001 |
| Other | 0.50 (0.23, 1.10) | 0.086 | 1.00 (0.00, 0.00) | <0.001 |
| Education category (Ref: No formal schooling) | | | | |
| Primary | 1.29 (0.72, 2.31) | 0.389 | 1.07 (0.59, 1.95) | 0.827 |
| Secondary | 0.84 (0.47, 1.51) | 0.568 | 0.75 (0.41, 1.38) | 0.354 |
| Tertiary | 0.44 (0.20, 0.96) | 0.039 | 0.35 (0.09, 1.35) | 0.128 |
| Sector (Ref: Urban) | | | | |
| Rural | 1.06 (0.87, 1.30) | 0.563 | 1.44 (0.95, 2.18) | 0.087 |
| Estate | 0.43 (0.27, 0.68) | <0.001 | 1.29 (0.62, 2.66) | 0.493 |
| Rural/estate | 0.97 (0.71, 1.32) | 0.834 | 1.76 (0.93, 3.34) | 0.084 |
| SES quintile (Ref: Poorest quintile) | | | | |
| 2 | 0.68 (0.53, 0.87) | 0.002 | 0.78 (0.49, 1.26) | 0.312 |
| 3 | 0.65 (0.51, 0.84) | 0.001 | 0.68 (0.40, 1.15) | 0.152 |
| 4 | 0.63 (0.48, 0.82) | 0.001 | 0.86 (0.47, 1.58) | 0.622 |
| Richest quintile | 0.56 (0.42, 0.76) | <0.001 | 0.48 (0.25, 0.89) | 0.02 |
| IHD | 1.21 (0.89, 1.63) | 0.219 | 1.63 (1.01, 2.62) | 0.045 |
| Rose angina | 0.96 (0.55, 1.68) | 0.895 | 1.58 (0.55, 4.52) | 0.398 |
| Stroke | 2.41 (1.39, 4.16) | 0.002 | 7.52 (4.06, 13.95) | <0.001 |
| Hypertension | 1.33 (1.09, 1.63) | 0.006 | 1.10 (0.73, 1.64) | 0.653 |
| Diabetes | 1.35 (1.08, 1.68) | 0.008 | 2.03 (1.33, 3.08) | 0.001 |
| Asthma | 1.28 (0.97, 1.70) | 0.083 | 1.26 (0.72, 2.19) | 0.424 |
| COPD | 0.94 (0.48, 1.87) | 0.867 | 1.25 (0.59, 2.65) | 0.567 |
| Liver disease | 2.49 (0.75, 8.33) | 0.138 | 2.82 (0.78, 10.14) | 0.113 |
| Cancer | 2.81 (1.22, 6.47) | 0.015 | 2.42 (0.53, 11.06) | 0.255 |
| Depression | 2.62 (1.40, 4.92) | 0.003 | 1.86 (0.34, 10.11) | 0.473 |
| Musculoskeletal | 3.44 (1.48, 8.04) | 0.004 | 1.52 (0.56, 4.15) | 0.414 |
| Constant | 0.04 (0.02, 0.08) | <0.001 | 0.00 (0.00, 0.00) | <0.001 |

(17.3%). The percentage of people reporting problems generally increased with age for all dimensions. In the youngest age group (18–24), 15.5% of people reported a problem with pain/discomfort, 10.4% reported a problem with anxiety/depression, and 6.1% reported a problem with mobility. In the oldest age group (75+), 61.7% reported a problem with mobility, 61.0% with pain and discomfort, and 36.1% with usual activities.

| Usual activities | | Pain/discomfort | | Anxiety/depression | |
|---|---|---|---|---|---|
| OR (95% CI) | *P*-value | OR (95% CI) | *P*-value | OR (95% CI) | *P*-value |
| 0.69 (0.54, 0.88) | 0.003 | 0.69 (0.59, 0.80) | <0.001 | 0.59 (0.49, 0.70) | <0.001 |
| 1.05 (1.04, 1.06) | <0.001 | 1.03 (1.03, 1.04) | <0.001 | 1.02 (1.01, 1.02) | <0.001 |
| 2.73 (2.02, 3.69) | <0.001 | 1.52 (1.24, 1.87) | <0.001 | 2.12 (1.69, 2.65) | <0.001 |
| 1.81 (0.93, 3.55) | 0.082 | 1.95 (1.23, 3.09) | 0.005 | 1.88 (1.15, 3.07) | 0.011 |
| 3.35 (2.34, 4.81) | <0.001 | 1.68 (1.28, 2.20) | <0.001 | 1.84 (1.35, 2.51) | <0.001 |
| 0.99 (0.28, 3.49) | 0.992 | 1.01 (0.43, 2.40) | 0.976 | 0.48 (0.21, 1.13) | 0.093 |
| 1.21 (0.75, 1.96) | 0.44 | 1.09 (0.73, 1.62) | 0.691 | 1.33 (0.89, 1.98) | 0.161 |
| 0.87 (0.54, 1.40) | 0.571 | 0.83 (0.57, 1.22) | 0.354 | 1.01 (0.69, 1.46) | 0.974 |
| 0.84 (0.34, 2.09) | 0.709 | 0.65 (0.38, 1.12) | 0.118 | 1.29 (0.72, 2.30) | 0.397 |
| 1.27 (0.96, 1.68) | 0.099 | 0.87 (0.71, 1.06) | 0.16 | 0.86 (0.69, 1.08) | 0.194 |
| 1.06 (0.63, 1.80) | 0.823 | 0.94 (0.62, 1.43) | 0.763 | 0.91 (0.57, 1.43) | 0.67 |
| 1.54 (1.00, 2.38) | 0.051 | 0.93 (0.71, 1.23) | 0.628 | 0.75 (0.54, 1.04) | 0.082 |
| 0.65 (0.47, 0.90) | 0.009 | 0.68 (0.55, 0.85) | <0.001 | 0.67 (0.52, 0.85) | 0.001 |
| 0.57 (0.40, 0.80) | 0.001 | 0.69 (0.55, 0.86) | 0.001 | 0.63 (0.48, 0.83) | 0.001 |
| 0.53 (0.34, 0.81) | 0.004 | 0.63 (0.50, 0.81) | <0.001 | 0.59 (0.45, 0.79) | <0.001 |
| 0.39 (0.26, 0.60) | <0.001 | 0.60 (0.47, 0.77) | <0.001 | 0.59 (0.43, 0.79) | 0.001 |
| 1.26 (0.87, 1.84) | 0.223 | 0.92 (0.68, 1.25) | 0.599 | 1.19 (0.86, 1.66) | 0.299 |
| 1.25 (0.68, 2.30) | 0.479 | 1.81 (1.10, 2.99) | 0.02 | 1.67 (1.03, 2.70) | 0.038 |
| 4.52 (2.57, 7.95) | <0.001 | 1.52 (0.88, 2.61) | 0.134 | 2.72 (1.50, 4.95) | 0.001 |
| 1.49 (1.13, 1.96) | 0.004 | 1.07 (0.88, 1.30) | 0.501 | 1.10 (0.88, 1.36) | 0.4 |
| 1.49 (1.11, 1.98) | 0.007 | 1.32 (1.08, 1.61) | 0.006 | 1.21 (0.96, 1.52) | 0.108 |
| 1.07 (0.71, 1.63) | 0.739 | 1.17 (0.91, 1.50) | 0.233 | 1.22 (0.92, 1.61) | 0.159 |
| 1.58 (0.82, 3.05) | 0.169 | 1.59 (0.96, 2.64) | 0.072 | 0.81 (0.45, 1.46) | 0.486 |
| 0.99 (0.33, 3.01) | 0.99 | 1.50 (0.50, 4.52) | 0.47 | 0.76 (0.28, 2.02) | 0.58 |
| 12.52 (3.60, 43.52) | <0.001 | 2.01 (0.92, 4.43) | 0.082 | 2.43 (1.10, 5.37) | 0.028 |
| 3.22 (1.37, 7.57) | 0.007 | 3.16 (1.70, 5.87) | <0.001 | 9.56 (5.18, 17.64) | <0.001 |
| 3.74 (1.57, 8.91) | 0.003 | 1.98 (0.96, 4.05) | 0.063 | 1.84 (0.89, 3.77) | 0.098 |
| 0.00 (0.00, 0.01) | <0.001 | 0.18 (0.10, 0.30) | <0.001 | 0.13 (0.08, 0.23) | <0.001 |

The results of the multivariate logistic regressions of the odds of reporting any issue in each domain is shown in Table 4. The odds of reporting any issue were lower in males compared to females in all domains ($p<0.001$), and the richest quintile compared to the poorest quintile for four domains ($p\leq0.001$). Muslims had higher odds of problems for all domains, than Sinhalese. People with stroke had higher odds of problems with selfcare (OR 7.52; 95% CI

4.06, 13.95; p<0.001), usual activities (OR 4.52; 95% CI 2.57, 7.95; p<0.001), and higher odds of problems across the remaining domains than people without stroke. People with cancer had a higher likelihood of problems with usual activities (OR 12.52; 95% CI 3.60, 43.52; p<0.001) than those without cancer.

The results of weighted robust OLS regression and Tobit regressions are shown in Table 5. Regressions which included the number of chronic conditions are shown in Appendix Table A2. The Tobit regression results show significant trends in disutility for female gender (male utility vs female = 0.077; 95% CI 0.054, 0.100; p<0.001), increasing age (disutility 0.007 per year increase in age; 95% CI 0.006, 0.007; p<0.001), lower SES quintile (utility of richest quintile vs poorest quintile 0.099; 95% CI 0.061, 0.137; p<0.001), and for certain disease conditions particularly stroke (disutility of disease vs no disease 0.249; 95% CI 0.158, 0.340; p<0.001), diabetes (0.064; 95% CI 0.032, 0.096; p<0.001), cancer (0.254; 95% CI 0.138,

***Table 5 Disutility associated with chronic disease using robust OLS and Tobit regressions***

| | OLS (robust) | | | | | Tobit | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Coefficient** | **SE** | **95% CI** | ***P*-value** | | **Coefficient** | **SE** | **95% CI** | ***P*-value** | |
| Gender (Ref: Female) | | | | | | | | | | |
| Male | 0.0376 | 0.0050 | (0.028, 0.047) | 0.000 | *** | 0.0772 | 0.0117 | (0.054, 0.100) | 0.000 | *** |
| Age | -0.0031 | 0.0002 | (-0.004, -0.003) | 0.000 | *** | -0.0066 | 0.0004 | (-0.007, -0.006) | 0.000 | *** |
| Ethnic group (Ref: Sinhala) | | | | | | | | | | |
| Sri Lankan Tamil | -0.0430 | 0.0074 | (-0.058, -0.028) | 0.000 | *** | -0.1017 | 0.0154 | (-0.132, -0.072) | 0.000 | *** |
| Indian Tamil | -0.0467 | 0.0177 | (-0.081, -0.012) | 0.008 | ** | -0.1048 | 0.0350 | (-0.173, -0.036) | 0.003 | ** |
| Muslim | -0.0598 | 0.0123 | (-0.084, -0.036) | 0.000 | *** | -0.1104 | 0.0225 | (-0.155, -0.066) | 0.000 | *** |
| Other | 0.0394 | 0.0180 | (0.004, 0.075) | 0.028 | * | 0.0959 | 0.0645 | (-0.030, 0.222) | 0.137 | |
| Education category (Ref: No formal schooling) | | | | | | | | | | |
| Primary | 0.0052 | 0.0235 | (-0.041, 0.051) | 0.826 | | -0.0072 | 0.0345 | (-0.075, 0.060) | 0.834 | |
| Secondary | 0.0557 | 0.0219 | (0.013, 0.099) | 0.011 | * | 0.0658 | 0.0334 | (0.000, 0.131) | 0.049 | * |
| Tertiary | 0.0723 | 0.0235 | (0.026, 0.118) | 0.002 | ** | 0.1132 | 0.0442 | (0.027, 0.200) | 0.010 | * |
| Sector (Ref: Urban) | | | | | | | | | | |
| Rural | 0.0038 | 0.0062 | (-0.008, 0.016) | 0.538 | | 0.0178 | 0.0151 | (-0.012, 0.048) | 0.239 | |
| Estate | 0.0206 | 0.0158 | (-0.010, 0.052) | 0.192 | | 0.0494 | 0.0300 | (-0.010, 0.108) | 0.100 | |
| Rural/estate | 0.0041 | 0.0097 | (-0.015, 0.023) | 0.674 | | 0.0207 | 0.0216 | (-0.022, 0.063) | 0.337 | |
| SES quintile (Ref: Poorest quintile) | | | | | | | | | | |
| 2 | 0.0286 | 0.0088 | (0.011, 0.046) | 0.001 | ** | 0.0650 | 0.0171 | (0.031, 0.099) | 0.000 | *** |
| 3 | 0.0399 | 0.0080 | (0.024, 0.056) | 0.000 | *** | 0.0847 | 0.0173 | (0.051, 0.119) | 0.000 | *** |
| 4 | 0.0419 | 0.0086 | (0.025, 0.059) | 0.000 | *** | 0.0953 | 0.0190 | (0.058, 0.133) | 0.000 | *** |
| Richest quintile | 0.0467 | 0.0086 | (0.030, 0.063) | 0.000 | *** | 0.0989 | 0.0194 | (0.061, 0.137) | 0.000 | *** |

| | OLS (robust) | | | | | Tobit | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Coefficient** | **SE** | **95% CI** | ***P*-value** | | **Coefficient** | **SE** | **95% CI** | ***P*-value** | |
| IHD | -0.0196 | 0.0153 | (-0.050, 0.010) | 0.201 | | -0.0210 | 0.0230 | (-0.066, 0.024) | 0.362 | |
| Rose angina | -0.0224 | 0.0174 | (-0.057, 0.012) | 0.198 | | -0.0585 | 0.0349 | (-0.127, 0.010) | 0.094 | |
| Stroke | -0.1959 | 0.0402 | (-0.275, -0.117) | 0.000 | *** | -0.2493 | 0.0464 | (-0.340, -0.158) | 0.000 | *** |
| Hypertension | -0.0282 | 0.0092 | (-0.046, -0.010) | 0.002 | ** | -0.0315 | 0.0154 | (-0.062, -0.001) | 0.040 | * |
| Diabetes | -0.0343 | 0.0099 | (-0.054, -0.015) | 0.001 | ** | -0.0641 | 0.0162 | (-0.096, -0.032) | 0.000 | *** |
| Asthma | -0.0224 | 0.0105 | (-0.043, -0.002) | 0.034 | * | -0.0322 | 0.0209 | (-0.073, 0.009) | 0.125 | |
| COPD | -0.0367 | 0.0246 | (-0.085, 0.011) | 0.135 | | -0.0399 | 0.0374 | (-0.113, 0.034) | 0.287 | |
| Liver disease | -0.0532 | 0.0543 | (-0.160, 0.053) | 0.328 | | -0.0790 | 0.0948 | (-0.265, 0.107) | 0.405 | |
| Cancer | -0.1777 | 0.0457 | (-0.267, -0.088) | 0.000 | *** | -0.2539 | 0.0592 | (-0.370, -0.138) | 0.000 | *** |
| Depression | -0.1321 | 0.0287 | (-0.188, -0.076) | 0.000 | *** | -0.2113 | 0.0392 | (-0.288, -0.134) | 0.000 | *** |
| Musculoskeletal | -0.1177 | 0.0337 | (-0.184, -0.052) | 0.000 | *** | -0.1816 | 0.0476 | (-0.275, -0.088) | 0.000 | *** |
| Constant | 0.9339 | 0.0253 | (0.884, 0.984) | 0.000 | *** | 1.1939 | 0.0464 | (1.103, 1.285) | 0.000 | *** |
| | | | | | | | | | | |
| Adjusted $R^2$ | 0.243 | | | | | 0.242 | | | | |

**Notes:** Data are weighted as described in text. Reference group for each disease is "no disease". Significance of difference with reference group denoted by *** P-value < 0.001, ** 0.001 ≤ P-value < 0.01, * 0.01 ≤ P-value < 0.05.

0.370; p<0.001), depression (0.211; 95% CI 0.134, 0.288; p<0.001) and musculoskeletal conditions (0.181; 95% CI 0.088, 0.275; p<0.001). As with the univariate analysis (Table 1), the Tobit regression suggests variations in disutility by race, where Sri Lankan Tamils, Indian Tamils and Muslims have lower utility values than Sinhalese (Table 5). Compared to the Tobit regression coefficients, most of the robust OLS regression coefficients have similar statistical significance and are similar in direction for demographic characteristics and disease conditions, as well as magnitude for many of the disease conditions. The adjusted R2 of both models are very similar (0.243 for robust OLS compared to 0.242 for the Tobit model).

The regression model including the number of chronic conditions per person is shown in Appendix Table A2. The coefficients remain very similar for the characteristics of gender, sex, ethnicity, education, sector, and SES quintile, in both the robust OLS and Tobit models, whilst most of the disutility is transferred from the individual chronic conditions to the number of chronic conditions. There is a utility gradient seen in the number of chronic conditions, with people with three or more conditions having a disutility of 0.21 (95% CI 0.04, 0.37, p=0.017) in the Tobit model, compared to people with no chronic conditions.

Appendix Figure A1 plots the utility values calculated using the Sri Lankan value set against those calculated using the Indian value set, and is weighted. The fitted cubic spline with 95% confidence interval, suggests that utility values calculated using the Sri Lankan value set are much lower than the Indian value set at (Sri Lankan) utility values below -0.37 (95% CI -0.52, -0.26) and values above 0.25 (95% CI 0.20, 0.29). The Bland Altman plot (Appendix Figure A2) comparing utility values shows that the Sri Lankan utility values are on average lower than

the Indian utility values, with a mean difference of -0.081, with 98% of observations found within a difference in utility values of -0.33 and 0.09.

## 3.4 DISCUSSION

This study updates the mean utility values (also known as EQ-5D-5L values, scores or weights) presented by Kularatna et al (25), by providing national-level data covering all districts of Sri Lanka, from a larger sample size of 6,415 adults, and using the EQ-5D-5L instrument instead of EQ-5D-3L. Mean utility values calculated in this study are very similar to those in Kularatna et al (25)– almost identical – in several domains, including utility values by age group and for the total population. However, one major difference is the utility values by gender. Whereas Kularatna found that mean utility values were similar by gender, in this sample, mean utility values were higher for males than for females. After adjusting for age, demographic factors and health conditions, the utility for males was higher by 0.04 in the robust OLS ($p<0.001$), and by 0.08 ($p<0.001$) in the Tobit regression model.

The dimensions of pain/discomfort and mobility had the highest percentage of participants who reported a problem, followed by problems in anxiety/depression. In an unstandardized comparison with studies from the past decade, the percentage of participants that reported a mobility problem in our study (21%) was higher than in Vietnam (10%) (26); lower than in high-income countries such as Australia (26%) (27), New Zealand (28%) (20), and Germany (35%) (28) that have an older population structure; and lower than in Thailand (28%) (9) and India (33%) (15), which have a similar or younger age structure to Sri Lanka. The percentage reporting pain/discomfort in Sri Lanka (32%) was similar to Vietnam (34%) (26) and less than Thailand (53%) (9), India (55%) (15), Australia (44%) (27), Germany (57%) (28) and New Zealand (62%) (20). Comparisons between countries of people reporting problems by dimension are complex, as a person's experience for each dimension is an interaction of biological, psychological, sociocultural, and environmental factors, and age-standardised analyses are needed. For example, when considering the 75+ years age group only, it appears that a similar or higher percentage of people in Sri Lanka have a problem with mobility (62%) compared to 46% in New Zealand (20), 50% in Germany (28), and 60% in Australia (27).

Our results provide a catalogue of utility values that can be used in health economic evaluations, similar to catalogues produced by Sullivan for the USA and the UK (5, 6). This is particularly useful for modelling exercises. Each coefficient presented in Table 5 represents a disutility associated with each condition after controlling for demographic features such as age, gender, ethnicity, level of education, socioeconomic status and disease conditions. Our study has a relatively small sample size of 6,415 participants compared to the sample sizes in Sullivan's

studies of 38,678 in the US and 79,522 in the UK. This leads to wider confidence intervals around conditions that affect a smaller proportion of people. Therefore, we also presented disutility values after controlling for the number of chronic conditions (Appendix Table A2). These tables can be used to calculate the impacts of disease on an individual's utility value. For example, if a 40-year-old male, whose baseline utility value calculated from his responses to the EQ-5D-5L was 0.900, had a stroke, we could model his new utility value as 0.900 – 0.249 = 0.651, using the disutility of a stroke from the Tobit regression in Table 5. Alternatively, we could use the coefficients from Appendix Table A2, where we included the disutility of having one chronic condition (-0.065), and the adjusted disutility for stroke (-0.189), resulting in a utility value of 0.900 – 0.065 – 0.189 = 0.646. If this 40-year-old male had a stroke and diabetes, then the utility value would be 0.900 – 0.249 – 0.064 = 0.587 using the disutility of diabetes (-0.064) from Table 5, or 0.900 – 0.124 – 0.189 – 0.001 = 0.586 using the disutility of having two chronic conditions (-0.124), and adjusted disutilities for stroke (-0.189) and diabetes (-0.001) from Appendix Table A2. The differences are minor, and the decision to use either method could be based on what diseases are being modelled for. For example, in a modelling exercise focusing only on the incidence of IHD and stroke, Table 5 can be used, whereas a modelling exercise that evaluates multiple chronic diseases, or models conditions that may not be specified in the catalogue could use the coefficients generated after controlling for the number of chronic conditions (Appendix Table A2). In modelling exercises, we can reduce the utility value for each year lived by -0.007 and apply discounting to the overall utility values, as demonstrated by Sullivan et al (5).

The decision to use disutility values produced by the robust OLS or Tobit regressions, depends on the preference of the researcher. Researchers who believe that health utility is censored at 1, can use the values produced by the robust OLS regression, whilst those who believe that health utility is not censored at 1, can use the values produced by the Tobit regression (18, 19). Half of the unweighted dataset (and 54% of the weighted dataset) had a utility value of 1, which also supports the use of Tobit regression results (22).

Our study has several limitations. The sample size of 6,415, is sufficient to make estimates of mean utility values and disutility with reasonable certainty for factors such as age, gender, and education category. A larger sample size would be desirable still for ethnicities other than the Sinhalese ethnicity, and disease status estimates.

It would be ideal to use a directly measured EQ-5D-5L Sri Lankan value set, however no such set is currently available. Nevertheless, using the cross-walked EQ-5D-5L value set appears to be more appropriate than using another country's EQ-5D-5L value set, given the known differences in the valuation of disease states in different contexts (3). Compared to utility values calculated using the EQ-5D-5L value set for India (15), utilities derived from the value

set from Sri Lanka appear to be generally lower, particularly for Sri Lankan utility values above 0.25 (Appendix Figure A1 and A2). These differences could be due to several reasons: Sri Lankans may value some disease states less (4); or, be less tolerant of deviations from good health (29, 30); or, the value set may give lower utilities than a directly valued EQ-5D-5L utility set, thus over-estimating disutility of disease states (31); or, due to methodological differences in the Indian valuation which used a combination of TTO and DCE, whereas the Sri Lankan valuation used TTO. These differences warrant further investigation, which is beyond the scope of this paper, particularly to determine if a directly valued EQ-5D-5L utility set for Sri Lanka would be beneficial.

## 3.5 CONCLUSION

This study updates population norms and mean EQ-5D-5L utility values for Sri Lanka by demographic features and disease status using nationally representative data. It also presents estimates for utility values for a variety of chronic conditions. Whilst these estimates should be confirmed using even larger datasets, such large nationally representative datasets covering multiple chronic conditions will remain scarce given resource requirements. Accordingly, these estimates present an interim catalogue of utility values that could be used by researchers interested in calculating QALYs for analysing the cost-utility of public health interventions.

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# APPENDIX

## Text A1 Estimation of household socioeconomic status using principal components analysis

The SLHAS Wave 1 uses an asset index approach to generate a proxy measure of each household's living standard. The index was computed by using principal components analysis (PCA) of a set of householdlevel variables relating to asset ownership or household characteristics. Variables were selected from those used in recent Sri Lanka Household Income and Expenditure Surveys conducted by the Department of Census and Statistics, selecting those with most predictive performance, and excluding some assets that are only relevant to agricultural households (e.g., tractor, thresher, fishing equipment). Variables were either dichotomous (e.g., household has a car) or categorical (e.g., type of drinking water source), apart from one ordinal variable (number of bedrooms). Dichotomous variables consisted of whether the household possessed each of the following items: radio/cassette player, television, VCD/DVD player, washing machine, fridge, electric fan, domestic phone, mobile phone, computer, internet access, camera/video camera, bicycle, motorcycle/scooter, three-wheeler, motor car/van, and bus/lorry/tipper.

Categorical variables were transformed into dichotomous indicators by creating separate dummy variables for each category. They consisted of the following (numbers in parentheses indicates number of categories in each): flooring material (5), material of wall (7), type of housing tenure (12), drinking water source (16), type of toilet (4), method of household garbage disposal (6), lighting power source (5), cooking fuel (13), and type of cooking place (3).

There was a small percentage of missing values in each variable (2–3%). These were imputed with either the PSU or stratum level mean of the variable or failing those the district/sector or national means. The principal component factor or index obtained by PCA after combining all these variables was then used to divide the sample into population weighted quantiles of equal size. Separate indices were not estimated for urban or rural sectors, but analysis indicates little difference between sectors in how the national index performs.

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Rannan-Eliya RP, Wijemunige N, Perera P, Kapuge Y, Gunawardana N, Sigera C, et al. Prevalence of diabetes and pre-diabetes in Sri Lanka: a new global hotspot-estimates from the Sri Lanka Health and Ageing Survey 2018/2019. BMJ Open Diabetes Res Care. 2023;11(1). Supplementary Text S1.

*Table A1 Sources of information used to determine conditions of interest*

| Condition | Participants with condition (n) | Selfreported only (%) | Medical records only (%) | Examination or laboratory tests only (%) | Self-reported and medical record (%) |
|---|---|---|---|---|---|
| Ischaemic heart disease | 366 | 22.1 | 2.5 | Not applicable | 75.4 |
| Stroke | 101 | 35.6 | 21.8 | Not applicable | 42.6 |
| Hypertension | 1,498 | 26.2 | 1.2 | 8.4 | 64.2 |
| Diabetes | 1,070 | 29.3 | 0.6 | 0.6 | 69.5 |
| Asthma | 566 | 64.1 | 1.1 | Not applicable | 34.8 |
| COPD | 95 | 67.4 | 0.0 | Not applicable | 32.6 |
| Liver disease | 19 | 52.6 | 0.0 | Not applicable | 47.4 |
| Cancer | 45 | 28.9 | 4.4 | Not applicable | 66.7 |
| Depression | 64 | 50.0 | 4.7 | Not applicable | 45.3 |
| Musculoskeletal disorders | 51 | 56.9 | 5.9 | Not applicable | 37.3 |
| Neurological | 18 | 66.7 | 11.1 | Not applicable | 22.2 |
| Chronic kidney disease | 10 | 10.0 | 0.0 | Not applicable | 90.0 |

*Table A2 Results of Robust OLS and Tobit regression, including number of chronic diseases*

| | OLS (robust) | | | | | Tobit | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Coefficient | SE | 95% CI | *P*-value | | Coefficient | SE | 95% CI | *P*-value | |
| Gender (Ref: Female) | | | | | | | | | | |
| Male | 0.0376 | 0.0050 | (0.028, 0.047) | 0.000 | *** | 0.0772 | 0.0117 | (0.054, 0.100) | 0.000 | *** |
| Age | -0.0032 | 0.0002 | (-0.004, -0.003) | 0.000 | *** | -0.0066 | 0.0004 | (-0.007, -0.006) | 0.000 | *** |
| Ethnic group (Ref: Sinhala) | | | | | | | | | | |
| Sri Lankan Tamil | -0.0426 | 0.0074 | (-0.057, -0.028) | 0.000 | *** | -0.1007 | 0.0154 | (-0.131, -0.070) | 0.000 | *** |
| Indian Tamil | -0.0469 | 0.0176 | (-0.081, -0.012) | 0.008 | ** | -0.1038 | 0.0348 | (-0.172, -0.036) | 0.003 | ** |
| Muslim | -0.0599 | 0.0123 | (-0.084, -0.036) | 0.000 | *** | -0.1100 | 0.0226 | (-0.154, -0.066) | 0.000 | *** |
| Other | 0.0391 | 0.0181 | (0.004, 0.075) | 0.031 | * | 0.0966 | 0.0646 | (-0.030, 0.223) | 0.134 | |
| Education category (Ref: No schooling) | | | | | | | | | | |
| Primary educated | 0.0037 | 0.0235 | (-0.042, 0.050) | 0.876 | | -0.0095 | 0.0344 | (-0.077, 0.058) | 0.782 | |
| Secondary educated | 0.0544 | 0.0219 | (0.012, 0.097) | 0.013 | * | 0.0640 | 0.0333 | (-0.001, 0.129) | 0.055 | |
| Tertiary educated | 0.0712 | 0.0235 | (0.025, 0.117) | 0.002 | ** | 0.1113 | 0.0442 | (0.025, 0.198) | 0.012 | * |
| Sector (Ref: Urban) | | | | | | | | | | |
| Rural | 0.0038 | 0.0063 | (-0.008, 0.016) | 0.544 | | 0.0176 | 0.0151 | (-0.012, 0.047) | 0.246 | |
| Estate | 0.0210 | 0.0158 | (-0.010, 0.052) | 0.185 | | 0.0505 | 0.0301 | (-0.008, 0.109) | 0.093 | |
| Rural/estate | 0.0038 | 0.0097 | (-0.015, 0.023) | 0.700 | | 0.0204 | 0.0216 | (-0.022, 0.063) | 0.344 | |

| | OLS (robust) | | | | | Tobit | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Coefficient** | **SE** | **95% CI** | ***P*-value** | | **Coefficient** | **SE** | **95% CI** | ***P*-value** | |
| SES quintile (Ref: Poorest quintile) | | | | | | | | | | |
| 2 | 0.0289 | 0.0088 | (0.012, 0.046) | 0.001 | ** | 0.0657 | 0.0171 | (0.032, 0.099) | 0.000 | *** |
| 3 | 0.0401 | 0.0080 | (0.024, 0.056) | 0.000 | *** | 0.0862 | 0.0173 | (0.052, 0.120) | 0.000 | *** |
| 4 | 0.0419 | 0.0086 | (0.025, 0.059) | 0.000 | *** | 0.0970 | 0.0190 | (0.060, 0.134) | 0.000 | *** |
| Richest quintile | 0.0468 | 0.0086 | (0.030, 0.064) | 0.000 | *** | 0.0998 | 0.0194 | (0.062, 0.138) | 0.000 | *** |
| IHD | 0.0055 | 0.0236 | (-0.041, 0.052) | 0.817 | | 0.0391 | 0.0351 | (-0.030, 0.108) | 0.266 | |
| Rose angina | -0.0039 | 0.0249 | (-0.053, 0.045) | 0.875 | | 0.0092 | 0.0454 | (-0.080, 0.098) | 0.840 | |
| Stroke | -0.1705 | 0.0434 | (-0.256, -0.085) | 0.000 | *** | -0.1889 | 0.0535 | (-0.294, -0.084) | 0.000 | *** |
| Hypertension | -0.0107 | 0.0193 | (-0.048, 0.027) | 0.581 | | 0.0323 | 0.0314 | (-0.029, 0.094) | 0.305 | |
| Diabetes | -0.0162 | 0.0196 | (-0.055, 0.022) | 0.406 | | -0.0013 | 0.0309 | (-0.062, 0.059) | 0.966 | |
| Asthma | -0.0054 | 0.0198 | (-0.044, 0.033) | 0.784 | | 0.0315 | 0.0337 | (-0.035, 0.098) | 0.350 | |
| COPD | -0.0181 | 0.0295 | (-0.076, 0.040) | 0.541 | | 0.0176 | 0.0451 | (-0.071, 0.106) | 0.696 | |
| Liver | -0.0409 | 0.0614 | (-0.161, 0.079) | 0.505 | | -0.0316 | 0.1037 | (-0.235, 0.172) | 0.761 | |
| Cancer | -0.1569 | 0.0482 | (-0.251, -0.062) | 0.001 | ** | -0.1866 | 0.0653 | (-0.315, -0.059) | 0.004 | ** |
| Depression | -0.1140 | 0.0326 | (-0.178, -0.050) | 0.000 | *** | -0.1483 | 0.0468 | (-0.240, -0.057) | 0.002 | ** |
| Musculoskeletal | -0.0767 | 0.0480 | (-0.171, 0.017) | 0.110 | | -0.0682 | 0.0681 | (-0.202, 0.065) | 0.317 | |
| Number of chronic conditions (Ref: 0) | | | | | | | | | | |
| 1 | -0.0107 | 0.0182 | (-0.046, 0.025) | 0.556 | | -0.0646 | 0.0306 | (-0.125, -0.005) | 0.035 | * |
| 2 | -0.0324 | 0.0346 | (-0.100, 0.035) | 0.349 | | -0.1237 | 0.0553 | (-0.232, -0.015) | 0.025 | * |
| 3+ | -0.0763 | 0.0547 | (-0.184, 0.031) | 0.163 | | -0.2049 | 0.0859 | (-0.373, -0.036) | 0.017 | * |
| Constant | 0.9347 | 0.0254 | (0.885, 0.984) | 0.000 | *** | 1.1960 | 0.0000 | (0.000, 0.000) | 0.000 | *** |
| Adjusted-$R^2$ | 0.244 | | | | | 0.242 | | | | |

***Figure A1 Utility using Sri Lankan EQ-5D-5L value set versus Indian EQ-5D-5L value set for SLHAS participants in Sri Lanka***

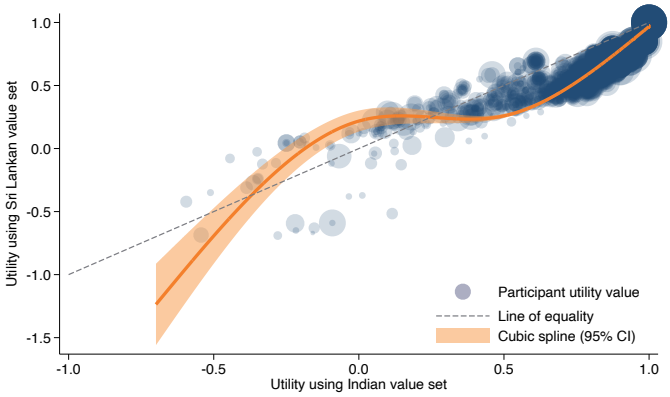
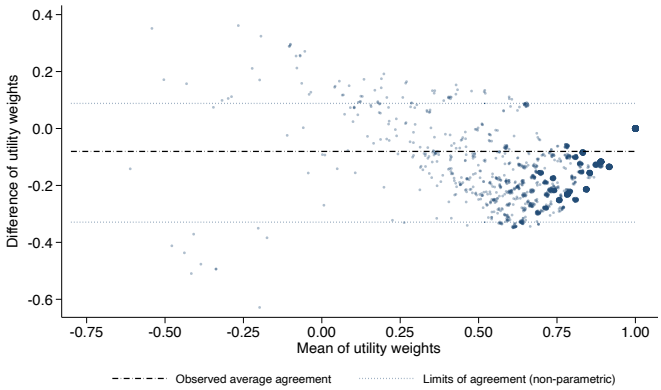



***Figure A2 Bland Altman plot of utility using Sri Lankan EQ-5D-5L value set versus Indian EQ-5D-5L value set for SLHAS participants in Sri Lanka***




**Notes:** The mean difference of utility weights was -0.081. 98% of observations lay between a difference of 0.33 and 0.09. Points are jittered to show where multiple points are superimposed more clearly.

# Chapter 4

# Health outcomes and healthcare utilization associated with four undiagnosed chronic conditions: evidence from nationally representative survey data in Sri Lanka

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# ABSTRACT


## Background

Low awareness of chronic conditions raises the risk of poorer health outcomes and may result in healthcare utilization and spending in response to symptoms of undiagnosed conditions. Little evidence exists, particularly from lower-middle-income countries, on the health and healthcare use of undiagnosed people with an indication of a condition. This study aimed to compare health (physical, mental and health-related quality of life (HRQoL)) and healthcare (inpatient and outpatient visits and out-of-pocket (OOP) medical spending) outcomes of undiagnosed Sri Lankans with an indication of coronary heart disease (CHD), hypertension, diabetes and depression with the outcomes of their compatriots who were diagnosed or had no indication of these conditions.

## Methods

This study used a nationally representative survey of Sri Lankan adults to identify people with an indication of CHD, hypertension, diabetes, or depression, and ascertain if they were diagnosed. Outcomes were self-reported measures of physical and mental functioning (12-Item Short Form Survey (SF-12)), HRQoL (EQ-5D-5L), inpatient and outpatient visits, and OOP spending. For each condition, we estimated the mean of each outcome for respondents with a) no indication, b) an indication without diagnosis, and c) a diagnosis. We adjusted the group-differences in these means for sociodemographic covariates using ordinary least squares (OLS) regression for physical and mental function, Tobit regression for HRQoL, and a generalized linear model (GLM) for healthcare visits and OOP spending.

## Results

An indication of each of CHD and depression, which are typically symptomatic, was associated with a lower adjusted mean of physical (CHD 2.65, 95% CI 3.66, 1.63; depression 5.78, 95% CI 6.91, 4.64) and mental functioning (CHD 2.25, 95% CI 3.38, 1.12; depression 6.70, 95% CI 7.97, 5.43) and, for CHD, more annual outpatient visits (2.13, 95% CI 0.81, 3.44) compared with no indication of the respective condition. There were no such differences for indications of hypertension and diabetes, which are often asymptomatic.

## Conclusions

Living with undiagnosed CHD and depression was associated with worse health and, for CHD, greater utilization of healthcare. Diagnosis and management of these symptomatic conditions can potentially improve health partly through substitution of effective healthcare for that which primarily responds to symptoms.

## 4.1 BACKGROUND

The burden of non-communicable diseases (NCDs) is large and growing in low- and middle-income countries (LMICs) (1). In Sri Lanka, cardiovascular and metabolic diseases account for more than a quarter of the disease burden, compared to less than one-fifth in high-income countries (2).

A large proportion of people living with NCDs or their risk factors are undiagnosed (3-6). In South Asia, around two-thirds of men with hypertension are undiagnosed, compared to 31% in high-income, Western countries (3). Over half of diabetics in LMICs are undiagnosed (4). In Sri Lanka, 47% and 38% of people with indications of hypertension and diabetes, respectively, are undiagnosed (7, 8). There is also substantial underdiagnosis of CHD (9-11), and likely underdiagnosis of depression (12), a condition with a bidirectional relationship with CHD (13), diabetes (14), and their risk factors (15) in LMICs.

People at early stages of developing a chronic condition are often asymptomatic, particularly for hypertension and diabetes. When symptoms do emerge, treatment may primarily respond to the symptoms without managing the underlying, still undiagnosed, condition (16-21). If undiagnosed people with indications of chronic conditions experience worse health, make greater use of healthcare, and incur more OOP spending, then there may be potential for earlier diagnosis and management not only to slow or prevent disease onset but also to improve health immediately and reduce pressures on health systems and household finances.

There is little evidence from LMICs to determine whether people with an indication but not a diagnosis of a chronic health condition do experience worse health and make greater use of healthcare. An Indonesian study found that people with an indication of diabetes or hypertension that was undiagnosed did not have significantly higher healthcare utilization and expenditures, but undiagnosed people with an indication of a heart problem were more frequent users of outpatient care than people without these conditions (22). In China, physical and mental functioning of people with an indication of hypertension without diagnosis were similar to those of people with no indication (23). Even for high-income countries, there is limited evidence on health and healthcare utilization associated with having an indication of a chronic condition without a diagnosis. One small-scale study in Finland found that the physical functioning of people with an indication of hypertension without diagnosis was lower than that of people without hypertension (24). A subnational study in Japan found that people with undiagnosed depression had lower physical and mental functioning, HRQoL, and more healthcare utilization than people without depression (25). Each of these studies focused on a limited set of outcomes of one or two chronic conditions.

Using nationally representative data from Sri Lanka, this study aimed to add to the limited evidence from LMICs on the association between having an indication without diagnosis of each of four major chronic conditions – CHD, hypertension, diabetes, and depression – and both health (physical, mental, and HRQoL) and healthcare (inpatient and outpatient utilization, and OOP medical spending) outcomes.

## 4.2 METHODS

We used data from the Sri Lanka Health and Ageing Study (SLHAS) conducted from 9 November 2018 to 14 November 2019 (26). A multi-stage cluster random sampling design, stratified by district, residential sector and area socioeconomic status (SES) was used to collect data in 297 sampling units selected by probability-proportionate-to-size sampling in all districts of Sri Lanka (27). Within each sampling unit (smallest administrative division), households were randomly selected and one adult (18 years and older) was randomly chosen from each household roster, with oversampling of those aged ≥70 years. After application of sampling weights, the sample was representative of the adult population of Sri Lanka in 2019 by gender, age, geographical region, area SES and ethnicity (27).

Data were collected using a computer-assisted personal interviewing platform, iFormBuilder (Zerion Software Inc., Herndon, VA, USA), with built-in skip logic and checks for unlikely values during data entry. During data cleaning, less likely values were cross-checked using manually recorded clinic checklists.

### 4.2.1 Identification of chronic conditions

In addition to completing a questionnaire, each respondent was asked to bring their medical records to the interview and to give consent for the enumerator to consult these records. An inventory of each respondent's medicines was taken. Blood pressure, weight and height were measured, and a blood sample was taken. Blood pressure was measured two times, 10 minutes apart, on one occasion using an OMRON HEM-7320 blood pressure monitor (OMRON Healthcare Co., Ltd., Kyoto, Japan) by a trained enumerator following standard procedure (7). We used the mean of the two measurements. Participants were asked to fast for 12 hours prior to attending the clinic for data collection. A venous blood sample was taken from all consenting participants, and those who provided an initial fasting sample underwent an oral glucose tolerance test (8). Samples were stored within 6-10 hours of initial collection in a field freezer (TwinBird Freezer SC-DF25, Twinbird Corporation, Niigita, Japan and Glacio 55L Portable Cooler Fridge PFN-E-WEA-L-GR, New Aim Pty Ltd, Melbourne, Australia) at -40oC to -20oC for transport to the Sri Lanka Medical Research Institute (Colombo) for testing.

For each of four chronic conditions – CHD, hypertension, diabetes, and depression – we distinguished between respondents who a) had been diagnosed (diagnosed), b) showed an indication but had not been diagnosed (indicated), and c) showed no indication and had not been diagnosed (no condition). A respondent was defined as diagnosed with CHD if they reported ever being diagnosed with angina, myocardial infarction or coronary artery disease, or their medical records indicated such a diagnosis. They were defined as indicated for CHD if they were not diagnosed but they satisfied the criteria on the Rose angina questionnaire of ever having chest pain that appeared upon exertion, was situated at any level of the sternum or left anterolateral chest and arm, which caused the respondent to slow down or stop while walking, and was relieved within ten minutes of rest, or they reported ever having severe chest pain across the front of the chest for thirty minutes or more (28, 29). The Rose angina questionnaire is a standardized tool for detecting angina based on self-reported symptoms that has been used in a wide range of research and clinical settings (11, 28) and has been validated for use in Sri Lanka (30).

A respondent was categorised as diagnosed with hypertension if they reported a diagnosis or their medical records showed this, or they reported taking antihypertensives in the past 14 days. They were defined as indicated for hypertension if they were not diagnosed and had a systolic blood pressure of at least 140 mmHg or a diastolic blood pressure of at least 90 mmHg.

A respondent was identified as diagnosed with diabetes if they reported a diagnosis or their medical records showed this, or they reported taking oral hypoglycaemics or insulin in the past 14 days. They were defined as indicated for diabetes if they were not diagnosed but had a fasting plasma sugar of 126 mg/dL or more, or a random (6 participants had not fasted) or oral glucose tolerance test showed a plasma sugar of 200 mg/dL or more (8).

A respondent was categorised as diagnosed with depression if they reported a diagnosis or their medical records showed this. They were indicated for depression if it had not been diagnosed but they scored 10 or more on the Patient Health Questionnaire (PHQ-9) questionnaire (31). A score ≥ 10 maximises sensitivity and specificity for major depression (32) and is the threshold validated and used in Sri Lanka (31).

### 4.2.2 Outcomes

We used the physical component score (PCS) and mental component score (MCS) from the SF-12 questionnaire (33) to measure physical and mental health functioning, respectively. Both scores were calculated for each respondent using an algorithm developed from a sample in the United States, where scores were standardized to give a mean score of 50 and a standard deviation of 10 (33). Scores below 50 indicate poorer function.

For each respondent, HRQoL was obtained from their responses to the EQ-5D-5L questionnaire (34). The EQ-5D-5L is a multi-attribute utility instrument used to measure health status in five domains (mobility, self-care, usual activities, pain and discomfort, anxiety, and depression) with five levels of severity ranging from "no problems" to "extreme/unable". Each combination of responses was mapped to a utility value using tariffs derived from Sri Lankan data (35), where 1 represents "perfect health" and 0 represents death, and where negative values (states worse than death) are possible.

We measured healthcare utilization with self-reported inpatient stays, which included any admission to a bed in a public or private hospital, and outpatient visits. Outpatient visits covered any visit to a facility that did not require admission or an overnight stay, and included public and private specialist and general clinics, allied health visits (e.g. to see a physiotherapist or dietician), public health clinics, such as medical officer of health and midwife clinics, visits to a pharmacy, laboratory or imaging center, and non-Western medicine clinics. The SLHAS randomly varied recall periods across participants in order to analyze the impact of recall periods on reported healthcare utilization in a study separate from this one. They were 1, 6 and 12 months (22%, 18% and 60% of the sample) for inpatient visits and 7, 14 and 28 days (20%, 20% and 60% of the sample) for outpatient visits. Data on the number of inpatient and outpatient encounters over a specified recall period were annualized.

Self-reported OOP spending for direct medical costs, including hospitalization and consultation fees, medicine and medical supplies, investigations, and informal payments were annualized. Amounts were converted to US dollars using the average US dollar exchange rate for the month the respondent was interviewed, as reported by the Central Bank of Sri Lanka, as an appropriate way to handle the devaluation of the local currency (36).

### 4.2.3 Covariates

Socio-demographic characteristics included age in 10year age groups (18-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+), sex (male, female), ethnicity (Sinhala, Tamil, Muslim/Moor/Malay, Other), education (no formal, primary, secondary and tertiary), sector (urban, rural, estate, rural/estate) and province of residence, SES, household size (number of persons), and proportions of household members aged under 15 years and above 60 years. SES was proxied by quintile groups of an index obtained as the first principal component of an analysis of household assets, water and sanitation facilities, housing quality and other assets (37) (Appendix Text A1). Standard body mass index (BMI) categories (normal < 25 kg/m2, overweight 25-29.9 kg/m2, obese ≥ 30 kg/m2), which were used in the sensitivity analysis, were calculated based on the weight in kilograms measured by an OMRON BF511 Body Composition Monitor (OMRON Healthcare Co., Ltd., Kyoto, Japan) and height measured in centimetres by a seca 240 mechanical measuring rod (stadiometer) (seca, Hamburg, Germany).

### 4.2.4 Statistical analysis

We estimated the mean of each outcome for each group defined as having no condition, being indicated, and being diagnosed for each of the four chronic conditions (CHD, hypertension, diabetes, and depression). We used a z-test to test the null of no difference in the means for indicated vs no condition, and diagnosed vs no condition. We used multivariate regression to estimate differences in the mean of each outcome between the three groups (no condition, indicated, and diagnosed) adjusted for the covariates (with age groups interacted with sex). For regressions of PCS and MCS scores, which are normally distributed, we used OLS. For HRQoL, following much analysis (38-40), we assumed a Tobit model to account for censoring at 1 that arose from anchoring EQ-5D-based utility values at that value for "full health", and used maximum likelihood estimation. For regressions of inpatient and outpatient visits, which are counts data, and OOP spending, which are skewed data with many zero values, we used a GLM with a Poisson distribution, a log link and robust standard errors. Correct specification of the conditional mean is sufficient for the consistency of this pseudo-maximum-likelihood estimator (41), which performs well with many zeros [40] and is often used to model medical spending data [41]. We present estimates from these models of average marginal effects (AME): the change in the mean of the outcome associated with a unit change in an independent variable that is estimated for each observation and averaged over the sample. We repeated the multivariate regressions extended to include BMI, which is usually positively associated with higher risk of CHD, hypertension and diabetes (42, 43) but can also be associated with poorer health outcomes after controlling for these and other conditions (44). In all analyses, we applied sample weights and estimated robust standard errors adjusted for sample stratification and clustering. A p-value less than 0.05 was considered as statistically significant.

Data were missing for PCS, MCS and HRQoL (<5%), inpatient and outpatient visits (<3.5%), OOP spending (<3%), and covariates (<1%). To avoid selection bias that may result if participants with missing data were excluded, we assumed that data were missing at random and imputed them using multiple imputation with chained equations and predictive mean matching using 10 nearest neighbors (Appendix Text A2). As a sensitivity analysis, we also performed a complete case analysis instead of using multiply imputed data. All analyses were performed using Stata 17.0 (45).

## 4.3 RESULTS

Table 1 shows characteristics of the analysis sample after imputation. The mean age was 50.1 years (standard deviation (SD) 17.2) and 51% were female. A majority (82.1%) had secondary education or above. More than half (54.9%) of the sample were in the rural sector. The average household size was 2.98 (SD 1.4), with the proportion of household members aged above 60 years and below 15 years being 0.23 (SD 0.33) and 0.07 (SD 0.16), respectively, on average. Characteristics of the complete cases sample were very similar (Appendix Table S1).

***Table 1 Sample characteristics, n=6,665***

| | n / mean | % / SD |
|---|---|---|
| Age, mean (SD) | 50.1 | 17.2 |
| Sex | | |
| Male | 3,268 | 49.0 |
| Female | 3,397 | 51.0 |
| Ethnicity | | |
| Sinhala | 4,707 | 70.6 |
| Tamil | 1,504 | 22.6 |
| Muslim | 428 | 6.4 |
| Other | 26 | 0.4 |
| Education | | |
| No formal schooling | 258 | 3.9 |
| Primary educated | 937 | 14.1 |
| Secondary educated | 5,199 | 78.0 |
| Tertiary educated | 272 | 4.1 |
| Sector | | |
| Urban | 2,024 | 30.4 |
| Rural | 3,661 | 54.9 |
| Estate | 170 | 2.6 |
| Rural/Estate | 810 | 12.2 |
| Province | | |
| Western | 1,435 | 21.5 |
| Central | 976 | 14.6 |
| Southern | 851 | 12.8 |
| Northern | 691 | 10.4 |
| Eastern | 553 | 8.3 |
| North-Western | 548 | 8.2 |
| North-Central | 477 | 7.2 |
| Uva | 467 | 7.0 |
| Sabaragamuwa | 667 | 10.0 |
| SES quintile | | |
| Poorest | 1,568 | 23.5 |
| Poorer | 1,328 | 19.9 |
| Middle | 1,245 | 18.7 |
| Richer | 1,220 | 18.3 |
| Richest | 1,304 | 19.6 |

| | n / mean | % / SD |
|---|---|---|
| Household size, mean (SD) | 2.98 | 1.4 |
| Proportion below 15, mean (SD) | 0.07 | 0.16 |
| Proportion above 60, mean (SD) | 0.23 | 0.33 |

**Notes:** Columns shows n (%) unless specified as mean (SD). Sample weights not applied. SES is socioeconomic status, SD is standard deviation. The percentages for SES quintile groups are not 20% because the groups were constructed to account for 20% after the application of sample weights.

Table 2 shows, for each of the four chronic conditions, estimates of the population percentages with an indication but no diagnosis (indicated), a diagnosis (diagnosed), and with neither an indication nor diagnosis (no condition). We estimated that 5.7% (95% CI 5.0, 6.5) of the adult population of Sri Lanka had an indication of CHD but had not been diagnosed and 3.9% (95% CI 3.4, 4.4) had been diagnosed with CHD. Meanwhile, 13.0% (95% CI 11.8, 14.2) of the population had an indication of hypertension with no diagnosis, and 16.7% (95% CI 15.5, 17.8) had diagnosed hypertension. For diabetes, 7.2% (95% CI 6.4, 8.0) of the population had an indication of diabetes, and 13.6% (95% CI 12.3, 14.8) had a diagnosis. We estimated that 4.3% (95% CI 3.6%, 4.9%) of the population had an indication of depression and only 1.0% (0.7%, 1.3%) of the population had a diagnosis.

***Table 2 Estimated prevalence of chronic conditions by indication and diagnosis***

| | n | % (95% CI) |
|---|---|---|
| CHD | | |
| No condition | 5,896 | 90.4 (89.4, 91.3) |
| Indicated | 382 | 5.7 (5.0, 6.5) |
| Diagnosed | 387 | 3.9 (3.4, 4.4) |
| Hypertension | | |
| No condition | 4,132 | 70.3 (68.7, 71.9) |
| Indicated | 975 | 13.0 (11.8, 14.2) |
| Diagnosed | 1,558 | 16.7 (15.5, 17.8) |
| Diabetes | | |
| No condition | 5,054 | 79.2 (77.8, 80.6) |
| Indicated | 499 | 7.2 (6.4, 8.0) |
| Diagnosed | 1,112 | 13.6 (12.3, 14.8) |
| Depression | | |
| No condition | 6,224 | 94.8 (94.1, 95.5) |
| Indicated | 377 | 4.3 (3.6, 4.9) |
| Diagnosed | 64 | 1.0 (0.7, 1.3) |

**Notes:** Imputed data used (N=6,665). Sample weights applied for percentage and confidence intervals (CI).

There was substantial multimorbidity (Appendix Table S2). For example, we estimated that among those who had an indication or diagnosis of CHD, 52.0% (95% CI 47.0, 57.1) also had an indication or diagnosis of hypertension and 32.7% (95% CI 27.6, 37.7) had an indication or diagnosis of diabetes. Of those with an indication or diagnosis of depression, we estimated that 42.2% (95% CI 35.0, 49.4) had an indication/diagnosis of hypertension, 32.5% (95% CI 25.7, 39.4) had an indication/diagnosis of diabetes, and 22.3% (95% CI 16.6, 27.9) had an

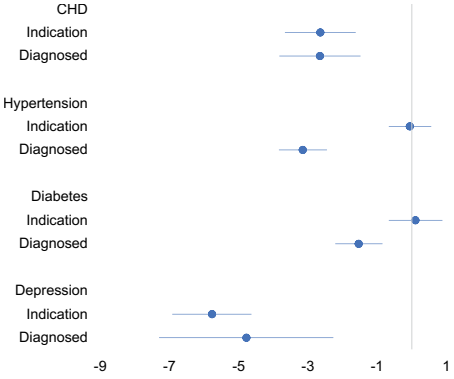
indication/diagnosis of CHD. There was also a substantial overlap between hypertension and diabetes.

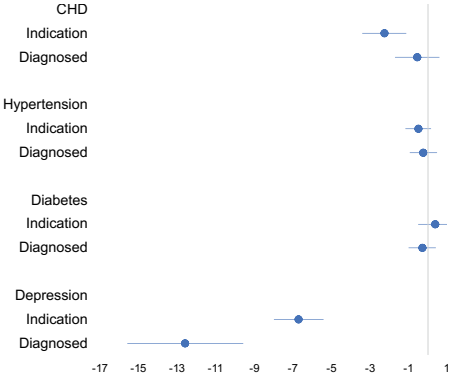
Table 3 shows the estimated mean of each outcome by category of each chronic condition and Fig 1 shows the estimated adjusted difference in means between those indicated with each condition and those without that condition as well as the respective difference between those diagnosed with each condition and those without that condition (point estimates in Appendix Table S3). Without and with adjustment, the mean PCS scores with an indication and with a diagnosis of CHD was lower – indicating lower physical functioning – than the mean score of those without any indication or diagnosis of CHD. After adjustment, the mean PCS score of those with an indication of CHD was 2.7 points (95% CI 1.6, 3.7) lower than the mean score of those without CHD. The mean difference between those diagnosed with CHD and those without the condition was the same (2.7, 95% CI 1.5, 3.8). Having an indication of CHD was associated with an adjusted mean MCS score that was 2.3 points (95% CI 1.1, 3.4) lower (worse mental functioning) than the respective score without CHD. Compared with not having CHD, a diagnosis of that condition was not associated with any difference in mental functioning even before adjusting for covariates. Point estimates show that respondents with an indication of CHD had lower mental functioning than those diagnosed with the condition, although the 95% CIs of the adjusted mean differences overlap. Compared with not having CHD, mean HRQoL was lower among those with an indication of CHD, and lower still for those with a diagnosis, with only the difference for those with a diagnosis statistically significant at the 0.05 level.

Compared with not having CHD, an indication of the condition and a diagnosis of it were each associated with more outpatient visits and higher OOP spending on healthcare, on average. Those diagnosed with CHD also had more inpatient admissions, on average. After adjustment, an indication of CHD was estimated to be associated with 2.1 (95% CI 0.8, 3.4) more outpatient visits per annum and $29.08 (95% CI -$1.49, $59.64) higher OOP spending per annum than the respective means for those without CHD. After adjustment, only mean inpatient admissions remained significantly higher for those with a CHD diagnosis than for those without the condition (0.18, 95% CI 0.03, 0.34), with no significant differences seen in outpatient visits and OOP spending.

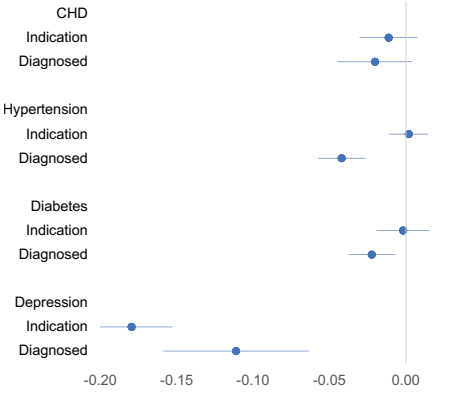
An indication of hypertension and an indication of diabetes were both associated with lower mean PCS scores and HRQoL compared with not having the respective condition. After adjustment for covariates, these differences were not statistically significant, while diagnosed hypertension and diagnosed diabetes were associated with lower PCS scores (hypertension 3.15 95% CI 2.46, 3.84; diabetes 1.53 95% 0.86, 2.21) and HRQoL (hypertension 0.04 95% CI 0.03, 0.06; diabetes 0.02 95% CI, 0.01, 0.04), and with more outpatient visits (hypertension

***Figure 1 Adjusted differences in mean health and healthcare outcomes between indication or diagnosis and absence of each chronic condition***

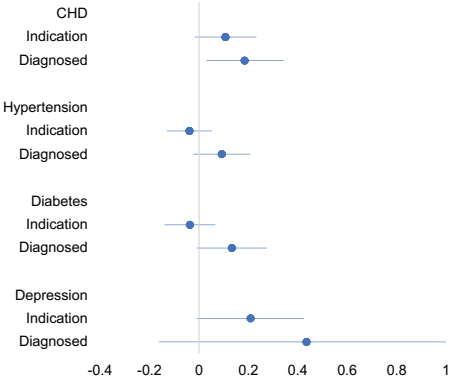


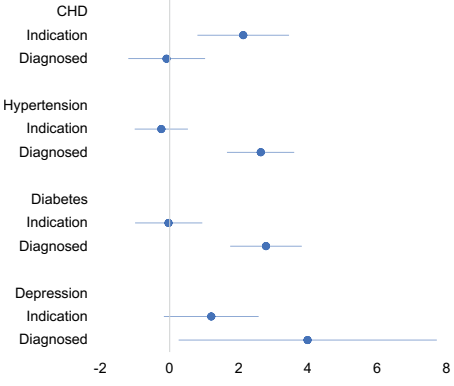

C HRQoL




D Inpatient visits (annual)




E Outpatient visits (annual)




F Out-of-pocket spending (USD/year)

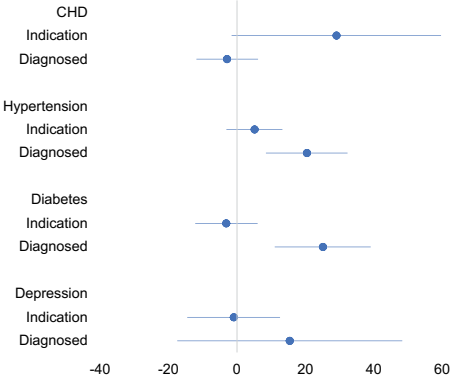


*Table 3 Mean health and healthcare outcomes by indication and diagnosis of chronic conditions*

| | Health functioning (SF-12) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Physical (95% CI) | | Mental (95% CI) | | HRQoL (95% CI) | | Inpatient visits (95% CI) | | Outpatient visits (95% CI) | | OOP spending, USD (95% CI) | |
| All | 48.93 (48.60, 49.25) | | 50.39 (50.05, 50.73) | | 0.87 (0.86, 0.87) | | 0.23 (0.19, 0.27) | | 4.95 (4.52, 5.37) | | 17.52 (14.50, 20.54) | |
| CHD | | | | | | | | | | | | |
| No condition | 49.44 (49.12, 49.76) | | 50.57 (50.23, 50.92) | | 0.87 (0.87, 0.88) | | 0.21 (0.17, 0.25) | | 4.67 (4.24, 5.11) | | 15.70 (12.63, 18.78) | |
| Indicated | 45.88 (44.52, 47.24) | *** | 47.44 (46.00, 48.88) | *** | 0.83 (0.81, 0.86) | ** | 0.24 (0.17, 0.32) | | 7.85 (5.77, 9.93) | *** | 35.15 (16.68, 53.62) | ** |
| Diagnosed | 41.37 (39.58, 43.16) | *** | 50.54 (48.86, 52.21) | | 0.75 (0.71, 0.79) | *** | 0.61 (0.38, 0.84) | *** | 6.98 (5.35, 8.61) | ** | 33.76 (15.81, 51.70) | ** |
| Hypertension | | | | | | | | | | | | |
| No condition | 50.44 (50.13, 50.75) | | 50.37 (49.97, 50.78) | | 0.89 (0.89, 0.90) | | 0.20 (0.15, 0.25) | | 4.26 (3.77, 4.75) | | 12.09 (9.02, 15.15) | |
| Indicated | 48.77 (48.01, 49.53) | *** | 50.58 (49.79, 51.36) | | 0.86 (0.84, 0.88) | *** | 0.17 (0.11, 0.23) | | 4.27 (3.33, 5.20) | | 17.33 (8.42, 26.24) | |
| Diagnosed | 42.66 (41.86, 43.46) | *** | 50.33 (49.64, 51.01) | | 0.76 (0.74, 0.78) | *** | 0.39 (0.29, 0.50) | *** | 8.35 (7.32, 9.38) | *** | 40.59 (28.13, 53.06) | *** |
| Diabetes | | | | | | | | | | | | |
| No condition | 49.81 (49.50, 50.12) | | 50.37 (50.03, 50.72) | | 0.88 (0.88, 0.89) | | 0.19 (0.16, 0.22) | | 4.37 (3.94, 4.79) | | 13.32 (10.41, 16.23) | |
| Indicated | 48.39 (47.32, 49.46) | * | 50.77 (49.85, 51.69) | | 0.85 (0.83, 0.87) | ** | 0.17 (0.08, 0.25) | | 4.48 (3.27, 5.69) | | 13.97 (1.86, 26.07) | |

| | Health functioning (SF-12) | | | | HRQoL (95% CI) | | Inpatient visits (95% CI) | | Outpatient visits (95% CI) | | OOP spending, USD (95% CI) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Physical (95% CI) | | Mental (95% CI) | | | | | | | | | |
| Diagnosed | 44.03 (43.15, 44.91) | *** | 50.29 (49.38, 51.19) | | 0.78 (0.76, 0.80) | *** | 0.47 (0.23, 0.71) | ** | 8.58 (7.19, 9.96) | *** | 43.97 (29.22, 58.71) | *** |
| Depression | | | | | | | | | | | | |
| No condition | 49.36 (49.06, 49.66) | | 50.81 (50.46, 51.17) | | 0.88 (0.87, 0.89) | | 0.20 (0.17, 0.24) | | 4.82 (4.40, 5.24) | | 16.72 (13.85, 19.60) | |
| Indicated | 40.62 (38.72, 42.51) | *** | 43.93 (42.02, 45.85) | *** | 0.64 (0.61, 0.68) | *** | 0.71 (0.21, 1.21) | ** | 7.12 (5.30, 8.94) | ** | 26.75 (-2.16, 55.65) | |
| Diagnosed | 42.96 (39.08, 46.83) | ** | 37.18 (34.16, 40.20) | *** | 0.70 (0.63, 0.78) | *** | 0.36 (0.01, 0.70) | | 7.51 (4.15, 10.86) | | 55.37 (-7.61, 118.35) | * |

**Notes:** Statistical significance when comparing to mean of no condition denoted by *** p<0.001, ** p<0.01, *p<0.05. Mean values calculated on weighted, imputed data (N=6,665). HRQoL is health-related quality of life, calculated using utility values obtained from responses to the EQ-5D-5L questionnaire.

2.63 95% CI 1.67, 3.60; diabetes 2.79 95% 1.75, 3.82) and OOP spending (hypertension $20.42 95% CI $8.59, $32.26; diabetes $25.10, 95% CI $11.15, $39.05), on average, compared with not having the respective conditions.

Mean PCS, MCS, and HRQoL scores were all significantly lower both for people with an indication of depression and for those diagnosed with depression than for those without depression. This was true without and with adjustment for covariates. Both unadjusted and adjusted estimates indicate that those with an indication of depression and those diagnosed with the condition had similar mean PCS and HRQoL scores. After adjustment, diagnosed depression was associated with a mean MCS score that was 12.58 points (95% CI 9.59, 15.58) lower than the mean for those with no depression, while those with an indication of depression also had a lower MCS score, though half as large in magnitude (6.70, 95% CI 5.43, 7.97).

Adding BMI as an additional covariate in the multivariate models had little impact on the magnitude and significance of the estimates of the partial associations of the outcomes with both an indication of each condition and its diagnosis (Appendix Table S4). Complete case analysis yielded partial associations of similar direction, magnitude, and significance as those estimated using the multiply-imputed dataset (Appendix Table S5).

## 4.4 DISCUSSION

In LMICs, high prevalence of undiagnosed chronic conditions (3-6, 12), particularly cardiovascular disease risk factors, has rightly aroused concern about an iceberg of NCD that could strain health systems ill-prepared to respond to a double burden of disease (46). These concerns motivate a push for earlier diagnosis of chronic conditions, which could well be a health system priority. Assessment of the likely consequences of such a policy requires better evidence on the health and healthcare utilization of people with an indication but not a diagnosis of chronic conditions. If they have poor health and make heavy use of healthcare, then diagnosis, and consequent treatment, may bring immediate improvement in health while straining a health system less than would be the case if the newly diagnosed were previously light users of healthcare.

This study of a representative sample of the adult population of Sri Lanka revealed heterogeneity by type of chronic condition in the health and healthcare utilization of those with an indication but not a diagnosis of a condition. We found that having an indication but not a diagnosis of either CHD or depression – both symptomatic conditions – was associated with worse physical and mental health functioning and, for depression, worse HRQoL, after adjustment for age, ethnicity, education, sector and province of residence, wealth quintile, household size and composition and the other chronic conditions of interest. Point estimates suggest that

indications of these two conditions may also be associated with greater utilization of healthcare and higher OOP medical spending, although most of these estimates do not reach conventional levels of statistical significance after adjustment. In contrast, having an indication but not a diagnosis of either hypertension or diabetes – two conditions that can remain asymptomatic for some time – was not partially associated with worse health functioning and HRQoL, nor with higher healthcare utilization and OOP spending, after adjustment. These findings suggest that the health, healthcare, and economic burdens of undiagnosed chronic conditions may well depend, as would be logical, on the degree to which any condition is symptomatic. Those suffering symptoms of an undiagnosed condition may seek relief through medical treatment. Asymptomatic conditions would not be expected to induce the same loss of health and level of healthcare seeking.

We found that for each of CHD and depression, the likelihood of being diagnosed was lower than the likelihood of having an undiagnosed indication, while the opposite was true for hypertension and diabetes. This discrepancy may be partly due to the relatively higher cost and complexity of diagnosing the first two conditions. Health system constraints may slow the diagnosis of CHD and depression, which may partly explain the lower functioning and HRQoL of people with undiagnosed indications of these conditions. Less technology and skills are required to diagnose hypertension and diabetes, which may contribute to quicker diagnosis and less health impact among those not yet diagnosed.

We found that people with an indication of CHD had similar limitations in physical functioning and more limitations in mental functioning than people diagnosed with CHD, after adjustment. We estimated that an indication of CHD was associated with lower physical and mental functioning equal in magnitude to about 4–5% in the respective score. An indication of CHD was estimated to be associated with at least two outpatient visits per year more than the average with no indication of CHD after adjustment – a 46% increase. The absolute increase in the number of outpatient visits was similar to that associated with being diagnosed with CHD without adjustment. This is similar to findings in Indonesia, where people with undiagnosed "heart problems" had an additional 1.9 outpatient visits per year than those who did not have heart problems (22). After adjusting for covariates, we found that OOP spending of those with an indication of CHD was almost 85 percent higher than those with no indication of CHD, on average. As a result of these increases, the utilization of outpatient care and the OOP spending of people with an indication of CHD were similar to the average levels of those with diagnosed CHD, hypertension, and diabetes. In Indonesia, people with undiagnosed heart problems did report higher outpatient and inpatient medical expenses, though this was not statistically significant, but they also reported higher expenditures on self-treatment (22). The findings in Sri Lanka suggest that targeting people with an indication of CHD but not yet diagnosed should be prioritized given health and healthcare outcomes that are on par with

people already diagnosed with CHD risk factors. For hypertension and diabetes, screening to identify people with indications of these conditions can still be worthwhile to reverse or slow progression to worse outcomes observed among those who are eventually diagnosed (47).

After adjusting for covariates, we found that the lower levels of physical functioning and HRQoL associated with an indication of depression were as large as the respective reductions associated with diagnosed depression. As would be expected, an indication of depression was associated with a reduction in mental functioning that was a little more than half the magnitude of the reduction associated with diagnosed depression. However, on average, those with an indication of depression scored 13 percent lower in mental functioning than those with no indication of depression after full adjustment. These findings suggest that people with symptoms of depression experience substantial losses of health and related quality of life that, with the exception of mental functioning, were similar to those experienced by those diagnosed with depression. There were similarities with findings in Japan, where people with undiagnosed depression had lower physical and mental functioning than those without depression, and similar to those with diagnosed depression (25). The fact that reductions in health and quality of life associated with an indication of depression were substantially larger than those estimated for an indication of CHD gives further reason to increase efforts to identify Sri Lankans living with undiagnosed depression.

We found that indications of hypertension and diabetes were not associated with worse health and greater healthcare utilization, while these outcomes were associated with diagnosed hypertension and diabetes. These findings are consistent with evidence from Indonesia showing that outpatient use and OOP spending were higher for people with self-reported hypertension and diabetes but these outcomes were not higher for people with undiagnosed hypertension and diabetes (22). Our estimates are also consistent with other evidence that people with undiagnosed hypertension report better physical health than people diagnosed with the condition (24, 48). There are several potential explanations for these consistencies. First, people who are undiagnosed may have had the condition for a shorter period and are less likely to be symptomatic, and so may not have experienced a loss of health which would also cause their demand for healthcare to increase (22). Second, the association of diagnosed diabetes and hypertension with more outpatient visits and OOP spending is expected as these people should have had regular followup visits to manage their condition, while people with indications of diabetes and hypertension may not have sought additional healthcare as they had no perceived requirement. Lastly, among those with indications of hypertension and diabetes based on measurements taken in a single encounter, there are likely to be many false positives (22). As with awareness-treatment-control studies of hypertension and diabetes, there is a risk of misclassifying individuals without these conditions as having an indication of them. This

would dilute associations between true indications of hypertension or diabetes and health and healthcare outcomes.

There were several limitations in our study. Due to the nature of the field survey, we were limited to one measurement of biomarkers. The biomarkers used to define diabetes in this study were likely to be more precise than the symptomatic criteria used in a related study (22). Furthermore, single biomarker measurements for hypertension and diabetes are commonly used in cascades of care studies to assess the performance of healthcare systems (4, 49).

To identify undiagnosed heart problems (22) and depression (25), we used methods that are commonly used to estimate the prevalence of these conditions. While an indication of a chronic condition is often used to identify undiagnosed cases (22, 24, 25), there is variation in the positive predictive values of the indicator tools. Nevertheless, our study suggests, at the very least, that people with symptoms that are indicative of CHD and depression were likely to experience poorer health and healthcare outcomes than those without indications of these conditions. We did not assess whether the duration since diagnosis was associated with worse outcomes.

The algorithm used to calculate physical and mental health functioning scores has been validated in several other countries (50) but not in Sri Lanka. For comparisons within a country, it is expected that the US-based algorithm will provide similar results to a country-derived one (51), although we cannot be sure of this.

## 4.5 CONCLUSIONS

Undiagnosed people with indications of symptomatic conditions like CHD and depression, are likely to have poorer health and use more healthcare than people without these conditions. Outcomes can even be worse for the undiagnosed than for the diagnosed. This suggests that management of people with indications of CHD and depression should be prioritized as the burden of these undiagnosed conditions was almost as high as it was for those diagnosed with these conditions. Getting these people diagnosed and onto effective disease management programmes that pay attention to follow-up and treatment compliance may not raise demands on health systems by so much since the undiagnosed are already heavy users of healthcare. In contrast, people with indications of typically asymptomatic conditions like hypertension and diabetes, show similar outcomes to those without these conditions. Here, diagnosis and effective management and control could still generate important health benefits by slowing disease progression.

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# APPENDIX

## Text A1 Estimation of household socioeconomic status using principal components analysis

The SLHAS Wave 1 uses an asset index approach to generate a proxy measure of each household's living standard. The index was computed by using principal components analysis (PCA) of a set of householdlevel variables relating to asset ownership or household characteristics. Variables were selected from those used in recent Sri Lanka Household Income and Expenditure Surveys conducted by the Department of Census and Statistics, selecting those with most predictive performance, and excluding some assets that are only relevant to agricultural households (e.g., tractor, thresher, fishing equipment). Variables were either dichotomous (e.g., household has a car) or categorical (e.g., type of drinking water source), apart from one ordinal variable (number of bedrooms). Dichotomous variables consisted of whether the household possessed each of the following items: radio/cassette player, television, VCD/DVD player, washing machine, fridge, electric fan, domestic phone, mobile phone, computer, internet access, camera/video camera, bicycle, motorcycle/scooter, three-wheeler, motor car/van, and bus/lorry/tipper.

Categorical variables were transformed into dichotomous indicators by creating separate dummy variables for each category. They consisted of the following (numbers in parentheses indicates number of categories in each): flooring material (5), material of wall (7), type of housing tenure (12), drinking water source (16), type of toilet (4), method of household garbage disposal (6), lighting power source (5), cooking fuel (13), and type of cooking place (3).

There was a small percentage of missing values in each variable (2–3%). These were imputed with either the PSU or stratum level mean of the variable or failing those the district/sector or national means. The principal component factor or index obtained by PCA after combining all these variables was then used to divide the sample into population weighted quantiles of equal size. Separate indices were not estimated for urban or rural sectors, but analysis indicates little difference between sectors in how the national index performs.

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Rannan-Eliya RP, Wijemunige N, Perera P, Kapuge Y, Gunawardana N, Sigera C, Jayatissa R, Herath HM, Gamage A, Weerawardena N, Sivagnanam I. Prevalence of diabetes and prediabetes in Sri Lanka: a new global hotspot–estimates from the Sri Lanka Health and Ageing Survey 2018/2019. BMJ Open Diabetes Research and Care. 2023 Feb 1;11(1):e003160.

## Text A2 Multiple imputation method

We used the mi impute family of functions in Stata to impute data. First, with registered variables with no missing values as "regular" variables: namely, participant age, sex, socioeconomic quintile, sector and district of residence, and ethnicity. Next, we registered variables of interest that had missing values as "imputed variables", including inpatient and outpatient visits (annualized), recall period of inpatient and outpatient visits, out-of-pocket expenditures, household size, number of people in the household below 15 and above 60, body mass index, smoking status, physical component score, mental component score, utility value, diagnosis status of CHD, hypertension, diabetes and depression. Multiple imputation was performed with chained equations (mi impute chained) and predictive mean matching (pmm) using 10 nearest neighbors (kn(10)).

***Table A1 Complete case and imputed sample characteristics***

| | **Complete case, unweighted (*N*=6,137)** | | **Imputed, unweighted (*N*=6,665)** | |
|---|---|---|---|---|
| | **n / mean** | **% / SD** | **n / mean** | **% / SD** |
| Age, mean (SD) | 49.8 | 17.2 | 50.1 | 17.2 |
| Sex | | | | |
| Male | 3,019 | 49.2 | 3,268 | 49.0 |
| Female | 3,118 | 50.8 | 3,397 | 51.0 |
| Ethnicity | | | | |
| Sinhala | 4,324 | 70.5 | 4,707 | 70.6 |
| Tamil | 1,384 | 22.6 | 1,504 | 22.6 |
| Muslim | 403 | 6.6 | 428 | 6.4 |
| Other | 26 | 0.4 | 26 | 0.4 |
| Education | | | | |
| No formal schooling | 227 | 3.7 | 258 | 3.9 |
| Primary educated | 847 | 13.8 | 937 | 14.1 |
| Secondary educated | 4,812 | 78.4 | 5,199 | 78.0 |
| Tertiary educated | 251 | 4.1 | 272 | 4.1 |
| Sector | | | | |
| Urban | 1,840 | 30.0 | 2,024 | 30.4 |
| Rural | 3,395 | 55.3 | 3,661 | 54.9 |
| Estate | 165 | 2.7 | 170 | 2.6 |
| Rural/Estate | 737 | 12.0 | 810 | 12.2 |
| Province | | | | |
| Western | 1,284 | 20.9 | 1,435 | 21.5 |
| Central | 886 | 14.4 | 976 | 14.6 |
| Southern | 788 | 12.8 | 851 | 12.8 |
| Northern | 644 | 10.5 | 691 | 10.4 |
| Eastern | 527 | 8.6 | 553 | 8.3 |

| | Complete case, unweighted (*N*=6,137) | | Imputed, unweighted (*N*=6,665) | |
|---|---|---|---|---|
| | **n / mean** | **% / SD** | **n / mean** | **% / SD** |
| North-Western | 523 | 8.5 | 548 | 8.2 |
| North-Central | 446 | 7.3 | 477 | 7.2 |
| Uva | 433 | 7.1 | 467 | 7.0 |
| Sabaragamuwa | 606 | 9.9 | 667 | 10.0 |
| | | | | |
| SES quintile | | | | |
| Poorest | 1,457 | 23.7 | 1,568 | 23.5 |
| Poorer | 1,221 | 19.9 | 1,328 | 19.9 |
| Middle | 1,131 | 18.4 | 1,245 | 18.7 |
| Richer | 1,110 | 18.1 | 1,220 | 18.3 |
| Richest | 1,218 | 19.8 | 1,304 | 19.6 |
| | | | | |
| Household size, mean (SD) | 2.98 | 1.4 | 2.98 | 1.4 |
| Proportion below 15, mean (SD) | 0.07 | 0.16 | 0.07 | 0.16 |
| Proportion above 60, mean (SD) | 0.22 | 0.33 | 0.23 | 0.33 |

***Table A2 Contingency table showing percentage (95% confidence interval) of people with comorbid conditions for each chronic condition state of CHD, hypertension, diabetes and depression***

| | Comorbid condition, % (95% CI) | | | |
|---|---|---|---|---|
| | **CHD** | **Hypertension** | **Diabetes** | **Depression** |
| CHD | - | 52.0 (47.0, 57.1) | 32.7 (27.6, 37.7) | 12.1 (8.9, 15.3) |
| Hypertension | 16.9 (15.1, 18.7) | - | 37.6 (34.8, 40.5) | 7.4 (6.1, 8.7) |
| Diabetes | 15.1 (12.9, 17.4) | 53.8 (50.3, 57.3) | - | 8.2 (6.4, 9.9) |
| Depression | 22.3 (16.6, 27.9) | 42.2 (35.0, 49.4) | 32.5 (25.7, 39.4) | - |
| Full sample | 9.6 (8.7, 10.6) | 29.7 (28.1, 31.3) | 20.8 (19.4, 22.2) | 5.2 (4.5, 5.9) |

**Notes:** Analysis on weighted, imputed data (N=6,665). 16.9% of people with hypertension have CHD, while 52.0% of people with CHD have hypertension. There are slight variations compared to prevalence estimates published individually for hypertension and diabetes given methodological differences in weighting for the full sample and use of imputed data.

*Table A3 Adjusted differences in mean health and healthcare outcomes between indication/diagnosis and absence of each chronic condition*

| | Health functioning (SF-12) | | | | HRQoL | | Inpatient visits | | Outpatient | | OOP spending, | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Physical (95% CI) | | Mental (95% CI) | | (95% CI) | | (95% CI) | | visits (95% CI) | | USD (95% CI) | |
| CHD (Ref: No condition) | | | | | | | | | | | | |
| Indicated | -2.65 (-3.66, -1.63) | *** | -2.25 (-3.38, -1.12) | *** | -0.01 (-0.03, 0.01) | | 0.11 (-0.02, 0.23) | | 2.13 (0.81, 3.44) | ** | 29.08 (-1.49, 59.64) | |
| Diagnosed | -2.66 (-3.82, -1.49) | *** | -0.55 (-1.68, 0.58) | | -0.02 (-0.04, 0.00) | * | 0.18 (0.03, 0.34) | * | -0.09 (-1.19, 1.02) | | -2.87 (-11.80, 6.07) | |
| Hypertension (Ref: No condition) | | | | | | | | | | | | |
| Indicated | -0.05 (-0.66, 0.55) | | -0.49 (-1.15, 0.16) | | 0.00 (-0.01, 0.01) | | -0.04 (-0.13, 0.05) | | -0.24 (-1.00, 0.52) | | 5.10 (-3.03, 13.23) | |
| Diagnosed | -3.15 (-3.84, -2.46) | *** | -0.24 (-0.93, 0.46) | | -0.04 (-0.06, -0.03) | *** | 0.09 (-0.02, 0.21) | | 2.63 (1.67, 3.60) | *** | 20.42 (8.59, 32.26) | ** |
| Diabetes (Ref: No condition) | | | | | | | | | | | | |
| Indicated | 0.11 (-0.66, 0.88) | | 0.38 (-0.50, 1.25) | | 0.00 (-0.02, 0.01) | | -0.04 (-0.14, 0.06) | | -0.03 (-0.99, 0.94) | | -3.11 (-12.17, 5.95) | |
| Diagnosed | -1.53 (-2.21, -0.86) | *** | -0.29 (-0.98, 0.41) | | -0.02 (-0.04, -0.01) | ** | 0.13 (-0.01, 0.27) | | 2.79 (1.75, 3.82) | *** | 25.10 (11.15, 39.05) | *** |
| Depression (Ref: No condition) | | | | | | | | | | | | |
| Indicated | -5.78 (-6.91, -4.64) | *** | -6.70 (-7.97, -5.43) | *** | -0.18 (-0.20, -0.16) | *** | 0.21 (-0.01, 0.42) | | 1.20 (-0.16, 2.57) | | -0.96 (-14.43, 12.51) | |
| Diagnosed | -4.79 (-7.30, -2.27) | *** | -12.58 (-15.58, -9.59) | *** | -0.11 (-0.16, -0.07) | *** | 0.44 (-0.16, 1.03) | | 3.99 (0.27, 7.71) | * | 15.43 (-17.39, 48.24) | |

**Notes:** Each column shows an outcome of interest. These models control for demographic features – age, sex, ethnicity, education, sector, province, socioeconomic quintile, household composition – and each chronic condition state (no condition, indication of condition, diagnosed condition). The statistical significance of the AME compared to no condition (indication vs no condition; diagnosed vs no condition) is denoted by *** p<0.001, ** p<0.01, * p<0.05. Analyses is on unweighted, imputed data (N=6,665). HRQoL is health-related quality of life, calculated using utility values obtained from responses to the EQ-5D-5L questionnaire.

| | Health functioning (SF-12) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Physical (95% CI) | | Mental (95% CI) | | HRQoL (95% CI) | | Inpatient visits (95% CI) | | Outpatient visits (95% CI) | | OOP spending, USD (95% CI) | |
| CHD (Ref: No condition) | | | | | | | | | | | | |
| Indication | -2.69 (-3.71, -1.67) | *** | -2.24 (-3.37, -1.11) | *** | -0.01 (-0.03, 0.01) | | 0.11 (-0.02, 0.23) | | 2.13 (0.81, 3.45) | ** | 29.81 (-0.41, 60.03) | |
| Diagnosed | -2.63 (-3.79, -1.47) | *** | -0.55 (-1.69, 0.58) | | -0.02 (-0.04, 0.00) | | 0.19 (0.03, 0.34) | * | -0.07 (-1.17, 1.04) | | -3.12 (-12.00, 5.75) | |
| Hypertension (Ref: No condition) | | | | | | | | | | | | |
| Indication | 0.10 (-0.51, 0.70) | | -0.54 (-1.20, 0.12) | | 0.01 (-0.01, 0.02) | | -0.04 (-0.13, 0.05) | | -0.25 (-1.01, 0.51) | | 4.21 (-3.83, 12.24) | |
| Diagnosed | -2.98 (-3.67, -2.29) | *** | -0.29 (-0.98, 0.41) | | -0.04 (-0.05, -0.02) | *** | 0.10 (-0.02, 0.21) | | 2.61 (1.64, 3.58) | *** | 18.49 (7.65, 29.34) | ** |
| Diabetes (Ref: No condition) | | | | | | | | | | | | |
| Indication | 0.27 (-0.51, 1.05) | | 0.33 (-0.55, 1.21) | | 0.00 (-0.01, 0.02) | | -0.03 (-0.14, 0.07) | | -0.01 (-0.98, 0.96) | | -3.99 (-12.69, 4.70) | |
| Diagnosed | -1.54 (-2.21, -0.86) | *** | -0.28 (-0.97, 0.41) | | -0.02 (-0.03, -0.01) | ** | 0.14 (-0.01, 0.28) | | 2.82 (1.78, 3.85) | *** | 24.94 (11.35, 38.52) | *** |
| Depression (Ref: No condition) | | | | | | | | | | | | |
| Indication | -5.75 (-6.89, -4.62) | *** | -6.71 (-7.98, -5.44) | *** | -0.18 (-0.20, -0.16) | *** | 0.20 (-0.01, 0.42) | | 1.18 (-0.18, 2.54) | | -1.37 (-14.17, 11.43) | |
| Diagnosed | -4.78 (-7.28, -2.27) | *** | -12.58 (-15.58, -9.59) | *** | -0.11 (-0.16, -0.07) | *** | 0.42 (-0.17, 1.01) | | 4.10 (0.34, 7.86) | * | 14.83 (-16.95, 46.61) | |
| BMI category (Ref: Normal) | | | | | | | | | | | | |
| Overweight | -0.55 (-1.04, -0.05) | * | 0.13 (-0.40, 0.66) | | -0.02 (-0.03, -0.01) | ** | -0.04 (-0.12, 0.04) | | -0.25 (-0.92, 0.41) | | 9.63 (0.93, 18.32) | * |
| Obese | -1.93 (-2.70, -1.16) | *** | 0.62 (-0.21, 1.45) | | -0.06 (-0.08, -0.05) | *** | 0.02 (-0.12, 0.17) | | 0.48 (-0.64, 1.61) | | 13.17 (-0.53, 26.86) | |

**Notes:** Each column shows an outcome of interest. These models use the same covariates as in Table S3, with additional control for body mass index (BMI) categories (normal<25kg/$m^2$, overweight 25-29.9kg/$m^2$, obese≥30kg/$m^2$). The statistical significance of the AME compared to no condition (indication vs no condition; diagnosed vs no condition) is denoted by *** p<0.001, ** p<0.01, * p<0.05. Analyses is on unweighted, imputed data (N=6,665). HRQoL is health-related quality of life, calculated using utility values obtained from responses to the EQ-5D-5L questionnaire.

*Table A4 Average marginal effects of chronic condition states on outcome variables, controlling for BMI*

| | Health functioning (SF-12) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Physical (95% CI) | | Mental (95% CI) | | HRQoL (95% CI) | | Inpatient visits (95% CI) | | Outpatient visits (95% CI) | | OOP spending, USD (95% CI) | |
| CHD (Ref: No condition) | | | | | | | | | | | | |
| Indication | -2.69 (-3.71, -1.67) | *** | -2.24 (-3.37, -1.11) | *** | -0.01 (-0.03, 0.01) | | 0.11 (-0.02, 0.23) | | 2.13 (0.81, 3.45) | ** | 29.81 (-0.41, 60.03) | |
| Diagnosed | -2.63 (-3.79, -1.47) | *** | -0.55 (-1.69, 0.58) | | -0.02 (-0.04, 0.00) | | 0.19 (0.03, 0.34) | * | -0.07 (-1.17, 1.04) | | -3.12 (-12.00, 5.75) | |
| Hypertension (Ref: No condition) | | | | | | | | | | | | |
| Indication | 0.10 (-0.51, 0.70) | | -0.54 (-1.20, 0.12) | | 0.01 (-0.01, 0.02) | | -0.04 (-0.13, 0.05) | | -0.25 (-1.01, 0.51) | | 4.21 (-3.83, 12.24) | |
| Diagnosed | -2.98 (-3.67, -2.29) | *** | -0.29 (-0.98, 0.41) | | -0.04 (-0.05, -0.02) | *** | 0.10 (-0.02, 0.21) | | 2.61 (1.64, 3.58) | *** | 18.49 (7.65, 29.34) | ** |
| Diabetes (Ref: No condition) | | | | | | | | | | | | |
| Indication | 0.27 (-0.51, 1.05) | | 0.33 (-0.55, 1.21) | | 0.00 (-0.01, 0.02) | | -0.03 (-0.14, 0.07) | | -0.01 (-0.98, 0.96) | | -3.99 (-12.69, 4.70) | |
| Diagnosed | -1.54 (-2.21, -0.86) | *** | -0.28 (-0.97, 0.41) | | -0.02 (-0.03, -0.01) | ** | 0.14 (-0.01, 0.28) | | 2.82 (1.78, 3.85) | *** | 24.94 (11.35, 38.52) | *** |
| Depression (Ref: No condition) | | | | | | | | | | | | |
| Indication | -5.75 (-6.89, -4.62) | *** | -6.71 (-7.98, -5.44) | *** | -0.18 (-0.20, -0.16) | *** | 0.20 (-0.01, 0.42) | | 1.18 (-0.18, 2.54) | | -1.37 (-14.17, 11.43) | |
| Diagnosed | -4.78 (-7.28, -2.27) | *** | -12.58 (-15.58, -9.59) | *** | -0.11 (-0.16, -0.07) | *** | 0.42 (-0.17, 1.01) | | 4.10 (0.34, 7.86) | * | 14.83 (-16.95, 46.61) | |
| BMI category (Ref: Normal) | | | | | | | | | | | | |
| Overweight | -0.55 (-1.04, -0.05) | * | 0.13 (-0.40, 0.66) | | -0.02 (-0.03, -0.01) | ** | -0.04 (-0.12, 0.04) | | -0.25 (-0.92, 0.41) | | 9.63 (0.93, 18.32) | * |
| Obese | -1.93 (-2.70, -1.16) | *** | 0.62 (-0.21, 1.45) | | -0.06 (-0.08, -0.05) | *** | 0.02 (-0.12, 0.17) | | 0.48 (-0.64, 1.61) | | 13.17 (-0.53, 26.86) | |

**Notes:** Each column shows an outcome of interest. These models use the same covariates as in Table S3, with additional control for body mass index (BMI) categories (normal <25 kg/m2, overweight 25-29.9 kg/m2, obese ≥ 30 kg/m2). The statistical significance of the AME compared to no condition (indication vs no condition; diagnosed vs no condition) is denoted by *** p<0.001, ** p<0.01, * p<0.05. Analyses is on unweighted, imputed data (N=6,665). HRQoL is health-related quality of life, calculated using utility values obtained from responses to the EQ-5D-5L questionnaire.

*Table A5 Average marginal effects of chronic condition states on outcome variables, using complete case analysis*

| | Health functioning (SF-12) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Physical (95% CI)** | | **Mental (95% CI)** | | **HRQoL (95% CI)** | | **Inpatient visits (95% CI)** | | **Outpatient visits (95% CI)** | | **OOP spending, USD (95% CI)** | |
| | *N = 6,313* | | *N = 6,313* | | *N = 6,350* | | *N = 6,411* | | *N = 6,432* | | *N = 6,443* | |
| CHD (Ref: No condition) | | | | | | | | | | | | |
| Indication | -2.67 (-3.69, -1.65) | *** | -2.35 (-3.49, -1.21) | *** | -0.01 (-0.03, 0.01) | | 0.11 (-0.01, 0.23) | | 2.16 (0.83, 3.48) | ** | 30.26 (-0.95, 61.46) | |
| Diagnosed | -2.55 (-3.71, -1.39) | *** | -0.44 (-1.58, 0.70) | | -0.02 (-0.04, 0.00) | * | 0.18 (0.03, 0.32) | * | -0.11 (-1.22, 1.00) | | -3.02 (-11.92, 5.89) | |
| Hypertension (Ref: No condition) | | | | | | | | | | | | |
| Indication | -0.03 (-0.64, 0.59) | | -0.56 (-1.22, 0.09) | | 0.00 (-0.01, 0.01) | | -0.04 (-0.13, 0.05) | | -0.31 (-1.06, 0.44) | | 4.78 (-3.02, 12.58) | |
| Diagnosed | -3.21 (-3.90, -2.52) | *** | -0.33 (-1.02, 0.37) | | -0.04 (-0.06, -0.03) | *** | 0.10 (-0.02, 0.21) | | 2.63 (1.66, 3.59) | *** | 19.99 (8.45, 31.52) | *** |
| Diabetes (Ref: No condition) | | | | | | | | | | | | |
| Indication | 0.14 (-0.62, 0.90) | | 0.42 (-0.46, 1.29) | | 0.00 (-0.02, 0.02) | | -0.04 (-0.14, 0.06) | | -0.10 (-1.04, 0.83) | | -3.24 (-12.30, 5.82) | |
| Diagnosed | -1.54 (-2.22, -0.86) | *** | -0.24 (-0.94, 0.45) | | -0.02 (-0.04, -0.01) | ** | 0.13 (-0.01, 0.27) | | 2.76 (1.73, 3.79) | *** | 25.25 (11.10, 39.39) | *** |
| Depression (Ref: No condition) | | | | | | | | | | | | |
| Indication | -5.74 (-6.88, -4.60) | *** | -6.77 (-8.03, -5.51) | *** | -0.18 (-0.21, -0.15) | *** | 0.21 (0.00, 0.42) | | 1.15 (-0.21, 2.52) | | -1.70 (-13.56, 10.17) | |
| Diagnosed | -4.63 (-7.11, -2.15) | *** | -12.62 (-15.59, -9.65) | *** | -0.11 (-0.15, -0.07) | *** | 0.44 (-0.16, 1.05) | | 3.93 (0.22, 7.65) | * | 15.49 (-17.58, 48.56) | |

**Notes:** Each column shows an outcome of interest. These models use the same covariates as Table S3, however analyses is on (unweighted) non-imputed data. The statistical significance of the AME compared to no condition (indication vs no condition; diagnosed vs no condition) is denoted by *** p<0.001, ** p<0.01, * p<0.05. HRQoL is health-related quality of life, calculated using utility values obtained from responses to the EQ-5D-5L questionnaire.

# Chapter 5

# Optimizing cardiovascular disease risk screening in a low-resource setting: cost-effectiveness of program modifications in Sri Lanka modelled with nationally representative survey data

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# ABSTRACT


## Background

While screening for cardiovascular disease (CVD) risk can help low-resource health systems deliver low-cost, effective prevention, evidence is needed to adapt international screening guidelines for maximal impact in local settings. We aimed to establish how the cost-effectiveness of CVD risk screening in Sri Lanka varies with who is screened, how risk is assessed, and what thresholds are used for prescription of medicines.

## Methods

We used data for people aged 35 years and over from a 2018/19 nationally representative survey in Sri Lanka. We modelled the costs and quality adjusted life years (QALYs) for 128 screening program scenarios distinguished by a) age group screened, b) risk tool used, c) definition of high CVD risk, d) blood pressure threshold for treatment of high-risks, and e) prescription of statins to all diabetics. We used the current program as the base case. We used a Markov model of a one-year screening program with a lifetime horizon and a public health system perspective.

## Results

Scenarios that included the WHO-2019 office-based risk tool dominated most others. Switching to this tool and raising the age threshold for screening from 35 to 40 years gave an incremental cost-effectiveness ratio (ICER) of $113/QALY. Lowering the CVD high-risk threshold from 20% to 10% and prescribing antihypertensives at a lower threshold to diabetics and people at high risk of CVD gave an ICER of $2,090/QALY. The findings were sensitive to allowing for disutility of daily medication.

## Conclusions

In Sri Lanka, CVD risk screening scenarios that used the WHO-2019 office-based risk tool, screened people above the age of 40, and lowered risk and blood pressure thresholds would likely be cost-effective, generating an additional QALY at less than half a GDP per capita.

## 5.1 BACKGROUND

Identification of people at high risk for cardiovascular disease (CVD) and managing them with a combination of lifestyle advice and pharmacological treatment is a cornerstone of the World Health Organization (WHO) Package of Essential Noncommunicable Disease Interventions (PEN) (1, 2). Using a total CVD risk approach, the PEN, supplemented by WHO HEARTS (3, 4), set out guidelines for screening and management of risk factors – hypertension, diabetes, and hypercholesterolaemia – in primary care settings in low- and middle-income countries (LMICs) to prevent CVD.

There is some evidence of improvement in clinical outcomes following PEN implementation (5) and on the cost-effectiveness of PEN variations in South Asia (6). However, a systematic review of CVD screening programs in LMICs emphasised the importance of assessing the appropriateness of international guidelines in local settings (7) Designing the pharmacological component of a CVD risk screening and treatment program involves specification of 1) the age groups to screen, 2) the CVD risk prediction tool to use, 3) the threshold to use to identify high CVD risk, 4) whether to lower the blood pressure treatment threshold for people with diabetes, and 5) whether to give statins to all people with diabetes regardless of CVD risk. These choices potentially have important consequences for cost and effectiveness (7-9).

Screening the working-age population can potentially detect CVD risks sufficiently early to avert negative outcomes. But with limited resources, screening at younger ages can have high opportunity costs and may weaken program effectiveness (7).

Most LMICs lack a CVD risk prediction tool derived from domestic data and must rely on tools derived from cohort data from another country (10) or from multiple countries (11). Validation for use in LMICs is difficult given the lack of accurate morbidity data and longitudinal datasets (12). The choice of tool may be largely determined by ease of use and WHO endorsement (13). Compared with an office-based tool, a laboratory-based tool, which requires a blood test for total cholesterol or a lipid profile, is more accurate but also more expensive.

CVD screening programs differ in the CVD risk threshold that is used to trigger statin treatment and, in some programs, to lower the blood pressure threshold for prescription of antihypertensives and determine follow-up frequency. Some countries use lower thresholds of 7.5% - 10% risk of a CVD event within ten years (14-16), while others use 20% and above (17, 18). Many LMICs adopt thresholds used in high-income countries despite possibly facing very different costs and impacts, or they adopt a suggested higher threshold assuming lower affordability (19) but without fully considering lower prices at which medicines may be available.

For prescription of antihypertensives, recent WHO guidelines recommend lower blood pressure thresholds for diabetics (≥130/80 mmHg) (3, 4), and for people at high risk of CVD (≥130 mmHg) (20). Several guidelines recommend statins for diabetics without consideration of CVD risk (3, 21, 22).

Since 2011, Sri Lanka has set up over 1,000 Healthy Lifestyle Centres (HLCs) to detect people with high CVD risk and associated risk factors (23, 24). CVD risk screening and treatment guidelines were published in 2012 (25). In 2018, these were updated by reducing the CVD risk threshold from 30% to 20% for prescription of statins, and broadening the age group screened from 40-65 years to 35 years and above (17). There was no published analysis of the health and cost consequences of these changes. Nor has there been analysis of the cost-effectiveness of the current program compared with alternatives that would screen at 40 years and above, use an alternative CVD risk tool, lower the CVD risk threshold to 10% in line with several high-income countries, lower the blood pressure treatment threshold for diabetics and those with high CVD risk, and prescribe statins for all diabetics. By conducting such cost-effectiveness analysis, this study aimed to help decision makers in Sri Lanka, and possibly elsewhere, optimise the CVD risk screening program.

## 5.2 METHODS

### 5.2.1 Data

We used data from the Sri Lanka Health and Ageing Study (SLHAS), which is a nationally-representative sample of 6,665 adults aged 18 years and older interviewed in 2018/9. The sample was selected using stratified, multi-stage cluster random sampling (26). Weights were applied to make the sample representative of the adult population of Sri Lanka in 2019. The dataset had risk factor data needed to simulate screening and predict CVD events for each individual (27). Except for smoking, each predictor was missing at random in <1% of the sample. Smoking status was missing for 2.9% of all participants, 3.8% of females, and 4.1% of urban participants. We used chained multiple imputation to impute missing data.

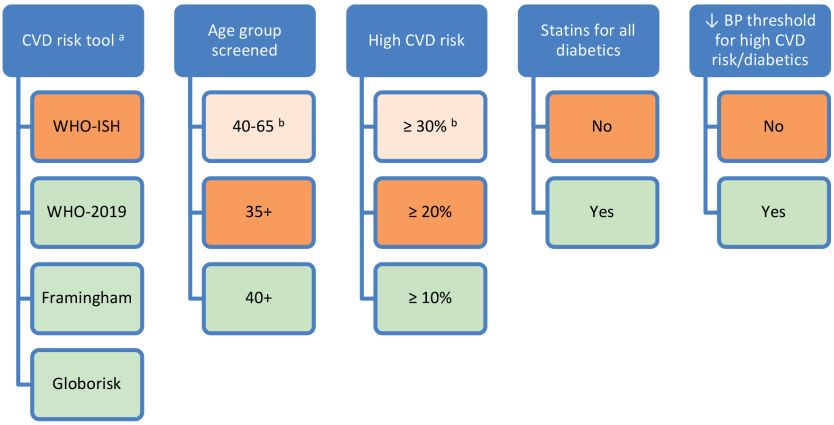
### 5.2.2 Screening scenarios

We simulated screening of a cohort of adults aged 35 years and older with no previous history of CVD (angina, coronary artery disease, myocardial infarction or stroke). We modelled programs that would screen at 70% of the capacity of HLCs (20 patients per week in 1,000 HLCs) for 48 weeks of one year (672,000 people), with follow-up of the cohort for 10-years.

We modelled two main modifications to the current screening protocol that would change the risk prediction tool and the age group screened (**Figure 1**). We compared eight screening tools

consisting of office- and laboratory-based versions of each of WHO International Society of Hypertension (WHO-ISH) (11), WHO-2019 (28), Framingham (10), and Globorisk (29) (current protocol: office-based WHO-ISH). We used tool-specific definitions of each risk factor used for predictions (Appendix Table A1). We compared three age groups: 40-65 years (previous protocol), 35 years and older (35+) (current protocol), and 40 years and older (40+). In all scenarios modelled, screening included glucose tests. Scenarios that used lab-based risk tools also included cholesterol tests in the initial screening.

***Figure 1 Screening and treatment parameters modelled in previous protocol, current protocol and potential scenarios***




**Notes:** [a] Office- and lab-based risk tools modelled. Current protocol deviates from previous protocol only in age group screened and definition of high CVD risk. [b] These parameter values were only assessed as part of the previous protocol. In all, there were 129 scenarios (8×2×2×2×2 + 1) including the base case. In the main text, we show results for scenarios that used WHO-ISH and WHO-2019 tools. Results for scenarios that used Framingham and Globorisk are in Additional file 1.

### 5.2.3 Treatment scenarios

In all scenarios modelled, those with blood pressure ≥ 140/90 would be given antihypertensives. Those with fasting blood glucose ≥ 126 mg/dL or random blood glucose ≥ 200 mg/dL would be given hypoglycaemics. In scenarios with lab-based risk tools, those with a total cholesterol ≥ 300 mg/dL would be given statins.

We modelled scenarios that differed in the criteria used to treat additional groups with statins and antihypertensives. First, we varied the CVD high-risk threshold that is used to determine eligibility for statins, and for lowering the blood pressure threshold in some scenarios, from 30% (previous protocol) to 20% (current protocol) to 10% (potential protocol). Second, we modelled giving statins to all diabetics irrespective of total cholesterol and CVD risk. Third, we

modelled lowering the blood pressure threshold for prescription of antihypertensives to 130/80 for all diabetics and those classified as high CVD risk.

We modelled follow-up according to the Sri Lankan screening guidelines (17). Anyone classified as high CVD risk was assumed to be followed up and given a glucose test twice per year. Those who were not high CVD risk but who qualified for any medication were assumed to be followed up and given a glucose test once per year, with an additional follow-up in the initial year. We assumed that all those qualifying for these medications continued to require them after the first year of follow-up. For scenarios with laboratory-based risk tools, total cholesterol was assumed to be measured on each follow-up visit if the initial CVD risk was high. For diabetics, we only modelled follow-up for management of CVD risk, not for diabetes management.

### 5.2.4 Outcomes

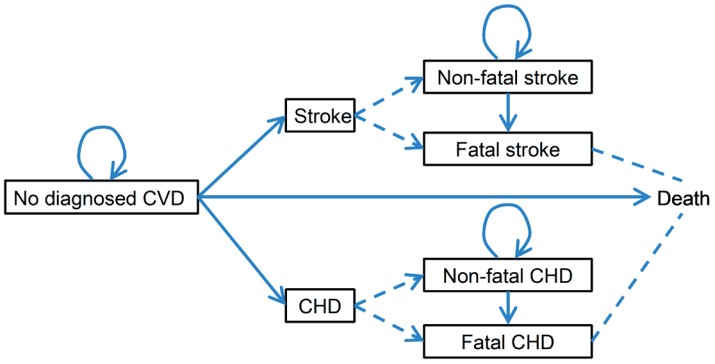
We used a Markov model with a 1-year cycle for the first 10 years of modelling (Figure 2). For all scenarios, we fed each individual's risk factor data into the WHO-2019 laboratory risk tool to estimate the 10-year probability of developing each of coronary heart disease (CHD) and stroke assuming that this tool would be the most accurate for the Sri Lankan population (Appendix Figure A1). We converted the 10-year probabilities to 1year probabilities (Appendix Text A2). The WHO-2019 tool defined CHD as International Classification of Disease-10 (ICD-10) code I21-I25, and stroke as I60-I69. We utilised 2019 Global Burden of Disease estimates of deaths and incidence of ischaemic heart disease and stroke, by sex and five-year age group (30) to produce mortality ratios for each individual age (Appendix Figure A2).

The transition probabilities for a non-fatal event to death in subsequent cycles were obtained by transforming 5-year mortality rates post CHD from 1990-1999 in the Framingham cohort (31) and post stroke from 2000-2004 in a Singaporean cohort study (32). The transition probability from no diagnosed CVD, to death without any CVD event was calculated by age and sex using WHO life tables (33). Since the focus is on primary prevention, we did not model multiple CVD events, which would be influenced by the intensity of secondary prevention (34). Mortality risks from non-fatal events included elevated mortality risk caused by any subsequent CVD event. We assumed that all people alive at the end of 10 years will transition to death using the probability of natural death for that age group, regardless of whether they had a CVD event or not. Cycles continued for each participant until death or the participant reached 100 years of age. Each transition was half-cycle corrected.

The baseline utility at the start of year 1 was calculated for each participant using a Sri Lankan valuation of their responses to the EQ-5D-5L questionnaire (35). For each subsequent yearly cycle, we calculated the utility for each individual by applying the marginal disutility of one

year increase in age, as well as non-fatal stroke and non-fatal CHD for people who transitioned to these states (Table 4).

***Figure 2 Markov model of population with no known history of CVD***




**Notes:** All participants started with no diagnosed CVD. Each solid arrow shows a possible transition at each cycle. Dashed lines with arrow show the breakdown within the same cycle: e.g., a stroke event is either non-fatal or fatal, and fatal stroke is related to death.

### 5.2.5 Impact of treatment

We used estimates from a metanalysis (37) for the effects of statins on the probabilities of non-fatal stroke and myocardial infarction (as a proxy for CHD). We used another metanalysis (38) for the effects of antihypertensives on the risks of CHD and stroke. We used the conservative estimates of these effects for a baseline blood pressure of 140-159 mmHg. Since this meta-analysis did not distinguish between effects of antihypertensives on CHD and stroke mortality, we used the estimated effect on cardiovascular disease mortality for both conditions. We also assumed, conservatively, that there would be no reduction of CHD or stroke risk after treatment of 10 years, though treatment would continue for the individual's lifetime.

### 5.2.6 Costs

We calculated costs over a lifetime horizon from a public health system perspective. Medicines costs, laboratory costs, admission costs for CHD and stroke, and costs of usual care for 2019 were calculated using locally available data (Appendix Text A1). All costs were converted to December 2019 US dollars (US$1 = LKR 181.63), which is the time the SLHAS was completed, the year for which most cost data were available, and an effective way to handle costing in a setting with fluctuating inflation (42).

*Table 4 Input and sensitivity parameters*

| Parameter | Value (95% CI) | Distribution | Source |
|---|---|---|---|
| **Events** | | | |
| 10-year probability of CHD / stroke event | Risk factor specific rates | | WHO CVD Risk Chart Working Group (28) |
| 10-year probability of death from CVD event | Age-sex specific proportion applied to CHD events and stroke events | ± 10% (uniform) | Global Burden of Disease Collaborative Network (30) |
| 1-year probability of death without previous CVD event | Age-sex specific natural mortality from life-tables. | | World Health Organization (33) |
| 1-year probability of dying after non-fatal CHD event | 0.03 (0.01, 0.04) | limits of 95% CI (β) | Velagaleti, Pencina, Murabito (31) |
| 1-year probability of dying after non-fatal stroke event | 0.10 | ± 20% (uniform) | Sun, Lee, Heng (32) |
| **Statin treatment** | | | |
| Cost for one year of treatment of atorvastatin 20 mg per day (USD) | 3.98 | ± 10% (Uniform) | IHP analysis (36) |
| RR of non-fatal MI | 0.74 (0.67, 0.81) | 95% CI (log normal) | Mills, Wu, Chong (37) |
| RR of non-fatal stroke | 0.86 (0.78, 0.95) | 95% CI (log normal) | Mills, Wu, Chong (37) |
| RR of fatal MI | 0.82 (0.75, 0.91) | 95% CI (log normal) | Mills, Wu, Chong (37) |
| RR of fatal stroke | 0.92 (0.80, 1.07) | 95% CI (log normal) | Mills, Wu, Chong (37) |
| **Antihypertensive treatment** | | | |
| Cost for one year of treatment of enalapril 5 mg per day (USD) | 2.21 | Gamma distribution, assuming 10% standard deviation | IHP analysis (36) |
| Cost for one year of treatment of nifedipine SR 20 mg per day (USD) | 0.78 | Gamma distribution, assuming 10% standard deviation | IHP analysis (36) |
| RR of non-fatal MI | 0.86 (0.76, 0.96) | 95% CI (log normal) | Brunstrom and Carlberg (38) |
| RR of non-fatal stroke | 0.86 (0.72, 1.01) | 95% CI (log normal) | Brunstrom and Carlberg (38) |
| RR of fatal MI | 0.86 (0.65, 1.14) | 95% CI (log normal) | Brunstrom and Carlberg (38) |
| RR of fatal stroke | 0.86 (0.65, 1.14) | 95% CI (log normal) | Brunstrom and Carlberg (38) |

| Parameter | Value (95% CI) | Distribution | Source |
|---|---|---|---|
| **Anti-diabetic treatment** | | | |
| Cost of one year of treatment with metformin 500 mg three times a day (USD) | 6.27 | Gamma distribution, assuming 10% standard deviation | IHP analysis (36) |
| **Screening costs (USD)** | | | |
| Glucose test | 0.17 | Gamma distribution, assuming 10% standard deviation | IHP analysis (36) |
| Total cholesterol test | 0.19 | Gamma distribution, assuming 10% standard deviation | IHP analysis (36) |
| Consultation | 1.96 | Gamma distribution, assuming 10% standard deviation | Amarasinghe, Dalpatadu and Rannan-Eliya (39),<br>Ministry of Health (24) |
| **Adjustment of annual usual care costs** | | | |
| Inflation of usual inpatient and outpatient care costs for general public | 1.00 | ± 20% (uniform) | Authors' analysis (Appendix Text A1) |
| Inflation of usual inpatient care costs for people with CHD | 2.85 (1.79, 4.54) | 95% CI (log normal) | Authors' analysis (Appendix Text A1) |
| Inflation of usual inpatient care costs for people with stroke | 1.09 (0.53, 2.26) | 95% CI (log normal) | Authors' analysis (Appendix Text A1) |
| Inflation of usual outpatient care costs for people with CHD | 1.95 (1.45, 2.61) | 95% CI (log normal) | Authors' analysis (Appendix Text A1) |
| Inflation of usual outpatient care costs for people with stroke | 1.97 (0.83, 4.69) | 95% CI (log normal) | Authors' analysis (Appendix Text A1) |
| **Event costs (USD)** | | | |
| Cost of myocardial infarction admission | 318 | ± 10% (uniform) | Perera, Rannan-Eliya, Senanayake (40), Amarasinghe, Dalpatadu and Rannan-Eliya (39) |
| Cost of stroke admission | 241 | ± 10% (uniform) | Perera, Rannan-Eliya, Senanayake (40), Amarasinghe, Dalpatadu and Rannan-Eliya (39) |
| **Disutilities** | | | |
| Non-fatal MI | -0.0210 (-0.066, 0.024) | 95% CI (log normal) | Wijemunige, Gamage, Rannan-Eliya (41) |
| Non-fatal stroke | -0.2493 (-0.340, -0.158) | 95% CI (log normal) | Wijemunige, Gamage, Rannan-Eliya (41) |
| 1 year increase in age | -0.0066 (-0.007, -0.006) | 95% CI (log normal) | Wijemunige, Gamage, Rannan-Eliya (41) |

**Notes:** A log normal distribution was used for disutility as the confidence interval for non-fatal MI spanned positive and negative values.

*Table 5 Incremental costs, QALYs and ICERs of selected scenarios*

| Scenario | CVD risk tool | High CVD risk | Ages screened | Statins all diabetics | HTN medication at lower BP |
|---|---|---|---|---|---|
| Base | WHO-ISH, office | ≥ 20% | 35+ | NO | NO |
| A | WHO 2019, office | ≥ 20% | 35+ | NO | NO |
| B | WHO 2019, office | ≥ 20% | 40+ | NO | NO |
| C | WHO-ISH, office | ≥ 30% | 40-65 | NO | NO |
| D | WHO 2019, office | ≥ 10% | 40+ | NO | NO |
| E | WHO 2019, office | ≥ 10% | 40+ | NO | YES |
| F | WHO 2019, office | ≥ 10% | 40+ | YES | YES |

**Notes:** Scenario labels as used in Figure 3. CEF = cost-effectiveness frontier. * ICERs are calculated from the closest least costly scenario on the CEF. For example, moving from scenario D to scenario E costs $1,511/QALY ($10.1 million - $6.2 million) / (8,747 QALYs – 6,129 QALYs).

## 5.2.7 Cost-effectiveness analysis

The base-case scenario was the current Sri Lanka CVD screening program (Figure 1). An incremental cost-effectiveness ratio (ICER) was calculated for each alternative scenario. Incremental costs were plotted against incremental QALYs, and cost-effectiveness frontiers drawn. We identified scenarios that were strongly dominated (another scenario produced more QALYs at lower cost) or weakly dominated (another scenario produced more total QALYs at a lower ICER). As there were no cost-effectiveness thresholds (CET) derived from local data, we compared ICERs to a threshold of gross domestic product (GDP) per capita (43). We also used lower thresholds of half and a quarter of a GDP per capita based on application of an approach to estimate CETs (44-46). We used 2019 GDP per capita in current US dollars of $4,083 (47). All costs and QALYs were discounted at 3% per year (7). Subgroup analysis of costs and impact was performed by 5-year age-groups for selected scenarios.

## 5.2.8 Sensitivity analysis

In a deterministic sensitivity analysis, we tested sensitivity to increasing the effect of antihypertensives on the risk of non-fatal stroke to the higher estimate at SBP ≥ 160 mmHg (33). We tested reducing the discount rate to 0% and raising it to 6%. We tested the effect of lowering the utility score for myocardial infarction to a value similar to that of stroke (48, 49). We also tested changing the cost of usual care to 80% and 120% of the value used, and changed the ratio used to inflate the cost of usual care for all people with CHD and stroke to 1 and 3.

In a separate oneway sensitivity analysis, we applied a disutility of 0.00384 to all participants newly prescribed medication, based on a small study from a high-income country (50) to account for a possible burden of taking long-term daily medications (50-52). Although this

| % of screened people newly commenced on: | | | | | | | |
|---|---|---|---|---|---|---|---|
| Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incre-mental costs (million $) | Incre-mental QALYs | ICER ($/QALY) | ICER from previous scenario on CEF* ($/QALY) |
| 19.8 | 2.4 | 8.1 | 21.2 | [Base] | [Base] | [Base] | [Base] |
| 19.8 | 2.1 | 8.1 | 21.4 | -0.6 | -426 | Cost saving | - |
| 21.7 | 2.7 | 8.5 | 22.5 | 0.1 | 1,007 | 113 | 113 |
| 21.2 | 0.9 | 8.8 | 22.3 | 1.5 | -153 | Dominated | - |
| 21.7 | 14.5 | 8.5 | 26.1 | 6.2 | 6,129 | 1,009 | 1,185 |
| 30.5 | 14.5 | 8.5 | 27.2 | 10.1 | 8,747 | 1,159 | 1,511 |
| 30.5 | 31.1 | 8.5 | 28.5 | 19.0 | 13,010 | 1,464 | 2,090 |

value aimed to capture the inconvenience of taking medications, "pill disutility" could also apply to the possibility of side-effects (50).

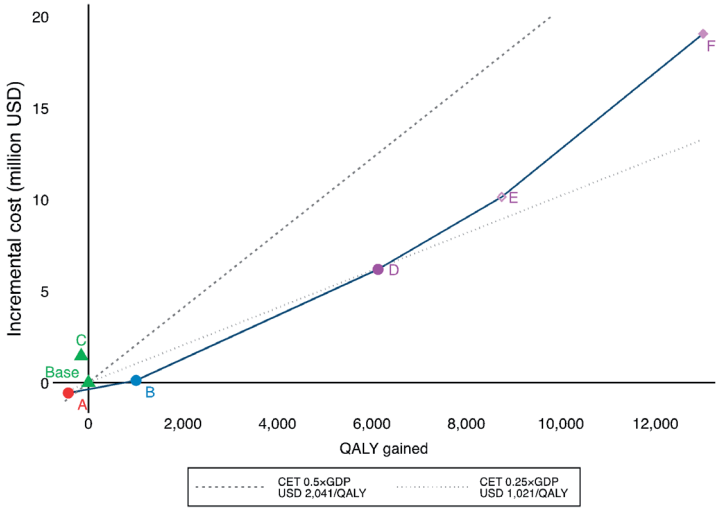
Probabilistic sensitivity analysis (PSA) was performed on all scenarios on the cost-effectiveness frontier that used WHO-ISH or WHO 2019 risk tools, which are most likely to be considered by the Sri Lankan Ministry of Health (MOH). 1,000 simulations were performed, randomly drawing from the distributions in Table 1, and cost-effectiveness acceptability curves (CEAC) were plotted.

We reported using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist (53) (Appendix Table A2). All analyses were done using Stata V.17.0 (Stata, College Station, Texas, USA).

## 5.3 RESULTS

Table 5 shows the percentage of people newly prescribed medications, the incremental QALYs, incremental costs and ICERs compared to the base case, for selected scenarios that used the WHO-ISH or WHO-2019 risk tools. The same scenarios are shown along with the cost-effectiveness frontier in Figure 7. The base case, which modelled the current screening protocol (WHO-ISH office tool, 20% risk threshold, 35+), the old protocol (WHO-ISH office tool, 30% risk threshold, 40-65) and all non-dominated scenarios are included. The results for all other scenarios, including those that used the Globorisk and Framingham screening tools, are shown in Appendix Table A3 and Table A4. Table 5 also shows the ICER from the nearest scenario on the cost-effectiveness frontier.

*Figure 7 Cost-effectiveness frontier for all scenarios using WHO-ISH and WHO-2019 risk tools*




**Notes:** Letters denote scenarios labelled in Table 2. Triangles denote scenarios that used the WHO-ISH office tool, filled circles denote scenarios that used the WHO-2019 office tool. The hollow diamond denotes a scenario that used the WHO-2019 tool with hypertension medication at a lower blood pressure threshold. The full diamond denotes a scenario that used the WHO-2019 tool with statins for all diabetics and hypertension medication at a lower blood pressure.

Of the 672,000 people screened, the percentage of people newly commenced on at least one of the three medications ranged from 21.2% – 30.5% for antihypertensives, 0.9% – 14.5% for statins, 8.1% – 8.5% for antidiabetics, and 22.3% to 27.2%% for at least one of the three medications. The incremental cost ($19.0 million) of the most expensive scenario on the costeffectivenes frontier, for screening one cohort and following this cohort over a lifetime is estimated to be 1.5% of the government's annual recurrent health expenditure in 2019 ($1.3 billion).

The old protocol (Scenario C) was dominated by the current protocol (Scenario "Base" in Table 5). Switching from the WHO-ISH to WHO-2019 tool (Scenario A) was cost saving, with a small loss in QALYs. Using the WHO-2019 tool and changing the age group screened to 40+ (Scenario B) had an ICER of $113 compared to the base case. Reducing the risk threshold to 10% (Scenario D) resulted in a gain of 6,129 QALYs with an ICER of $1,009/QALY. Moving from one scenario to the next most effective scenario along the frontier cost around 0.25× to 0.5×GDP per capita per QALY).

### 5.3.1 WHO-2019 lab tool with cholesterol testing compared to WHO-2019 office tool

The incremental costs and QALYs gained from using the WHO-2019 lab tool are compared to the office tool in Appendix Figure A3 for four combinations of ages screened (35+ or 40+) and risk thresholds (10% or 20%). Compared with the base case, the ICER of most scenarios using the lab tool are below 0.5×GDP per capita per QALY. All are dominated by scenarios using the WHO-2019 office tool.

### 5.3.2 Statins for all diabetics and lowering BP threshold for high-risk individuals

The impact of adding statins for diabetics (SD) and a lowered blood pressure threshold (LBP) for high-risk individuals is shown in Figure 7 (Scenarios E and F) and Appendix Figure A4. Compared to the base case, adding SD and LBP to the scenarios using WHO-2019 office tools had an ICER of approximately 0.5×GDP per capita/QALY or less. However, most of the scenarios with SD or LBP lie above the cost-effectiveness frontier (meaning they are dominated by other more cost-effective alternatives). There are two exceptions: Scenario E, which added LBP to scenario D (WHO-2019, 10%, 40+) has an ICER of 1,511 (less than 0.5×GDP per capita/QALY) compared to scenario D, and lies on the cost-effectiveness frontier. Scenario F, which further adds SD to scenario E, also lies on the cost-effectiveness frontier, however it has a higher ICER of $2,090/QALY (0.5×GDP per capita/QALY) compared to scenario E.

### 5.3.3 Framingham and Globorisk tools

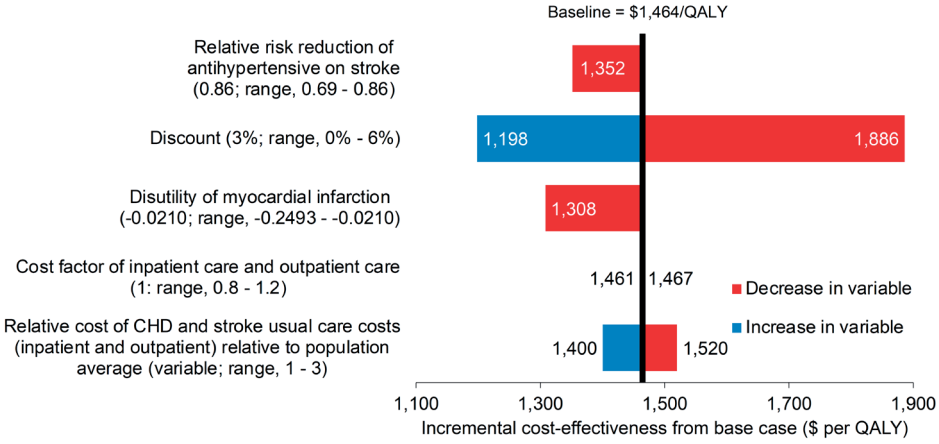
The impact of switching from WHO-2019 office to Framingham office and Globorisk office tools are shown in Appendix Figure A5. Almost all scenarios with Framingham and Globorisk tools are dominated by scenarios using WHO-2019 office tools. Globorisk scenario G, which uses a 20% threshold, lies on the cost-effectiveness frontier close to scenarios using the WHO-2019 tool with a 10% threshold. Whilst some scenarios on the cost-effectiveness frontier using the Globorisk tool generate the highest impact, they also have larger ICERs (0.8 – 2.3×GDP per capita/QALY) in comparison to the closest cheaper model on the frontier.

### 5.3.4 Sensitivity analysis

Results of the deterministic sensitivity analysis are shown in Figure 8 for the Scenario F (WHO-2019 office, 10% threshold, 40+, SD and LBP). Increasing the impact of antihypertensives on stroke reduced the ICER by 8% to $1,352/QALY from $1,464/QALY. Increasing the discount rate to 6% reduced the ICER to $1,198/QALY, whilst removing the discount rate increased the ICER to $1,886/QALY. Increasing the disutility of having a myocardial infarction reduced the ICER to $1,308/QALY. Deflating and inflating the estimated costs for usual care by 20% changed the ICER marginally. Reducing the relative costs of usual care for CHD stroke patients to be the same as the general population increased the ICER to $1,520/QALY, and

increasing the relative costs to be three times that of the general population reduced the ICER to $1,400 per QALY. Results from the PSA are shown in Appendix Figure A6. All scenarios on the cost-effectiveness frontier have more than an 90% probability of having an ICER of 0.5×GDP per capita/QALY or less.

***Figure 8 One-way sensitivity analysis assessing cost-effectiveness of Scenario F (WHO-2019 office, 10%, 40+, SD, LBP)***




**Notes:** SD = statins for diabetics, LBP = lowered blood pressure threshold/

## 5.3.5 Sensitivity to pill-taking disutility

Overall, when pill-taking disutility is included, the QALY gain is diminished and ICERs increase, particularly in scenarios which place a large proportion of individuals on new medication (Appendix Figure A7). Scenarios using the Globorisk tool (H, I) on the cost-effectiveness frontier, and scenarios using the Framingham and Globorisk tool with 10% thresholds move from costing less than 0.5×GDP per capita/QALY when the pill-taking disutility is set to 0 (Appendix Figure A5), to more than 0.5×GDP per capita/QALY when pill-taking disutility is -0.00384 (Appendix Figure A7).

## 5.3.6 Impact by age group

The incremental costs and impact by age group for Scenario F (WHO-2019 office, 10% threshold, 40+, SD and LBP scenario) are shown in Appendix Figure A8. In general, older age groups have lower ICERs than younger age groups.

## 5.4 DISCUSSION

Switching the Sri Lankan CVD screening program from the WHO-ISH to WHO-2019 office risk tool would be cost-effective and have a far higher impact, particularly if combined with lowering the highrisk threshold to 10%. Raising the lower age threshold for screening from 35 years to 40 years has a very low ICER of $113/QALY. Although lifetime exposure to low-density lipoprotein cholesterol, including in early adulthood can pose a great CVD risk, and so interventions should not neglect younger people (54), we recognise that the health system has limited screening capacity and resources. Given these constraints, greater impact and better cost-effectiveness are achieved by screening adults aged 40 and above. The ICER of younger age-groups is consistently higher than older age groups (Appendix Figure A8).

Prescribing antihypertensives at a lower threshold to people classified as high-risk of CVD and diabetics has an ICER of around 0.25×GDP per capita/QALY. Prescribing statins to all diabetics regardless of CVD risk is somewhat more expensive, with some scenarios costing around 0.5×GDP per capita/QALY. Age and gender-specific risk thresholds may be needed for statin initiation given possible side effects, which increase with age (19). However, a recent metanalysis did not find an increased risk in serious adverse events with low-intensity statin treatment (55). Nevertheless, in sensitivity analyses, when we modelled a disutility for taking medications, which could also include disutility from potential side-effects, ICERs for all scenarios increased. The scenarios using the WHO-2019 office tool on the cost-effectiveness frontier were robust, and remained on or very close to the new cost-effectiveness frontier, and still had ICERs less than 0.5×GDP per capita/ QALY. However, scenarios which resulted in larger proportions of people newly commenced on medications were more sensitive to "pill disutility".

Compared to the current screening protocol, using the WHO-2019 laboratory tool and including cholesterol testing costs less than 1×GDP per capita/ QALY. However, as it is dominated by scenarios that use the WHO-2019 office tool, it could be argued that the WHO-2019 office tool may be sufficient in resource-constrained environments.

The study used a public health system perspective, which is appropriate since CVD screening protocols are established by the MOH and public healthcare costs are of most interest to decision makers. A societal perspective would include travel costs to facilities, but also the likely much larger increase in labour productivity from reduced CVD events (56) that would be partially offset by future non-medical expenditures life (57). A lifetime perspective is used as CVD preventative treatment is longterm, and restricting analysis to a shorter time period would not capture long-term costs and benefits (58, 59).

While our modelling suggests that modifications to CVD risk screening in Sri Lanka would be highly cost effective, the efficiency gain may not materialise in a realworld situation (5, 60). Though limited in size and follow-up duration, some studies in LMICs suggest the impact of PEN interventions can be muted due to inadequate follow-up, high drug costs and poor adherence (61). Sri Lanka has very low drug costs, as well as an established system for follow-up, although public sector drug availability is facing pressures due to the economic crisis (62) that further underlines the importance of cost-effective preventative medicine (63).

Individual-level risk-factor data used in the model are collected in WHO STEPwise approach to surveillance (STEPS) surveys in LMICs (64), suggesting that similar analyses may be feasible in other LMICs with CVD screening programs.

Our findings may assist healthcare policy makers in Sri Lanka to further refine the CVD risk screening protocol for maximal impact. It enriches the evidence base to guide policy makers elsewhere in designing screening protocols that implement the PEN and HEARTS packages.

### 5.4.1 Limitations

As Sri Lanka does not have data to accurately estimate willingness to pay for QALYs, we could not define cost-effectiveness thresholds that could be used to identify program scenarios as highly, moderately, or not costeffective. Instead, we provided incremental cost per QALY for all scenarios on the cost-effectiveness frontier (43). We also compared the ICERs with thresholds of 0.25, 0.5 and 1×GDP per capita/QALY (65).

We did not recalibrate the CVD risk prediction tools for use in Sri Lanka given the lack of high-quality data on incidence of CVD in the country. However, we do not aim to establish whether each risk tool is accurate, and we did model scenarios that set high CVD risk at various thresholds for each tool.

Several limitations could lead to upwardly biased estimates of ICERs. First, we assumed no impact on morbidity and mortality beyond 10 years, although we modelled the costs of treatment and follow-up over a lifetime. It is possible that the reduction in CVD risks persist beyond 10 years. Second, since the focus was on cardiovascular disease, health gains from diabetes screening and management due to reduced microvascular complications, such as diabetic retinopathy, nephropathy and neuropathy, were not modelled, although the costs of hypoglycemics and yearly glucose checks were included. However, it is expected that most of the reduction in disease burden from diabetes and CVD risk screening programs will come from the prevention of cardiovascular disease, rather than the prevention of other complications of diabetes (66). Third, conservative estimates were used for impacts of treatment with antihypertensives and statins and for the disutility of myocardial infarction. The sensitivity analysis suggests less

conservative estimates would reduce the ICER by 18%. Fourth, we allowed for the potential disutility of pill taking in recognition of the possibility that when potentially a substantial number of people are put on medications many may experience side effects or simply resent the effort of routinely taking medicines. However, there is very little research available in LMICs to quantify this disutility, and we relied on an estimate from a small study in a HIC setting.

## 5.5 CONCLUSIONS

Subject to the acknowledged limitations, this study has delivered evidence that modifications to the CVD risk screening program in Sri Lanka would be cost effective. Changing to the WHO-2019 office screening tool, increasing the age at which screening starts to 40+, lowering the CVD risk threshold for statin treatment to 10%, lowering the blood pressure threshold of high-risk people for prescription of antihypertensives, and prescribing statins to diabetics, are all likely to generate health improvements at reasonable incremental costs.

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# APPENDIX

***Table A1 Variables and definitions used for screening tools***

| Risk assessment method | Screening Parameters | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | Smoking | Diabetes | SBP | SBP treatment | BMI | Total cholesterol | HDL cholesterol |
| WHO/ISH office | | | Within past year | OHG/insulin<br>FG ≥ 126 mg/dL<br>2h ≥ 200 mg/dL | | | | be 5 mmol/L for Sri Lanka | |
| WHO/ISH, lab | | | Within past year | OHG/insulin<br>FG ≥ 126 mg/dL<br>2h ≥ 200 mg/dL | | | | | |
| WHO-2019, office | | | Current | | | | | | |
| WHO-2019, lab | | | Current | Known diabetes<br>FG ≥ 126 mg/dL<br>2h ≥ 200 mg/dL | | | | | |
| Framingham office - D'Agostino (2008) | | | Current | OHG/insulin<br>FG ≥ 126 mg/dL | | | | | |
| Framingham lab - D'Agostino (2008) | | | Current | OHG/insulin<br>FG ≥ 126 mg/dL | | | | | |
| Globorisk office | | | Current | | | | | | |
| Globorisk lab | | | Current | OHG/insulin<br>FG ≥ 126 mg/dL<br>Random ≥ 200 mg/dL | | | | | |

Notes: OHG = oral hypoglycaemics, FG = fasting blood glucose, 2h = 2 hour post prandial or oral glucose tolerance test, Random = random blood glucose. Oral glucose tolerance and HbA1c test results in our cohort were not used for calculating risk by these tools, since its use in the community is limited. For tools that had 2h glucose criteria, random blood glucose results were considered when other criteria were not fulfilled.

*Table A2 CHEERS checklist*

| Topic | No. | Item | Location where item is reported |
|---|---|---|---|
| **Title** | | | |
| | 1 | Identify the study as an economic evaluation and specify the interventions being compared. | Title |
| **Abstract** | | | |
| | 2 | Provide a structured summary that highlights context, key methods, results, and alternative analyses. | Abstract |
| **Introduction** | | | |
| **Background and objectives** | 3 | Give the context for the study, the study question, and its practical relevance for decision making in policy or practice. | Context (general): Introduction, Paragraph 5<br>Context (local): Introduction, Paragraph 6<br>*Study question, practical relevance* - Introduction, Paragraph 6 |
| **Methods** | | | |
| **Health economic analysis plan** | 4 | Indicate whether a health economic analysis plan was developed and where available. | Not applicable |
| **Study population** | 5 | Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics). | Methods: Data, Paragraph 1 |
| **Setting and location** | 6 | Provide relevant contextual information that may influence findings. | Methods: Data, Paragraph 1 |
| **Comparators** | 7 | Describe the interventions or strategies being compared and why chosen. | Methods: Screening scenarios, Paragraph 2<br>Methods: Treatment scenarios, Paragraph 2<br>*Reasons* - Introduction Paragraph 2-6 |
| **Perspective** | 8 | State the perspective(s) adopted by the study and why chosen. | Costs<br>*Reasons* - Discussion, Paragraph 4 |
| **Time horizon** | 9 | State the time horizon for the study and why appropriate. | Methods: Impact of treatment<br>Methods: Costs<br>*Reasons* - Discussion, Paragraph 4 |
| **Discount rate** | 10 | Report the discount rate(s) and reason chosen. | Methods: Cost-effectiveness analysis |
| **Selection of outcomes** | 11 | Describe what outcomes were used as the measure(s) of benefit(s) and harm(s). | Methods: Outcomes, Paragraph 1-2 |
| **Measurement of outcomes** | 12 | Describe how outcomes used to capture benefit(s) and harm(s) were measured. | Methods: Outcomes, Paragraph 1-2 |
| **Valuation of outcomes** | 13 | Describe the population and methods used to measure and value outcomes. | Methods: Outcomes, Paragraph 1-2 |
| **Measurement and valuation of resources and costs** | 14 | Describe how costs were valued. | Methods: Costs<br>Appendix Text A1 |
| **Currency, price date, and conversion** | 15 | Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion. | Methods: Costs<br>Methods: Cost-effectiveness analysis |

| Topic | No. | Item | Location where item is reported |
|---|---|---|---|
| **Rationale and description of model** | 16 | If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed. | Methods: Screening scenarios, Treatment scenarios, Outcomes<br>Data availability statement |
| **Analytics and assumptions** | 17 | Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used. | Methods: Outcomes<br>Appendix Text A1 |
| **Characterising heterogeneity** | 18 | Describe any methods used for estimating how the results of the study vary for subgroups. | Methods: Cost-effectiveness analysis |
| **Characterising distributional effects** | 19 | Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations. | Not reported |
| **Characterising uncertainty** | 20 | Describe methods to characterise any sources of uncertainty in the analysis. | Methods: Sensitivity analysis, Paragraph 1-3 |
| **Approach to engagement with patients and others affected by the study** | 21 | Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study. | Not applicable |
| **Results** | | | |
| **Study parameters** | 22 | Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions. | Table 1 |
| **Summary of main results** | 23 | Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure. | Results, Paragraph 2-3<br>Table 2 |
| **Effect of uncertainty** | 24 | Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable. | Results: Sensitivity analysis |
| **Effect of engagement with patients and others affected by the study** | 25 | Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study | Not applicable |
| **Discussion** | | | |
| **Study findings, limitations, generalisability, and current knowledge** | 26 | Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice. | Discussion, Paragraph 1-3<br>Discussion: Limitations, Paragraph 1-3 |
| **Other relevant information** | | | |
| **Source of funding** | 27 | Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis | Funding statement |
| **Conflicts of interest** | 28 | Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements. | Competing interests statement |

**Notes:** CHEERS template from Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022;25. doi:10.1016/j.jval.2021.10.008

*Table A3 Incremental costs, QALYs and ICERs of all scenarios (sorted by incremental costs)*

| Scenario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incremental costs ($) | Incremental QALYs | ICER ($/QALY) | Dominance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Base | WHO-ISH, office | ≥20% | 35+ | | | 19.8 | 2.4 | 8.1 | 21.2 | 0.0 | 0 | | Base |
| A | WHO 2019, office | ≥20% | 35+ | | | 19.8 | 2.1 | 8.1 | 21.4 | -0.6 | -426 | | CS |
| B | WHO 2019, office | ≥20% | 40+ | | | 21.7 | 2.7 | 8.5 | 22.5 | 0.1 | 1,007 | 113 | ND |
| | WHO-ISH, office | ≥20% | 40+ | | | 21.7 | 2.8 | 8.5 | 22.3 | 0.7 | 1,362 | 481 | ND |
| C | WHO-ISH, office | ≥30% | 40-65 | | | 21.2 | 0.9 | 8.8 | 22.3 | 1.5 | -153 | -9,538 | SD |
| | WHO-ISH, office | ≥10% | 35+ | | | 19.8 | 6.1 | 8.1 | 21.3 | 2.0 | 1,593 | 1,274 | ED |
| | WHO-ISH, office | ≥10% | 40+ | | | 21.7 | 7.3 | 8.5 | 22.4 | 3.0 | 3,344 | 910 | ED |
| | WHO 2019, office | ≥20% | 35+ | | Y | 26.8 | 2.1 | 8.1 | 22.7 | 3.2 | 1,429 | 2,249 | SD |
| | WHO 2019, lab | ≥20% | 35+ | | | 19.8 | 7.3 | 8.1 | 23.7 | 3.7 | 1,225 | 2,985 | SD |
| | WHO-ISH, office | ≥20% | 35+ | | Y | 26.7 | 2.4 | 8.1 | 22.6 | 3.8 | 1,818 | 2,072 | SD |
| | WHO 2019, office | ≥20% | 40+ | | Y | 29.1 | 2.7 | 8.5 | 23.9 | 3.8 | 3,123 | 1,225 | SD |
| | WHO-ISH, lab | ≥20% | 35+ | | | 19.8 | 6.4 | 8.1 | 23.5 | 3.9 | 1,076 | 3,649 | SD |
| | WHO 2019, office | ≥10% | 35+ | | | 19.8 | 11.4 | 8.1 | 24.2 | 4.2 | 3,708 | 1,146 | ED |
| | WHO 2019, lab | ≥20% | 40+ | | | 21.7 | 8.2 | 8.5 | 24.6 | 4.2 | 2,939 | 1,430 | SD |
| | WHO-ISH, office | ≥20% | 40+ | | Y | 28.9 | 2.8 | 8.5 | 23.7 | 4.3 | 3,431 | 1,268 | SD |
| | WHO-ISH, lab | ≥20% | 40+ | | | 21.7 | 6.7 | 8.5 | 24.3 | 4.3 | 2,572 | 1,682 | SD |
| | WHO-ISH, office | ≥10% | 35+ | | Y | 26.7 | 6.1 | 8.1 | 22.6 | 5.8 | 3,401 | 1,698 | SD |
| | Globorisk, office | ≥20% | 35+ | | | 19.8 | 13.5 | 8.1 | 24.2 | 5.9 | 4,722 | 1,250 | ED |
| D | WHO 2019, office | ≥10% | 40+ | | | 21.7 | 14.5 | 8.5 | 26.1 | 6.2 | 6,129 | 1,009 | ND |
| | WHO-ISH, office | ≥10% | 40+ | | Y | 28.9 | 7.3 | 8.5 | 23.7 | 6.7 | 5,401 | 1,242 | SD |
| | Framingham, office | ≥20% | 35+ | | | 19.8 | 13.9 | 8.1 | 23.9 | 7.1 | 4,628 | 1,544 | SD |
| | WHO-ISH, lab | ≥10% | 35+ | | | 19.8 | 11.5 | 8.1 | 23.7 | 7.4 | 3,068 | 2,422 | SD |
| | WHO 2019, lab | ≥20% | 35+ | | Y | 26.7 | 7.3 | 8.1 | 25.0 | 7.5 | 3,044 | 2,457 | SD |
| | WHO-ISH, lab | ≥20% | 35+ | | Y | 26.7 | 6.4 | 8.1 | 24.8 | 7.8 | 2,883 | 2,694 | SD |
| | WHO 2019, lab | ≥20% | 40+ | | Y | 29.0 | 8.2 | 8.5 | 25.8 | 7.9 | 5,011 | 1,583 | SD |
| | WHO-ISH, lab | ≥20% | 40+ | | Y | 28.9 | 6.7 | 8.5 | 25.6 | 8.1 | 4,628 | 1,746 | SD |
| | WHO 2019, office | ≥10% | 35+ | | Y | 27.9 | 11.4 | 8.1 | 25.4 | 8.2 | 5,957 | 1,380 | SD |
| | Globorisk, office | ≥20% | 40+ | | | 21.7 | 17.0 | 8.5 | 26.1 | 8.2 | 7,390 | 1,112 | ED |
| | WHO-ISH, lab | ≥10% | 40+ | | | 21.7 | 13.0 | 8.5 | 24.6 | 8.3 | 5,025 | 1,647 | SD |
| | Framingham, office | ≥20% | 40+ | | | 21.7 | 17.7 | 8.5 | 25.8 | 9.9 | 7,433 | 1,332 | ED |
| | WHO 2019, office | ≥20% | 35+ | Y | | 19.8 | 20.6 | 8.1 | 24.1 | 10.0 | 4,646 | 2,161 | SD |
| | Globorisk, office | ≥20% | 35+ | | Y | 28.3 | 13.5 | 8.1 | 25.3 | 10.0 | 7,113 | 1,400 | SD |

| Scenario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incremental costs ($) | Incremental QALYs | ICER ($/QALY) | Dominance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| E | WHO 2019, office | ≥10% | 40+ | | Y | 30.5 | 14.5 | 8.5 | 27.2 | 10.1 | 8,747 | 1,159 | ND |
| | WHO-ISH, office | ≥20% | 35+ | Y | | 19.8 | 20.2 | 8.1 | 24.0 | 10.4 | 4,715 | 2,198 | SD |
| | WHO 2019, office | ≥20% | 40+ | Y | | 21.7 | 22.6 | 8.5 | 25.2 | 10.8 | 6,935 | 1,555 | SD |
| | Framingham, lab | ≥20% | 35+ | | | 19.8 | 17.5 | 8.1 | 26.3 | 10.8 | 5,519 | 1,957 | SD |
| | WHO 2019, lab | ≥10% | 35+ | | | 19.8 | 18.7 | 8.1 | 27.0 | 10.9 | 5,927 | 1,833 | SD |
| | WHO-ISH, office | ≥20% | 40+ | Y | | 21.7 | 21.9 | 8.5 | 25.0 | 11.0 | 6,835 | 1,613 | SD |
| | Framingham, office | ≥20% | 35+ | | Y | 27.8 | 13.9 | 8.1 | 25.1 | 11.0 | 6,828 | 1,615 | SD |
| | WHO-ISH, lab | ≥10% | 35+ | | Y | 27.1 | 11.5 | 8.1 | 24.9 | 11.4 | 4,961 | 2,294 | SD |
| | WHO-ISH, office | ≥10% | 35+ | Y | | 19.8 | 21.8 | 8.1 | 24.0 | 11.7 | 5,560 | 2,103 | SD |
| | WHO-ISH, lab | ≥10% | 40+ | | Y | 29.3 | 13.0 | 8.5 | 25.8 | 12.1 | 7,177 | 1,689 | SD |
| G | Globorisk, office | ≥20% | 40+ | | Y | 30.9 | 17.0 | 8.5 | 27.2 | 12.3 | 10,182 | 1,206 | ND |
| | WHO-ISH, office | ≥10% | 40+ | Y | | 21.7 | 23.9 | 8.5 | 25.0 | 12.6 | 7,905 | 1,593 | SD |
| | WHO 2019, office | ≥20% | 35+ | Y | Y | 26.8 | 20.6 | 8.1 | 24.1 | 13.0 | 6,314 | 2,052 | SD |
| | WHO 2019, lab | ≥10% | 40+ | | | 21.7 | 22.4 | 8.5 | 28.8 | 13.2 | 8,735 | 1,509 | SD |
| | Framingham, lab | ≥20% | 40+ | | | 21.7 | 20.9 | 8.5 | 27.8 | 13.2 | 8,253 | 1,596 | SD |
| | WHO-ISH, office | ≥20% | 35+ | Y | Y | 26.7 | 20.2 | 8.1 | 24.0 | 13.3 | 6,344 | 2,091 | SD |
| | WHO 2019, lab | ≥20% | 35+ | Y | | 19.8 | 23.3 | 8.1 | 26.3 | 13.3 | 5,372 | 2,482 | SD |
| | WHO-ISH, lab | ≥20% | 35+ | Y | | 19.8 | 23.0 | 8.1 | 26.1 | 13.7 | 5,498 | 2,498 | SD |
| | WHO 2019, office | ≥20% | 40+ | Y | Y | 29.1 | 22.6 | 8.5 | 25.2 | 13.7 | 8,848 | 1,554 | SD |
| | Framingham, office | ≥20% | 40+ | | Y | 30.3 | 17.7 | 8.5 | 26.9 | 13.7 | 9,990 | 1,375 | SD |
| | WHO 2019, lab | ≥20% | 40+ | Y | | 21.7 | 25.1 | 8.5 | 27.1 | 13.8 | 7,704 | 1,786 | SD |
| | WHO-ISH, office | ≥20% | 40+ | Y | Y | 28.9 | 21.9 | 8.5 | 25.0 | 14.0 | 8,697 | 1,606 | SD |
| | WHO-ISH, lab | ≥20% | 40+ | Y | | 21.7 | 24.5 | 8.5 | 26.9 | 14.0 | 7,697 | 1,825 | SD |
| | WHO 2019, office | ≥10% | 35+ | Y | | 19.8 | 27.3 | 8.1 | 26.7 | 14.0 | 7,611 | 1,841 | SD |
| | WHO-ISH, office | ≥10% | 35+ | Y | Y | 26.7 | 21.8 | 8.1 | 24.0 | 14.6 | 7,189 | 2,029 | SD |
| | WHO 2019, lab | ≥10% | 35+ | | Y | 28.2 | 18.7 | 8.1 | 28.0 | 14.8 | 8,209 | 1,808 | SD |
| | Framingham, lab | ≥20% | 35+ | | Y | 27.8 | 17.5 | 8.1 | 27.4 | 14.8 | 7,741 | 1,912 | SD |
| | Globorisk, office | ≥20% | 35+ | Y | | 19.8 | 28.3 | 8.1 | 26.6 | 15.2 | 8,140 | 1,867 | SD |
| | Framingham, office | ≥20% | 35+ | Y | | 19.8 | 26.4 | 8.1 | 26.4 | 15.3 | 7,309 | 2,100 | SD |
| | WHO-ISH, office | ≥10% | 40+ | Y | Y | 28.9 | 23.9 | 8.5 | 25.0 | 15.5 | 9,767 | 1,590 | SD |
| | WHO 2019, office | ≥10% | 40+ | Y | | 21.7 | 31.1 | 8.5 | 28.5 | 15.8 | 10,565 | 1,494 | ED |
| | WHO-ISH, lab | ≥10% | 35+ | Y | | 19.8 | 25.6 | 8.1 | 26.1 | 16.2 | 6,575 | 2,470 | SD |
| | WHO 2019, lab | ≥20% | 35+ | Y | Y | 26.7 | 23.3 | 8.1 | 26.3 | 16.3 | 7,025 | 2,316 | SD |

| Scenario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incremental costs ($) | Incremental QALYs | ICER ($/QALY) | Dominance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | WHO-ISH, lab | ≥20% | 35+ | Y | Y | 26.7 | 23.0 | 8.1 | 26.1 | 16.7 | 7,127 | 2,338 | SD |
| | WHO 2019, lab | ≥20% | 40+ | Y | Y | 29.0 | 25.1 | 8.5 | 27.1 | 16.7 | 9,598 | 1,744 | SD |
| | WHO-ISH, lab | ≥10% | 40+ | Y | | 21.7 | 27.6 | 8.5 | 26.9 | 16.8 | 8,998 | 1,863 | SD |
| | WHO-ISH, lab | ≥20% | 40+ | Y | Y | 28.9 | 24.5 | 8.5 | 26.9 | 17.0 | 9,558 | 1,781 | SD |
| | WHO 2019, lab | ≥10% | 40+ | | Y | 30.8 | 22.4 | 8.5 | 29.7 | 17.1 | 11,401 | 1,502 | ED |
| | Framingham, lab | ≥20% | 40+ | | Y | 30.4 | 20.9 | 8.5 | 28.9 | 17.1 | 10,840 | 1,580 | SD |
| | WHO 2019, office | ≥10% | 35+ | Y | Y | 27.9 | 27.3 | 8.1 | 26.7 | 17.2 | 9,697 | 1,770 | SD |
| | Globorisk, office | ≥20% | 40+ | Y | | 21.7 | 32.3 | 8.5 | 28.4 | 17.2 | 11,209 | 1,537 | ED |
| | Framingham, office | ≥20% | 40+ | Y | | 21.7 | 30.1 | 8.5 | 28.1 | 17.5 | 10,322 | 1,697 | SD |
| | Globorisk, lab | ≥20% | 35+ | | | 19.8 | 25.5 | 8.1 | 28.8 | 17.8 | 8,268 | 2,151 | SD |
| | Framingham, office | ≥20% | 35+ | Y | Y | 27.8 | 26.4 | 8.1 | 26.4 | 18.5 | 9,382 | 1,967 | SD |
| | Globorisk, office | ≥20% | 35+ | Y | Y | 28.3 | 28.3 | 8.1 | 26.6 | 18.5 | 10,387 | 1,777 | SD |
| | WHO 2019, lab | ≥10% | 35+ | Y | | 19.8 | 30.1 | 8.1 | 29.1 | 18.6 | 8,292 | 2,245 | SD |
| | Framingham, lab | ≥20% | 35+ | Y | | 19.8 | 29.3 | 8.1 | 28.7 | 18.6 | 8,102 | 2,300 | SD |
| F | WHO 2019, office | ≥10% | 40+ | Y | Y | 30.5 | 31.1 | 8.5 | 28.5 | 19.0 | 13,010 | 1,464 | ED |
| | WHO-ISH, lab | ≥10% | 35+ | Y | Y | 27.1 | 25.6 | 8.1 | 26.1 | 19.3 | 8,303 | 2,326 | SD |
| | WHO-ISH, lab | ≥10% | 40+ | Y | Y | 29.3 | 27.6 | 8.5 | 26.9 | 19.9 | 10,972 | 1,811 | SD |
| | WHO 2019, lab | ≥10% | 40+ | Y | | 21.7 | 33.6 | 8.5 | 30.7 | 20.3 | 11,276 | 1,803 | SD |
| | Framingham, lab | ≥20% | 40+ | Y | | 21.7 | 32.6 | 8.5 | 30.1 | 20.4 | 11,046 | 1,846 | SD |
| | Globorisk, lab | ≥20% | 40+ | | | 21.7 | 29.9 | 8.5 | 30.5 | 20.5 | 11,364 | 1,806 | SD |
| | Globorisk, office | ≥20% | 40+ | Y | Y | 30.9 | 32.3 | 8.5 | 28.4 | 20.6 | 13,854 | 1,488 | ED |
| | Framingham, office | ≥20% | 40+ | Y | Y | 30.3 | 30.1 | 8.5 | 28.1 | 20.7 | 12,752 | 1,626 | SD |
| | Framingham, office | ≥10% | 35+ | | | 19.8 | 31.6 | 8.1 | 31.7 | 21.2 | 10,727 | 1,976 | SD |
| | WHO 2019, lab | ≥10% | 35+ | Y | Y | 28.2 | 30.1 | 8.1 | 29.1 | 21.8 | 10,464 | 2,084 | SD |
| | Framingham, lab | ≥20% | 35+ | Y | Y | 27.8 | 29.3 | 8.1 | 28.7 | 21.8 | 10,207 | 2,139 | SD |
| | Globorisk, lab | ≥20% | 35+ | | Y | 29.4 | 25.5 | 8.1 | 29.5 | 21.9 | 10,971 | 1,999 | SD |
| | Globorisk, lab | ≥20% | 35+ | Y | | 19.8 | 32.9 | 8.1 | 30.4 | 23.2 | 9,521 | 2,437 | SD |
| | WHO 2019, lab | ≥10% | 40+ | Y | Y | 30.8 | 33.6 | 8.5 | 30.7 | 23.7 | 13,832 | 1,710 | SD |
| | Framingham, lab | ≥20% | 40+ | Y | Y | 30.4 | 32.6 | 8.5 | 30.1 | 23.7 | 13,516 | 1,754 | SD |
| | Globorisk, lab | ≥20% | 40+ | | Y | 31.9 | 29.9 | 8.5 | 31.1 | 24.5 | 14,399 | 1,702 | ED |
| | Globorisk, lab | ≥20% | 40+ | Y | | 21.7 | 36.4 | 8.5 | 31.8 | 25.0 | 12,557 | 1,993 | SD |
| | Globorisk, office | ≥10% | 35+ | | | 19.8 | 36.5 | 8.1 | 36.8 | 25.1 | 12,549 | 1,998 | SD |
| | Framingham, office | ≥10% | 35+ | | Y | 31.2 | 31.6 | 8.1 | 32.7 | 25.8 | 14,024 | 1,840 | SD |

| Scenario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incremental costs ($) | Incremental QALYs | ICER ($/QALY) | Dominance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Framingham, lab | ≥10% | 35+ | | | 19.8 | 35.6 | 8.1 | 34.8 | 26.5 | 11,557 | 2,291 | SD |
| | Globorisk, lab | ≥20% | 35+ | Y | Y | 29.4 | 32.9 | 8.1 | 30.4 | 26.8 | 12,159 | 2,201 | SD |
| | Framingham, office | ≥10% | 35+ | Y | | 19.8 | 39.3 | 8.1 | 33.8 | 26.9 | 12,044 | 2,231 | SD |
| | Framingham, office | ≥10% | 40+ | | | 21.7 | 40.0 | 8.5 | 35.7 | 27.5 | 14,968 | 1,835 | ED |
| | Globorisk, lab | ≥20% | 40+ | Y | Y | 31.9 | 36.4 | 8.5 | 31.8 | 28.6 | 15,536 | 1,840 | ED |
| | Globorisk, office | ≥10% | 40+ | | | 21.7 | 43.7 | 8.5 | 40.4 | 29.7 | 16,445 | 1,806 | ED |
| | Globorisk, office | ≥10% | 35+ | | Y | 33.7 | 36.5 | 8.1 | 37.6 | 30.7 | 16,616 | 1,850 | ED |
| | Framingham, office | ≥10% | 35+ | Y | Y | 31.2 | 39.3 | 8.1 | 33.8 | 30.9 | 15,272 | 2,021 | SD |
| | Framingham, lab | ≥10% | 35+ | | Y | 32.0 | 35.6 | 8.1 | 35.7 | 31.5 | 15,063 | 2,090 | SD |
| | Globorisk, office | ≥10% | 35+ | Y | | 19.8 | 45.9 | 8.1 | 38.6 | 31.7 | 14,178 | 2,236 | SD |
| | Framingham, lab | ≥10% | 35+ | Y | | 19.8 | 42.6 | 8.1 | 36.8 | 31.8 | 12,753 | 2,492 | SD |
| | Framingham, office | ≥10% | 40+ | Y | | 21.7 | 46.3 | 8.5 | 37.5 | 32.0 | 16,160 | 1,977 | SD |
| | Framingham, lab | ≥10% | 40+ | | | 21.7 | 43.1 | 8.5 | 38.0 | 32.0 | 15,604 | 2,052 | SD |
| | Framingham, office | ≥10% | 40+ | | Y | 34.7 | 40.0 | 8.5 | 36.5 | 32.2 | 18,920 | 1,703 | ED |
| H | Globorisk, office | ≥10% | 40+ | | Y | 36.7 | 43.7 | 8.5 | 41.1 | 35.3 | 21,002 | 1,681 | ND |
| | Globorisk, office | ≥10% | 40+ | Y | | 21.7 | 52.2 | 8.5 | 41.9 | 35.4 | 18,036 | 1,963 | SD |
| | Framingham, lab | ≥10% | 35+ | Y | Y | 32.0 | 42.6 | 8.1 | 36.8 | 36.1 | 16,193 | 2,232 | SD |
| | Framingham, lab | ≥10% | 40+ | Y | | 21.7 | 48.7 | 8.5 | 39.7 | 36.1 | 16,649 | 2,166 | SD |
| | Framingham, office | ≥10% | 40+ | Y | Y | 34.7 | 46.3 | 8.5 | 37.5 | 36.3 | 20,055 | 1,809 | SD |
| | Globorisk, office | ≥10% | 35+ | Y | Y | 33.7 | 45.9 | 8.1 | 38.6 | 36.7 | 18,163 | 2,022 | SD |
| | Framingham, lab | ≥10% | 40+ | | Y | 35.1 | 43.1 | 8.5 | 38.7 | 37.0 | 19,634 | 1,883 | SD |
| | Globorisk, lab | ≥10% | 35+ | | | 19.8 | 48.1 | 8.1 | 42.1 | 39.7 | 14,792 | 2,682 | SD |
| I | Globorisk, office | ≥10% | 40+ | Y | Y | 36.7 | 52.2 | 8.5 | 41.9 | 40.5 | 22,518 | 1,799 | ND |
| | Framingham, lab | ≥10% | 40+ | Y | Y | 35.1 | 48.7 | 8.5 | 39.7 | 40.6 | 20,628 | 1,968 | SD |
| | Globorisk, lab | ≥10% | 35+ | Y | | 19.8 | 51.3 | 8.1 | 43.1 | 42.2 | 15,236 | 2,771 | SD |
| | Globorisk, lab | ≥10% | 40+ | | | 21.7 | 54.1 | 8.5 | 44.5 | 42.9 | 18,496 | 2,318 | SD |
| | Globorisk, lab | ≥10% | 40+ | Y | | 21.7 | 56.2 | 8.5 | 45.2 | 44.5 | 18,808 | 2,364 | SD |
| | Globorisk, lab | ≥10% | 35+ | | Y | 34.9 | 48.1 | 8.1 | 42.6 | 45.4 | 19,017 | 2,385 | SD |
| | Globorisk, lab | ≥10% | 35+ | Y | Y | 34.9 | 51.3 | 8.1 | 43.1 | 47.6 | 19,436 | 2,449 | SD |
| | Globorisk, lab | ≥10% | 40+ | | Y | 37.9 | 54.1 | 8.5 | 44.7 | 48.4 | 23,216 | 2,086 | ED |
| J | Globorisk, lab | ≥10% | 40+ | Y | Y | 37.9 | 56.2 | 8.5 | 45.2 | 49.9 | 23,514 | 2,121 | ND |

**Notes:** Scenario labels as used in Figure 3 and Appendix Figures S3-S8. HTN = hypertension, Y = Yes, ND = Not dominated, SD = Dominated (strong dominance), ED = Dominated (extended dominance), CS = Cost saving.

*Table A4 Incremental costs, QALYs and ICERs of all models (sorted by scenario)*

| Sce-nario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incre-mental costs ($) | Incre-mental QALYs | ICER ($/ QALY) | Domi-nance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C | WHO-ISH, office | ≥30% | 40-65 | | | 21.2 | 0.9 | 8.8 | 22.3 | 1.5 | -153 | -9,538 | SD |
| Base | WHO-ISH, office | ≥20% | 35+ | | | 19.8 | 2.4 | 8.1 | 21.2 | 0.0 | 0 | | Base |
| | WHO-ISH, office | ≥20% | 35+ | | Y | 26.7 | 2.4 | 8.1 | 22.6 | 3.8 | 1,818 | 2,072 | SD |
| | WHO-ISH, office | ≥20% | 35+ | Y | | 19.8 | 20.2 | 8.1 | 24.0 | 10.4 | 4,715 | 2,198 | SD |
| | WHO-ISH, office | ≥20% | 35+ | Y | Y | 26.7 | 20.2 | 8.1 | 24.0 | 13.3 | 6,344 | 2,091 | SD |
| | WHO-ISH, office | ≥20% | 40+ | | | 21.7 | 2.8 | 8.5 | 22.3 | 0.7 | 1,362 | 481 | ND |
| | WHO-ISH, office | ≥20% | 40+ | | Y | 28.9 | 2.8 | 8.5 | 23.7 | 4.3 | 3,431 | 1,268 | SD |
| | WHO-ISH, office | ≥20% | 40+ | Y | | 21.7 | 21.9 | 8.5 | 25.0 | 11.0 | 6,835 | 1,613 | SD |
| | WHO-ISH, office | ≥20% | 40+ | Y | Y | 28.9 | 21.9 | 8.5 | 25.0 | 14.0 | 8,697 | 1,606 | SD |
| | WHO-ISH, office | ≥10% | 35+ | | | 19.8 | 6.1 | 8.1 | 21.3 | 2.0 | 1,593 | 1,274 | ED |
| | WHO-ISH, office | ≥10% | 35+ | | Y | 26.7 | 6.1 | 8.1 | 22.6 | 5.8 | 3,401 | 1,698 | SD |
| | WHO-ISH, office | ≥10% | 35+ | Y | | 19.8 | 21.8 | 8.1 | 24.0 | 11.7 | 5,560 | 2,103 | SD |
| | WHO-ISH, office | ≥10% | 35+ | Y | Y | 26.7 | 21.8 | 8.1 | 24.0 | 14.6 | 7,189 | 2,029 | SD |
| | WHO-ISH, office | ≥10% | 40+ | | | 21.7 | 7.3 | 8.5 | 22.4 | 3.0 | 3,344 | 910 | ED |
| | WHO-ISH, office | ≥10% | 40+ | | Y | 28.9 | 7.3 | 8.5 | 23.7 | 6.7 | 5,401 | 1,242 | ND |
| | WHO-ISH, office | ≥10% | 40+ | Y | | 21.7 | 23.9 | 8.5 | 25.0 | 12.6 | 7,905 | 1,593 | SD |
| | WHO-ISH, office | ≥10% | 40+ | Y | Y | 28.9 | 23.9 | 8.5 | 25.0 | 15.5 | 9,767 | 1,590 | SD |
| | WHO-ISH, lab | ≥20% | 35+ | | | 19.8 | 6.4 | 8.1 | 23.5 | 3.9 | 1,076 | 3,649 | SD |
| | WHO-ISH, lab | ≥20% | 35+ | | Y | 26.7 | 6.4 | 8.1 | 24.8 | 7.8 | 2,883 | 2,694 | SD |
| | WHO-ISH, lab | ≥20% | 35+ | Y | | 19.8 | 23.0 | 8.1 | 26.1 | 13.7 | 5,498 | 2,498 | SD |
| | WHO-ISH, lab | ≥20% | 35+ | Y | Y | 26.7 | 23.0 | 8.1 | 26.1 | 16.7 | 7,127 | 2,338 | SD |
| | WHO-ISH, lab | ≥20% | 40+ | | | 21.7 | 6.7 | 8.5 | 24.3 | 4.3 | 2,572 | 1,682 | SD |
| | WHO-ISH, lab | ≥20% | 40+ | | Y | 28.9 | 6.7 | 8.5 | 25.6 | 8.1 | 4,628 | 1,746 | SD |
| | WHO-ISH, lab | ≥20% | 40+ | Y | | 21.7 | 24.5 | 8.5 | 26.9 | 14.0 | 7,697 | 1,825 | SD |

| Sce-nario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incre-mental costs ($) | Incre-mental QALYs | ICER ($/ QALY) | Domi-nance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | WHO-ISH, lab | ≥20% | 40+ | Y | Y | 28.9 | 24.5 | 8.5 | 26.9 | 17.0 | 9,558 | 1,781 | SD |
| | WHO-ISH, lab | ≥10% | 35+ | | | 19.8 | 11.5 | 8.1 | 23.7 | 7.4 | 3,068 | 2,422 | SD |
| | WHO-ISH, lab | ≥10% | 35+ | | Y | 27.1 | 11.5 | 8.1 | 24.9 | 11.4 | 4,961 | 2,294 | SD |
| | WHO-ISH, lab | ≥10% | 35+ | Y | | 19.8 | 25.6 | 8.1 | 26.1 | 16.2 | 6,575 | 2,470 | SD |
| | WHO-ISH, lab | ≥10% | 35+ | Y | Y | 27.1 | 25.6 | 8.1 | 26.1 | 19.3 | 8,303 | 2,326 | SD |
| | WHO-ISH, lab | ≥10% | 40+ | | | 21.7 | 13.0 | 8.5 | 24.6 | 8.3 | 5,025 | 1,647 | SD |
| | WHO-ISH, lab | ≥10% | 40+ | | Y | 29.3 | 13.0 | 8.5 | 25.8 | 12.1 | 7,177 | 1,689 | SD |
| | WHO-ISH, lab | ≥10% | 40+ | Y | | 21.7 | 27.6 | 8.5 | 26.9 | 16.8 | 8,998 | 1,863 | SD |
| | WHO-ISH, lab | ≥10% | 40+ | Y | Y | 29.3 | 27.6 | 8.5 | 26.9 | 19.9 | 10,972 | 1,811 | SD |
| A | WHO 2019, office | ≥20% | 35+ | | | 19.8 | 2.1 | 8.1 | 21.4 | -0.6 | -426 | | CS |
| | WHO 2019, office | ≥20% | 35+ | | Y | 26.8 | 2.1 | 8.1 | 22.7 | 3.2 | 1,429 | 2,249 | SD |
| | WHO 2019, office | ≥20% | 35+ | Y | | 19.8 | 20.6 | 8.1 | 24.1 | 10.0 | 4,646 | 2,161 | SD |
| | WHO 2019, office | ≥20% | 35+ | Y | Y | 26.8 | 20.6 | 8.1 | 24.1 | 13.0 | 6,314 | 2,052 | SD |
| B | WHO 2019, office | ≥20% | 40+ | | | 21.7 | 2.7 | 8.5 | 22.5 | 0.1 | 1,007 | 113 | ND |
| | WHO 2019, office | ≥20% | 40+ | | Y | 29.1 | 2.7 | 8.5 | 23.9 | 3.8 | 3,123 | 1,225 | SD |
| | WHO 2019, office | ≥20% | 40+ | Y | | 21.7 | 22.6 | 8.5 | 25.2 | 10.8 | 6,935 | 1,555 | SD |
| | WHO 2019, office | ≥20% | 40+ | Y | Y | 29.1 | 22.6 | 8.5 | 25.2 | 13.7 | 8,848 | 1,554 | SD |
| | WHO 2019, office | ≥10% | 35+ | | | 19.8 | 11.4 | 8.1 | 24.2 | 4.2 | 3,708 | 1,146 | ED |
| | WHO 2019, office | ≥10% | 35+ | | Y | 27.9 | 11.4 | 8.1 | 25.4 | 8.2 | 5,957 | 1,380 | SD |
| | WHO 2019, office | ≥10% | 35+ | Y | | 19.8 | 27.3 | 8.1 | 26.7 | 14.0 | 7,611 | 1,841 | SD |
| | WHO 2019, office | ≥10% | 35+ | Y | Y | 27.9 | 27.3 | 8.1 | 26.7 | 17.2 | 9,697 | 1,770 | SD |
| D | WHO 2019, office | ≥10% | 40+ | | | 21.7 | 14.5 | 8.5 | 26.1 | 6.2 | 6,129 | 1,009 | ND |
| E | WHO 2019, office | ≥10% | 40+ | | Y | 30.5 | 14.5 | 8.5 | 27.2 | 10.1 | 8,747 | 1,159 | ND |
| | WHO 2019, office | ≥10% | 40+ | Y | | 21.7 | 31.1 | 8.5 | 28.5 | 15.8 | 10,565 | 1,494 | ED |
| F | WHO 2019, office | ≥10% | 40+ | Y | Y | 30.5 | 31.1 | 8.5 | 28.5 | 19.0 | 13,010 | 1,464 | ED |
| | WHO 2019, lab | ≥20% | 35+ | | | 19.8 | 7.3 | 8.1 | 23.7 | 3.7 | 1,225 | 2,985 | SD |

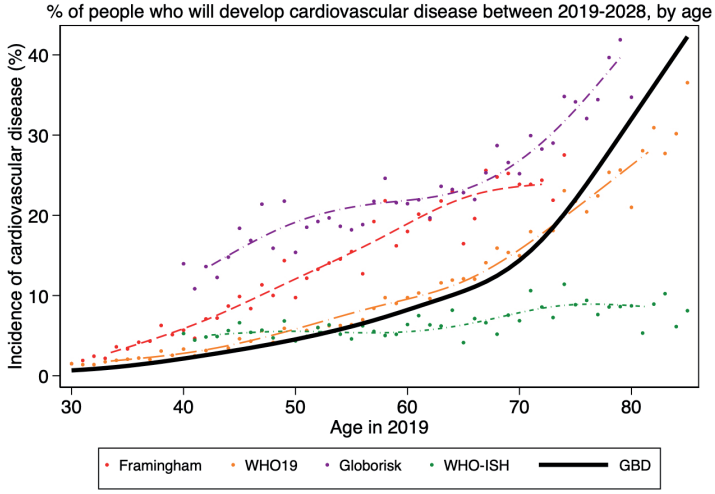
| Sce-nario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incre-mental costs ($) | Incre-mental QALYs | ICER ($/QALY) | Domi-nance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | WHO 2019, lab | ≥20% | 35+ | | Y | 26.7 | 7.3 | 8.1 | 25.0 | 7.5 | 3,044 | 2,457 | SD |
| | WHO 2019, lab | ≥20% | 35+ | Y | | 19.8 | 23.3 | 8.1 | 26.3 | 13.3 | 5,372 | 2,482 | SD |
| | WHO 2019, lab | ≥20% | 35+ | Y | Y | 26.7 | 23.3 | 8.1 | 26.3 | 16.3 | 7,025 | 2,316 | SD |
| | WHO 2019, lab | ≥20% | 40+ | | | 21.7 | 8.2 | 8.5 | 24.6 | 4.2 | 2,939 | 1,430 | SD |
| | WHO 2019, lab | ≥20% | 40+ | | Y | 29.0 | 8.2 | 8.5 | 25.8 | 7.9 | 5,011 | 1,583 | SD |
| | WHO 2019, lab | ≥20% | 40+ | Y | | 21.7 | 25.1 | 8.5 | 27.1 | 13.8 | 7,704 | 1,786 | SD |
| | WHO 2019, lab | ≥20% | 40+ | Y | Y | 29.0 | 25.1 | 8.5 | 27.1 | 16.7 | 9,598 | 1,744 | SD |
| | WHO 2019, lab | ≥10% | 35+ | | | 19.8 | 18.7 | 8.1 | 27.0 | 10.9 | 5,927 | 1,833 | SD |
| | WHO 2019, lab | ≥10% | 35+ | | Y | 28.2 | 18.7 | 8.1 | 28.0 | 14.8 | 8,209 | 1,808 | SD |
| | WHO 2019, lab | ≥10% | 35+ | Y | | 19.8 | 30.1 | 8.1 | 29.1 | 18.6 | 8,292 | 2,245 | SD |
| | WHO 2019, lab | ≥10% | 35+ | Y | Y | 28.2 | 30.1 | 8.1 | 29.1 | 21.8 | 10,464 | 2,084 | SD |
| | WHO 2019, lab | ≥10% | 40+ | | | 21.7 | 22.4 | 8.5 | 28.8 | 13.2 | 8,735 | 1,509 | SD |
| | WHO 2019, lab | ≥10% | 40+ | | Y | 30.8 | 22.4 | 8.5 | 29.7 | 17.1 | 11,401 | 1,502 | ED |
| | WHO 2019, lab | ≥10% | 40+ | Y | | 21.7 | 33.6 | 8.5 | 30.7 | 20.3 | 11,276 | 1,803 | SD |
| | WHO 2019, lab | ≥10% | 40+ | Y | Y | 30.8 | 33.6 | 8.5 | 30.7 | 23.7 | 13,832 | 1,710 | SD |
| | Framingham, office | ≥20% | 35+ | | | 19.8 | 13.9 | 8.1 | 23.9 | 7.1 | 4,628 | 1,544 | SD |
| | Framingham, office | ≥20% | 35+ | | Y | 27.8 | 13.9 | 8.1 | 25.1 | 11.0 | 6,828 | 1,615 | SD |
| | Framingham, office | ≥20% | 35+ | Y | | 19.8 | 26.4 | 8.1 | 26.4 | 15.3 | 7,309 | 2,100 | SD |
| | Framingham, office | ≥20% | 35+ | Y | Y | 27.8 | 26.4 | 8.1 | 26.4 | 18.5 | 9,382 | 1,967 | SD |
| | Framingham, office | ≥20% | 40+ | | | 21.7 | 17.7 | 8.5 | 25.8 | 9.9 | 7,433 | 1,332 | ED |
| | Framingham, office | ≥20% | 40+ | | Y | 30.3 | 17.7 | 8.5 | 26.9 | 13.7 | 9,990 | 1,375 | SD |
| | Framingham, office | ≥20% | 40+ | Y | | 21.7 | 30.1 | 8.5 | 28.1 | 17.5 | 10,322 | 1,697 | SD |
| | Framingham, office | ≥20% | 40+ | Y | Y | 30.3 | 30.1 | 8.5 | 28.1 | 20.7 | 12,752 | 1,626 | SD |
| | Framingham, office | ≥10% | 35+ | | | 19.8 | 31.6 | 8.1 | 31.7 | 21.2 | 10,727 | 1,976 | SD |
| | Framingham, office | ≥10% | 35+ | | Y | 31.2 | 31.6 | 8.1 | 32.7 | 25.8 | 14,024 | 1,840 | SD |
| | Framingham, office | ≥10% | 35+ | Y | | 19.8 | 39.3 | 8.1 | 33.8 | 26.9 | 12,044 | 2,231 | SD |

| Sce-nario | CVD risk tool | High CVD risk | Ages screened | % of screened people newly commenced on: Statins all diabetics | HTN medication at lower BP | Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incre-mental costs ($) | Incre-mental QALYs | ICER ($/QALY) | Domi-nance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Framingham, office | ≥10% | 35+ | Y | Y | 31.2 | 39.3 | 8.1 | 33.8 | 30.9 | 15,272 | 2,021 | SD |
| | Framingham, office | ≥10% | 40+ | | | 21.7 | 40.0 | 8.5 | 35.7 | 27.5 | 14,968 | 1,835 | ED |
| | Framingham, office | ≥10% | 40+ | | Y | 34.7 | 40.0 | 8.5 | 36.5 | 32.2 | 18,920 | 1,703 | ED |
| | Framingham, office | ≥10% | 40+ | Y | | 21.7 | 46.3 | 8.5 | 37.5 | 32.0 | 16,160 | 1,977 | SD |
| | Framingham, office | ≥10% | 40+ | Y | Y | 34.7 | 46.3 | 8.5 | 37.5 | 36.3 | 20,055 | 1,809 | SD |
| | Framingham, lab | ≥20% | 35+ | | | 19.8 | 17.5 | 8.1 | 26.3 | 10.8 | 5,519 | 1,957 | SD |
| | Framingham, lab | ≥20% | 35+ | | Y | 27.8 | 17.5 | 8.1 | 27.4 | 14.8 | 7,741 | 1,912 | SD |
| | Framingham, lab | ≥20% | 35+ | Y | | 19.8 | 29.3 | 8.1 | 28.7 | 18.6 | 8,102 | 2,300 | SD |
| | Framingham, lab | ≥20% | 35+ | Y | Y | 27.8 | 29.3 | 8.1 | 28.7 | 21.8 | 10,207 | 2,139 | SD |
| | Framingham, lab | ≥20% | 40+ | | | 21.7 | 20.9 | 8.5 | 27.8 | 13.2 | 8,253 | 1,596 | SD |
| | Framingham, lab | ≥20% | 40+ | | Y | 30.4 | 20.9 | 8.5 | 28.9 | 17.1 | 10,840 | 1,580 | SD |
| | Framingham, lab | ≥20% | 40+ | Y | | 21.7 | 32.6 | 8.5 | 30.1 | 20.4 | 11,046 | 1,846 | SD |
| | Framingham, lab | ≥20% | 40+ | Y | Y | 30.4 | 32.6 | 8.5 | 30.1 | 23.7 | 13,516 | 1,754 | SD |
| | Framingham, lab | ≥10% | 35+ | | | 19.8 | 35.6 | 8.1 | 34.8 | 26.5 | 11,557 | 2,291 | SD |
| | Framingham, lab | ≥10% | 35+ | | Y | 32.0 | 35.6 | 8.1 | 35.7 | 31.5 | 15,063 | 2,090 | SD |
| | Framingham, lab | ≥10% | 35+ | Y | | 19.8 | 42.6 | 8.1 | 36.8 | 31.8 | 12,753 | 2,492 | SD |
| | Framingham, lab | ≥10% | 35+ | Y | Y | 32.0 | 42.6 | 8.1 | 36.8 | 36.1 | 16,193 | 2,232 | SD |
| | Framingham, lab | ≥10% | 40+ | | | 21.7 | 43.1 | 8.5 | 38.0 | 32.0 | 15,604 | 2,052 | SD |
| | Framingham, lab | ≥10% | 40+ | | Y | 35.1 | 43.1 | 8.5 | 38.7 | 37.0 | 19,634 | 1,883 | SD |
| | Framingham, lab | ≥10% | 40+ | Y | | 21.7 | 48.7 | 8.5 | 39.7 | 36.1 | 16,649 | 2,166 | SD |
| | Framingham, lab | ≥10% | 40+ | Y | Y | 35.1 | 48.7 | 8.5 | 39.7 | 40.6 | 20,628 | 1,968 | SD |
| | Globorisk, office | ≥20% | 35+ | | | 19.8 | 13.5 | 8.1 | 24.2 | 5.9 | 4,722 | 1,250 | ED |
| | Globorisk, office | ≥20% | 35+ | | Y | 28.3 | 13.5 | 8.1 | 25.3 | 10.0 | 7,113 | 1,400 | SD |
| | Globorisk, office | ≥20% | 35+ | Y | | 19.8 | 28.3 | 8.1 | 26.6 | 15.2 | 8,140 | 1,867 | SD |
| | Globorisk, office | ≥20% | 35+ | Y | Y | 28.3 | 28.3 | 8.1 | 26.6 | 18.5 | 10,387 | 1,777 | SD |
| | Globorisk, office | ≥20% | 40+ | | | 21.7 | 17.0 | 8.5 | 26.1 | 8.2 | 7,390 | 1,112 | ED |

| Sce-nario | CVD risk tool | High CVD risk | Ages screened | Statins all diabetics | HTN medication at lower BP | % of screened people newly commenced on: Anti-hypertensive | Statin | Anti-diabetic | At least 1 medication | Incre-mental costs ($) | Incre-mental QALYs | ICER ($/QALY) | Domi-nance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| G | Globorisk, office | ≥20% | 40+ | | Y | 30.9 | 17.0 | 8.5 | 27.2 | 12.3 | 10,182 | 1,206 | ND |
| | Globorisk, office | ≥20% | 40+ | Y | | 21.7 | 32.3 | 8.5 | 28.4 | 17.2 | 11,209 | 1,537 | ED |
| | Globorisk, office | ≥20% | 40+ | Y | Y | 30.9 | 32.3 | 8.5 | 28.4 | 20.6 | 13,854 | 1,488 | ED |
| | Globorisk, office | ≥10% | 35+ | | | 19.8 | 36.5 | 8.1 | 36.8 | 25.1 | 12,549 | 1,998 | SD |
| | Globorisk, office | ≥10% | 35+ | | Y | 33.7 | 36.5 | 8.1 | 37.6 | 30.7 | 16,616 | 1,850 | ED |
| | Globorisk, office | ≥10% | 35+ | Y | | 19.8 | 45.9 | 8.1 | 38.6 | 31.7 | 14,178 | 2,236 | SD |
| | Globorisk, office | ≥10% | 35+ | Y | Y | 33.7 | 45.9 | 8.1 | 38.6 | 36.7 | 18,163 | 2,022 | SD |
| | Globorisk, office | ≥10% | 40+ | | | 21.7 | 43.7 | 8.5 | 40.4 | 29.7 | 16,445 | 1,806 | ED |
| H | Globorisk, office | ≥10% | 40+ | | Y | 36.7 | 43.7 | 8.5 | 41.1 | 35.3 | 21,002 | 1,681 | ND |
| | Globorisk, office | ≥10% | 40+ | Y | | 21.7 | 52.2 | 8.5 | 41.9 | 35.4 | 18,036 | 1,963 | SD |
| I | Globorisk, office | ≥10% | 40+ | Y | Y | 36.7 | 52.2 | 8.5 | 41.9 | 40.5 | 22,518 | 1,799 | ND |
| | Globorisk, lab | ≥20% | 35+ | | | 19.8 | 25.5 | 8.1 | 28.8 | 17.8 | 8,268 | 2,151 | SD |
| | Globorisk, lab | ≥20% | 35+ | | Y | 29.4 | 25.5 | 8.1 | 29.5 | 21.9 | 10,971 | 1,999 | SD |
| | Globorisk, lab | ≥20% | 35+ | Y | | 19.8 | 32.9 | 8.1 | 30.4 | 23.2 | 9,521 | 2,437 | SD |
| | Globorisk, lab | ≥20% | 35+ | Y | Y | 29.4 | 32.9 | 8.1 | 30.4 | 26.8 | 12,159 | 2,201 | SD |
| | Globorisk, lab | ≥20% | 40+ | | | 21.7 | 29.9 | 8.5 | 30.5 | 20.5 | 11,364 | 1,806 | SD |
| | Globorisk, lab | ≥20% | 40+ | | Y | 31.9 | 29.9 | 8.5 | 31.1 | 24.5 | 14,399 | 1,702 | ED |
| | Globorisk, lab | ≥20% | 40+ | Y | | 21.7 | 36.4 | 8.5 | 31.8 | 25.0 | 12,557 | 1,993 | SD |
| | Globorisk, lab | ≥20% | 40+ | Y | Y | 31.9 | 36.4 | 8.5 | 31.8 | 28.6 | 15,536 | 1,840 | ED |
| | Globorisk, lab | ≥10% | 35+ | | | 19.8 | 48.1 | 8.1 | 42.1 | 39.7 | 14,792 | 2,682 | SD |
| | Globorisk, lab | ≥10% | 35+ | | Y | 34.9 | 48.1 | 8.1 | 42.6 | 45.4 | 19,017 | 2,385 | SD |
| | Globorisk, lab | ≥10% | 35+ | Y | | 19.8 | 51.3 | 8.1 | 43.1 | 42.2 | 15,236 | 2,771 | SD |
| | Globorisk, lab | ≥10% | 35+ | Y | Y | 34.9 | 51.3 | 8.1 | 43.1 | 47.6 | 19,436 | 2,449 | SD |
| | Globorisk, lab | ≥10% | 40+ | | | 21.7 | 54.1 | 8.5 | 44.5 | 42.9 | 18,496 | 2,318 | SD |
| | Globorisk, lab | ≥10% | 40+ | | Y | 37.9 | 54.1 | 8.5 | 44.7 | 48.4 | 23,216 | 2,086 | ED |
| | Globorisk, lab | ≥10% | 40+ | Y | | 21.7 | 56.2 | 8.5 | 45.2 | 44.5 | 18,808 | 2,364 | SD |
| J | Globorisk, lab | ≥10% | 40+ | Y | Y | 37.9 | 56.2 | 8.5 | 45.2 | 49.9 | 23,514 | 2,121 | ND |

**Notes:** This table is identical to Appendix Table A3, however, rows are sorted by scenario, that is, by the columns CVD risk tool, High CVD risk, Ages screened, Statins all diabetics, and HTN medication at lower BP. Model labels as used in Figure 3 and Appendix Figures S3-S8. HTN = hypertension, Y = Yes, ND = Not dominated, SD = Dominated (strong dominance), ED = Dominated (extended dominance), CS = Cost saving.

***Figure A1 Comparison of percentage of people who will develop cardiovascular disease between 2019-2028 by age and prediction tool***

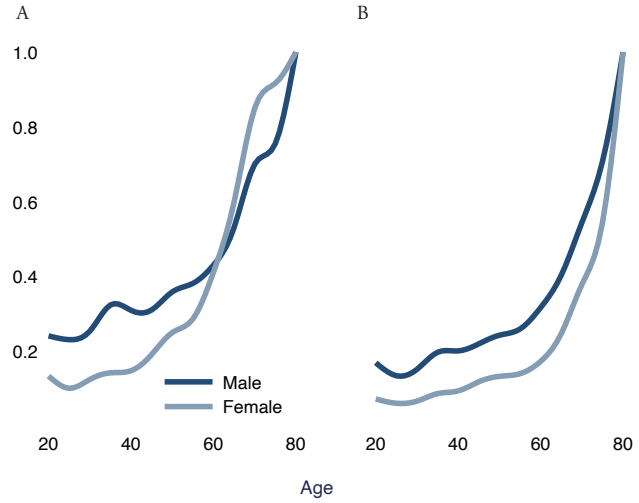



**Notes:** Figure A1 plots the predicted incidence of CVD over 10 years by age in 2019 using the WHO-ISH, WHO-2019, Globorisk and Framingham tools and SLHAS data, and compares it to the incidence of CVD obtained from extrapolating GBD incidence data.

GBD data for the incidence of ischaemic heart disease (GBD category 493) and stroke (GBD category 494) between 2010 and 2019 by 5-year age groups and gender were used to extrapolate the incident cases that were expected to happen from 2019 – 2029 by age group and gender. Cubic splines were fitted for each gender to smooth the 5-year age groups. The incident cases of ischaemic heart disease and stroke were summed to produce the incidence of cardiovascular disease between 2019 – 2028.

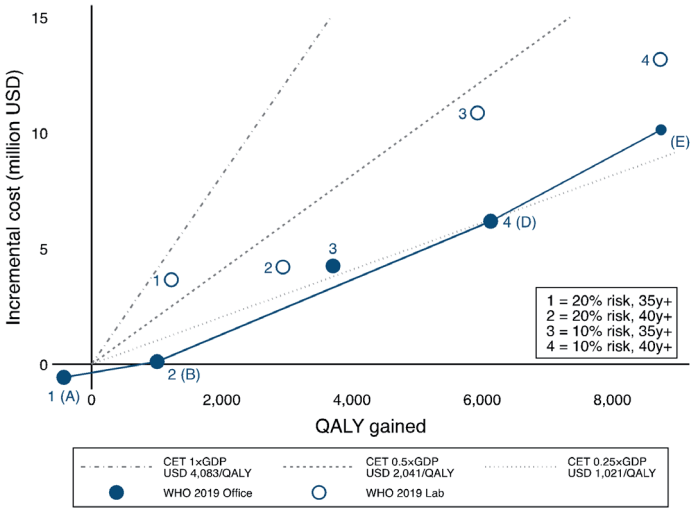
The predicted incidence of cardiovascular disease in the following 10 years (i.e. approximately 2019-2028) was calculated for each of the WHO-ISH, WHO-2019, Globorisk and Framingham tools using weighted data from SLHAS participants. The predicted incidence using WHO-2019 most closely follows the predicted incidence using GBD data. There is a limitation to this crude analysis: the WHO-2019 tool uses GBD regional incidence data for IHD and stroke for calibration, so it is not unexpected that the prediction using the WHO-2019 tool fits the GBD data best. However, there is a lack of an alternative data source to estimate incident CVD events.

***Figure A2 Mortality rates by age and gender, for coronary heart disease and stroke***



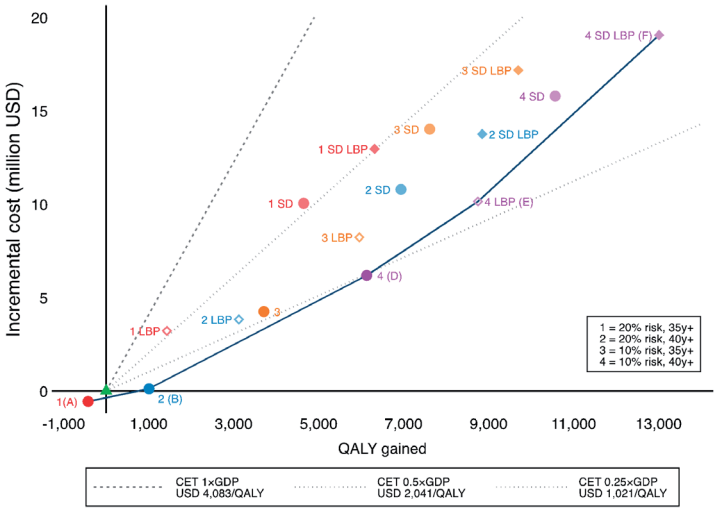

**Notes: A.** Coronary heart disease B. Stroke

***Figure A3 Comparison of ICERs of the current protocol, and proposed scenarios using the WHO-2019 lab tool versus WHO-2019 office tool***



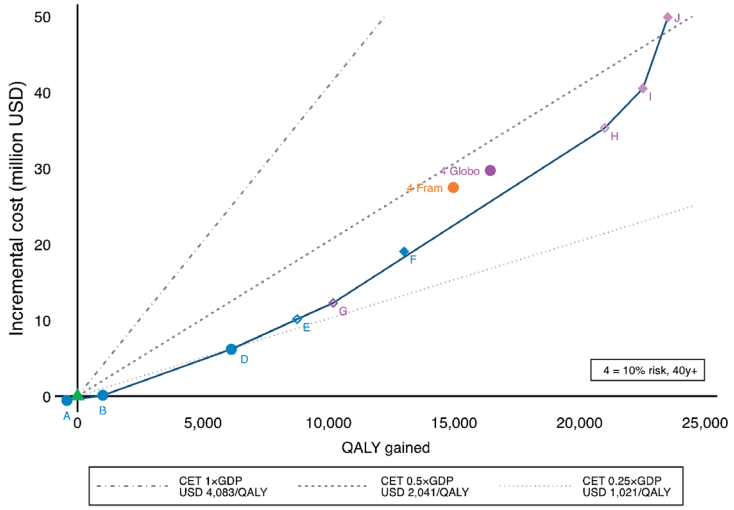

**Notes:** Scenarios A, B, D and E on the cost-effectiveness frontier shown in Table 2 and Figure 3 are shown.

*Figure A4 Cost-effectiveness frontier - LBP and SD for WHO 2019 office risk tool*




**Notes:** All scenarios used the WHO-2019 office tool. LBP = lowered blood pressure threshold, SD = statins for diabetics. Scenarios A, B, D, E, F on the cost-effectiveness frontier shown in Table 2 and Figure 3 are shown.

***Figure A5 Comparison of ICERs of the old program, and proposed programs using any risk tool, and modifying risk thresholds and age-groups screened***




**Notes:** Globo = Globorisk, Fram = Framingham. Triangles denote scenarios that used the WHO-ISH office tool. Hollow diamonds are tools that included LBP. Filled diamonds are tools that included SD and LBP. All risk tools were office based except for scenario L. Scenarios A, B, D, E, and F, which are shown in Table 2 and Figure 3 are on the cost-effectiveness frontier when considering scenarios which only use WHO-ISH and WHO-2019. When scenarios that used Globorisk and Framingham tools were included, only Scenario F was no longer on the cost-effectiveness frontier. Additionally, Globorisk scenarios G, H, I, and J were on the new cost-effectiveness frontier.

Scenario G: Globorisk office, 20%, 40+, LBP

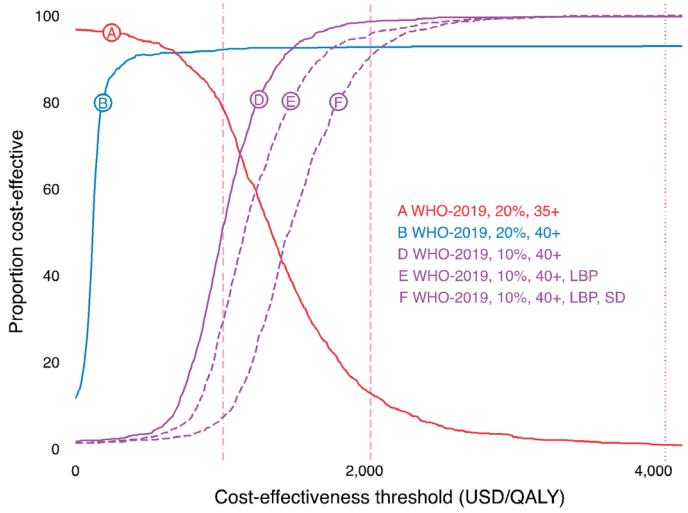
Scenario H: Globorisk office, 10%, 40+, LBP

Scenario I: Globorisk office, 10%, 40+, SD, LBP

Scenario J: Globorisk lab, 10%, 40+, SD, LBP

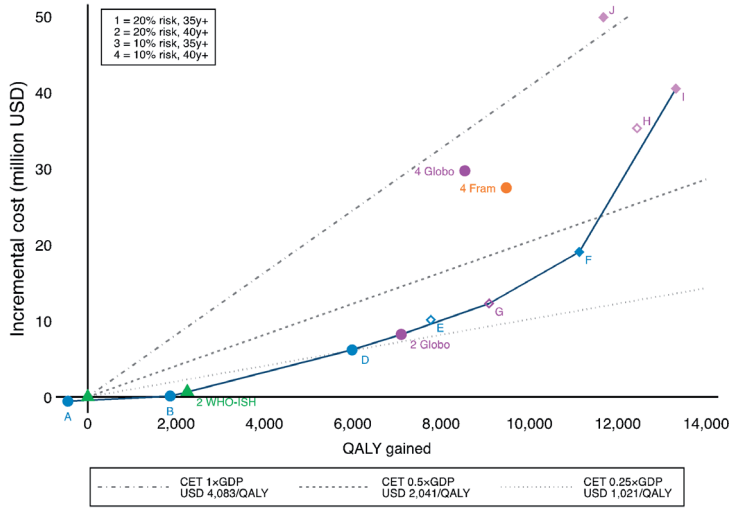
Scenarios H, I, J using Globorisk with a 10% threshold lie on the Cost-effectiveness frontier and have the highest QALYs gained out of all 129 scenarios modelled. Compared to the base case, Scenarios H and I cost below 0.5×GDP per capita/QALY, and Scenario J costs below 1×GDP per capita/QALY. However, moving from Scenario H to I and I to J costs 0.8 and 2.3×GDP per capita/QALY, respectively.

Figure A6 Probabilistic sensitivity analysis of scenarios on the cost-effectiveness frontier



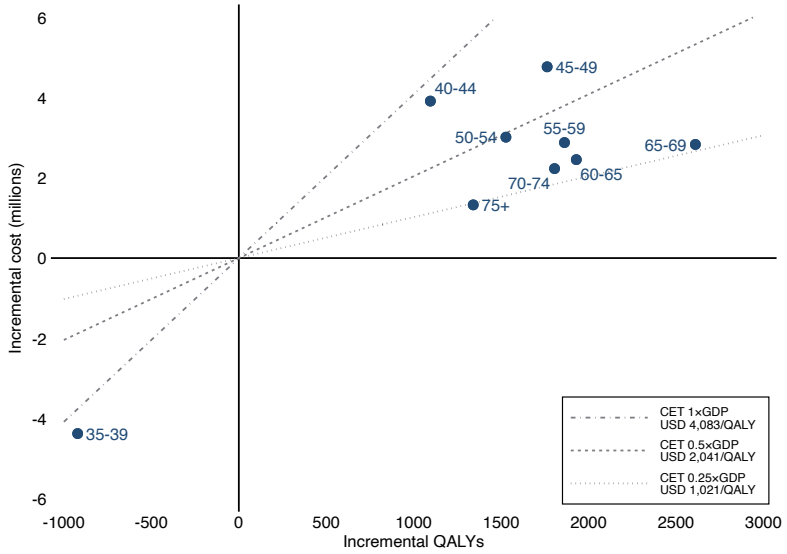

**Notes:** The probabilistic sensitivity traces are shown for scenarios A, B, D, E, and F, which were on the cost-effectiveness frontier (Figure 3). Dotted vertical lines show CET thresholds for 1 QALY at 0.25 (USD 1,021), 0.5 (USD 2,041) and 1 (USD 4,083)×GDP per capita.

***Figure A7 Impact on cost, impact and cost-effectiveness frontier, when including pill disutility***




**Notes**: Globo = Globorisk, Fram = Framingham. Triangles denote scenarios that used the WHO-ISH office tool. Hollow diamonds are scenarios that included LBP; filled diamonds are scenarios that used SD and LBP.
Scenarios A, B, D, G and I, which are on the cost-effectiveness frontier when considering all screening tools (Appendix Figure A5) remained on the frontier. However, scenarios E and H have moved slightly away from the frontier, and scenario J has moved well away from the frontier. Three programs have moved onto the frontier: F, and two additional programs labelled as 2 WHO-ISH (WHO-ISH Office, 20%, 40+) and 2 Globo (Globorisk Office, 20%, 40+).

***Figure A8 Incremental costs and QALYs by age category for Scenario G (WHO-2019 office, 10% threshold, 40+, SD and LBP) model compared to the base-case***




**Notes:** Age group 35-39 had negative QALYs and incremental cost as scenario F did not screen the 3539 age group, and the base case did.

## Text A1

Costs of medicines were calculated from data obtained from the Medical Supplies Division of the Ministry of Health (1). Laboratory costs were based on prices for reagents, consumables, and labour cost in the public sector in 2019. The cost of a consultation was calculating by dividing total public expenditure on outpatient care by the number of outpatient visits in 2019 (2, 3). We obtained the cost per hospital admission for each of CHD and stroke from a 2005 Sri Lanka public hospital survey of condition-specific costs and admissions (2, 4). We inflated these costs to 2019 values using the 2019:2005 ratio of total public inpatient expenditures.

### Costs of usual care

We also allocated a cost of usual medical care to all individuals based on an estimated average cost of inpatient and outpatient care by 10-year age groups using data from multiple sources (2-4). Usual costs for people with incident CHD or stroke in the first 10 years were increased by factors based on analysis of inpatient and outpatient contacts in people with CHD and stroke compared to those without.

Outpatient care

The total current expenditure on public outpatient care was calculated by applying the share of outpatient expenditure that is public (36%) to the total outpatient expenditure (Rs. 89,242 million) in 2019 (2, 3). Since some of this expenditure would be on people less than 18 years old, we adjusted the expenditure by the ratio of non-paediatric clinic visits to all clinic visits (0.98).

We used SLHAS Wave 1 data to estimate the weighted distribution of outpatient visits to the public sector by 10-year age groups (Appendix Table A5). The adult public expenditure on outpatient care was distributed amongst each age group based on each age group's proportion of outpatient visits. The total cost of each age group was divided by the estimated population of that age group to estimate an average annual cost for outpatient care per person of that age group (5).

Inpatient care

The total current expenditure on public inpatient care was calculated by applying the share of inpatient expenditure that is public (74%) to the total inpatient expenditure (Rs. 207,258 million) in 2019 (2, 3). To exclude expenditures on people less than 18 years old, we used

***Table A5 Distribution of inpatient and outpatient encounters, costs, and cost per capita***

| Age group | Distribution of visits | Total costs (million LKR) | Cost per capita (LKR) | Cost per capita (USD) |
|---|---|---|---|---|
| **Outpatient** | | | | |
| 18-24 | 12.49 | 3,920 | 1,748 | 9.6 |
| 25-34 | 10.04 | 3,151 | 1,064 | 5.9 |
| 35-44 | 17.47 | 5,483 | 1,786 | 9.8 |
| 45-54 | 16.13 | 5,063 | 1,938 | 10.7 |
| 55-64 | 20.67 | 6,488 | 2,853 | 15.7 |
| 65-74 | 17.33 | 5,440 | 3,544 | 19.5 |
| ≥ 75 | 5.88 | 1,846 | 2,537 | 14.0 |
| | | | | |
| **Inpatient** | | | | |
| 18-24 | 12.03 | 14,295 | 6,373 | 35.1 |
| 25-34 | 15.08 | 17,919 | 6,051 | 33.3 |
| 35-44 | 16.4 | 19,487 | 6,348 | 34.9 |
| 45-54 | 18.79 | 22,327 | 8,547 | 47.1 |
| 55-64 | 16.52 | 19,630 | 8,631 | 47.5 |
| 65-74 | 13.83 | 16,433 | 10,707 | 58.9 |
| ≥75 | 7.35 | 8,734 | 12,007 | 66.1 |

the percentage of bed-days used by people aged 18 years and over from the Public Hospital Inpatient Discharge Survey (PHIDS) (77%) (4)

Similar to the technique used for outpatient care, we used SLHAS Wave 1 data to estimate the weighted distribution of inpatient visits to the public sector by 10year age group, allocated total costs for each age group, and used the estimated population for each age group to estimate an average annual cost for inpatient care (5) (Appendix Table A5).

Adjusting costs for people with CHD and stroke

The SLHAS Wave 1 data collected information on number of inpatient and outpatient visits based on patient recall (6). Data were also collected on whether participants had CHD and stroke based on self-report and medical records. Annualised inpatient and outpatient numbers were calculated for all participants.

Negative binomial regressions were run for inpatient and outpatient encounters respectively, to determine the impact of having CHD and stroke on number of encounters, after controlling for age, gender and socioeconomic quintile. The coefficients were exponentiated to produce factors to increase annual usual inpatient and outpatient costs for individuals with CHD or stroke. The exponentiated values are also presented in Appendix Table A6.

***Table A6 Coefficients and 95% confidence intervals of negative binomial regression to assess the impact of CHD and stroke on inpatient and outpatient encounter numbers***

| | Log values | | Exponentiated values | |
|---|---|---|---|---|
| | **Coefficient** | **95% CI** | **Coefficient** | **95% CI** |
| **Inpatient** | | | | |
| CHD | 1.05 | (0.58 - 1.51) | 2.85 | (1.79 - 4.54) |
| Stroke | 0.09 | (-0.64 - 0.82) | 1.09 | (0.53 - 2.26) |
| | | | | |
| **Outpatient** | | | | |
| CHD | 0.67 | (0.37 - 0.96) | 1.95 | (1.45 - 2.61) |
| Stroke | 0.68 | (-0.19 - 1.54) | 1.97 | (0.83 - 4.69) |

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# Chapter 9

# Cost-Effectiveness and Distributional Impact of Opportunistic Screening for People at High-Risk of Cardiovascular Disease in Sri Lanka: A Modelling Study

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# ABSTRACT


## Background

While hypertension, diabetes, hypercholesterolemia and high-risk of cardiovascular disease can be easily diagnosed and treated with cost-effective medicines, a large proportion of people remain undiagnosed. We assessed the potential effectiveness, cost, and distributional impact of opportunistically screening for these chronic conditions at outpatient patient departments in Sri Lanka.

## Methods

We used nationally representative data on biomarkers and healthcare utilization in 2019 to model the screening of people aged 40+ without preexisting CVD and no reported diagnosis of hypertension, diabetes, or hypercholesterolemia. We modeled an intensive 1-month program that would screen a proportion of those making an outpatient visit to a public or private clinic and follow-up a proportion of those screened to confirm diagnoses. We also modelled a less intensive 1-year program. The main outcome was new diagnoses of any of the chronic conditions. Program costs were calculated and the socioeconomic distributions of individuals screened, new cases diagnosed, and treatments delivered were estimated. Sensitivity analyses varied the probability of screening and follow-up.

## Results

Using data on 2,380 survey participants who met the inclusion criteria, we estimated that the 1-month program would diagnose 8.2% (95% CI: 7.2, 9.3) of those with a chronic condition who would remain undiagnosed without the program. The 1-year program would diagnose 26.9% (95% CI: 25.0, 28.8) of the otherwise undiagnosed and would have a cost per person newly diagnosed of USD 6.82 (95% CI: 6.61, 7.03) in the public sector and USD 16.92 (95% CI: 16.37, 17.47) in the private sector. New diagnoses would be evenly distributed over the socioeconomic distribution, with public (private) clinics diagnosing a higher proportion of poorer (richer) individuals. Both programs would reduce underdiagnosis among males relative to females.

## Conclusions

Opportunistic screening for cardiovascular diseases at outpatient clinics in Sri Lanka could be cost-effective and equitable.

# 6.1 INTRODUCTION

In most low- and middle-income countries (LMICs), the burden of cardiovascular diseases is increasing (1) and reached 16% of all disability-adjusted life years (DALYs) in 2019 (2). In Sri Lanka, this burden is even higher at 29% of DALYs and ischemic heart disease, stroke, and diabetes mellitus accounted for 38% of mortality in 2019 (2). In high-income countries , these conditions caused 21% of DALYs and 27% of mortality (2). Screening for these diseases and their risk factors can hasten diagnosis, treatment, and control, and substantially reduce premature, avertable mortality (3). Diagnosis and management of hypertension, diabetes, and high-risk of CVD are considered "best-buys" (4), and is an important component of the Package of Essential Noncommunicable Disease Interventions for Primary Health Care in Low Resource Settings (PEN) (5). In programs screening for high-risk of CVD, risk factors, including hypertension, diabetes, and hypercholesterolemia, are detected and treated, which by extension, treats and reduces CVD risk (5).

In 2016, Sri Lanka's Ministry of Health (MOH) set targets to reduce the prevalence of hypertension by 25% and to reduce mortality due to diabetes and CVD by 20% by 2025 (6). It has set up 1,000 dedicated clinics–Healthy Lifestyle Centres–capable of screening nearly one million people a year for risk factors which lead to CVD (7-9). The screening assesses hypertension status, diabetes status, and CVD risk in people aged 35 and over without pre-existing CVD (9). While numbers screened have been increasing, only 605,000 people (7% of the target population) were screened in 2019, and only 28% of those screened were male (9).

Despite the potential for opportunistic screening for cardiovascular disease risk factors at routine medical consultations to deliver cost-effective interventions that help reorient primary care toward management of chronic diseases, it is not common in LMICs (3, 10). In Sri Lanka, where there is frequent use of outpatient (OP) care–around seven to eight visits per person per year (11)–opportunistic screening can potentially reach a much larger proportion of the target population.

This study aimed to assess the effectiveness, cost, and distributional impact of an opportunistic screening program for high-risk of CVD, along with hypertension, diabetes and hypercholesterolemia, implemented through OP visits of Sri Lankans aged 40 years and older without pre-existing CVD, and without a previous diagnosis of hypertension, diabetes or hypercholesterolemia.

# 6.2 MATERIALS AND METHODS

## 6.2.1 Survey design and measurements

We modelled the screening program using data on prevalence of CVD-related chronic conditions, their diagnoses, and healthcare utilization from the 2018/19 Sri Lanka Health and Ageing Study (SLHAS). This was a nationally representative, stratified, multi-stage cluster random sample of adults aged 18 years and older. Participants attended a field clinic close to their residence where a questionnaire was completed and biomarkers were measured (12). A medical history of hypertension, diabetes, hypercholesterolemia, and CVD was taken, along with self-reported use of healthcare and medication. Medical records, if brought to the field clinic, were checked for medications prescribed and diagnoses of hypertension, diabetes, hypercholesterolemia or CVD.

Each participant had their blood pressure (BP) measured, fasting blood glucose, and lipid profiles (Appendix Text A1). Most participants were asked how many OP visits they made to various types of healthcare facilities in a 28-day recall period. Others were randomly assigned to report OP visits in one of two other recall periods.

***Table 1 Criteria used to define disease state and diagnosis status of the chronic conditions of SLHAS participants for inclusion in modeling***

| Criteria by condition | Has condition | Already diagnosed |
|---|---|---|
| Hypertension | | |
| a) reported having been diagnosed with hypertension or their medical records showed this | ✓ | ✓ |
| b) reported taking antihypertensives in the past 14 days | ✓ | ✓ |
| c) had a systolic blood pressure of 140 mmHg or more, or a diastolic blood pressure of 90 mmHg or more | ✓ | |
| Diabetes | | |
| a) reported having been diagnosed with diabetes or their medical records showed this | ✓ | ✓ |
| b) reported taking oral hypoglycemics or insulin in the past 14 days | ✓ | ✓ |
| c) had a fasting blood glucose ≥ 126 mg/dL, a random glucose ≥ 200 mg/dL, or an oral glucose tolerance test result ≥ 200 mg/dL | ✓ | |
| Hypercholesterolemia or high CVD risk | | |
| a) reported having been diagnosed with hypercholesterolemia or their medical records showed this | ✓ | ✓ |
| b) reported taking a statin in the past 14 days | ✓ | ✓ |
| c) had a total cholesterol of 300 mg/dL or more | ✓ | |
| d) had a 10-year CVD risk based on the 2019 WHO risk charts (13) of 20% or more | ✓ | |

**Notes:** Only one applicable criteria under each condition needs to be fulfilled for a participant to be categorized as "has condition" and "already diagnosed". Criteria c) and d) are referred to as biomarker data in Calculations.

### 6.2.2 Classification

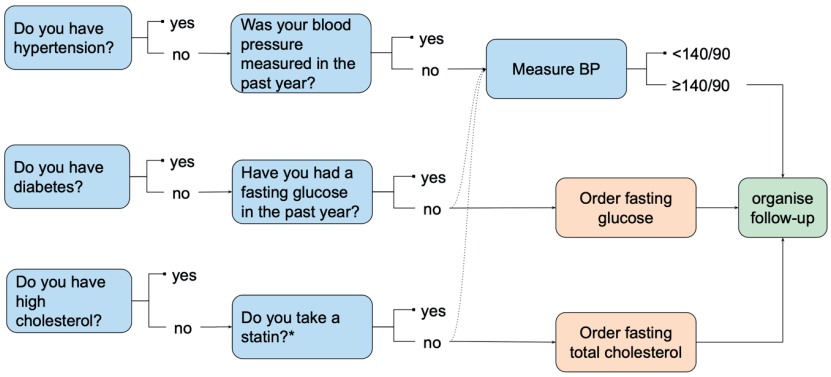
For the modelling exercise, we used the data on biomarkers, reported diagnoses and medication, medical records and criteria given in Table 1 to determine whether each participant had and was already diagnosed with any of three chronic conditions: i) hypertension, ii) diabetes, and iii) hypercholesterolemia or high-risk of CVD. A participant was "undiagnosed" if they fulfilled any criterion for "has condition" but did not satisfy any criterion for "already diagnosed". We grouped hypercholesterolemia and high-risk of CVD together as one condition since either is sufficient to prescribe statins according to respective guidelines (12). Participants with pre-existing CVD, which we defined as participants who reported or had medical records consistent with having been diagnosed with angina, coronary artery disease or myocardial infarction, were not eligible for screening.

We identified OP visits to public and private specialist clinics, public and private general clinics, and public Medical Officer of Health clinics as those at which opportunistic screening could potentially be initiated.

### 6.2.3 Intervention

We modeled a screening process (Figure 1, Appendix Text A1) that incorporates steps specified in the Sri Lankan Ministry of Health guidelines for screening (12). It begins with simple questions, similar to those asked in the SLHAS survey, for people without preexisting CVD, to ascertain whether a patient has a history of hypertension, diabetes or hypercholesterolemia. Negative answers trigger a further set of questions or BP measurement and ordering of a fasting glucose or cholesterol test, as appropriate. In most cases, a second follow-up appointment is arranged, either at the same clinic for a regular patient or at a nearby Healthy Lifestyle Centre, to repeat measurement of BP, review fasting glucose and cholesterol results, calculate CVD risk based on these measurements, diagnose hypertension or diabetes, determine whether a statin is required based on cholesterol and/or predicted CVD risk and explain the management plan to the patient where needed.

*Figure 1 Processes of the screening program for people without preexisting CVD*




We modeled a national program in which initial screenings would take place within a 28-day period which could be pitched as a CVD-riskscreening month. We assumed that screening would occur in 60% of OP visits to public facilities and 55% of OP visits to private clinics. These rates were based on estimates that process quality of care indicators, such as measuring BP in a known hypertensive patient or measuring blood glucose in a diabetic patient, were met in 70% and 65% of relevant OP consultations in the public and private sectors, respectively (14). This parameter was changed in sensitivity analyses.

In addition to a 28-day program, we modeled a program that would run less intensively for one year. In this program, we assumed screening would occur in 30% and 28% of OP visits to public and private facilities (that is, half the probability of the 28-day model), respectively. This program would place less demands on the day-to-day operation of clinics, but it would run over a longer period.

We assumed that 60% of those who would be screened in both the 28-day and 1-year programs would attend a follow-up visit irrespective of health status, sociodemographic characteristics, and type of facility initially visited, with this parameter varied in sensitivity analyses from 40% to 80%. A small intervention trial in the US, found that over 60% of participants who were screened and had been told they were at elevated risk for CVD had visited a doctor within three months (15).

### 6.2.4 Outcomes

The main outcomes were the number of people newly diagnosed with any of the three chronic conditions, this number as a proportion of those who would remain undiagnosed without the program, and the cost per person newly diagnosed. In secondary analysis, we estimated the number and proportion newly diagnosed for each of the three conditions separately.

### 6.2.5 Calculations

We used binomial probabilities to calculate the probability that a participant would get the initial screen based on the number of OP visits reported over a 28-day period (Appendix Text A1). For the 1-year program, we did not have data on OP visits over a 1-year period. Separately for public and private OP visits and by age, sex, and socioeconomic group, we estimated the proportion of participants that would have an OP visit in a year by extrapolating from a model of how the probability of having an OP visit varied for a 7-day, a 14-day and a 28-day recall period (see Appendix Text A1).

The number of patients screened was calculated by multiplying each participant's sample weight ($w_i$) by their probability of being screened ($p_i$) and summing over all participants ($\sum w_i p_i$). The weights scale the sample and make it representative of the population of Sri Lanka aged 40 years and over. We then calculated the number of patients followed-up by multiplying the number screened by the probability of follow-up (0.6). For each of the chronic conditions, the number of people that would be newly diagnosed by the screening program was the number followed-up who were identified to have that condition using the biomarker data but who were previously undiagnosed (Table 1). We also calculated the proportions of people with a chronic condition according to biomarker data but were undiagnosed and would be newly diagnosed by the screening program. For each chronic condition, we calculated how many were already diagnosed, how many would be newly diagnosed in the 28day program, how many would be additionally diagnosed in the 1-year program, and who would not be diagnosed in either program.

Following the same general procedure, we calculated the number of newly diagnosed cases identified through opportunistic screening at OP visits to public and private facilities separately. The weight of a participant who visited both sectors was distributed proportionately based on the number of visits to each sector and the respective probability of screening. Costs were calculated separately for the public and private sectors. Costs for the public sector were from a government budgetary perspective, and covered consumable, reagent and labour costs for laboratory testing and the cost for a follow-up visit. Costs for the private sector were from a patient perspective, covering prices of laboratory tests and the cost for a follow-up visit, although private sector doctors often do not charge when followingup reports ordered at a

previous appointment. Costs were based on prices quoted in the public and private sectors in 2021, which were converted to December 2021 US dollars (US$1=LKR 201.40) (16).

We used concentration curves and concentration indices (17) to assess socioeconomic inequality in the distributions of undiagnosed cases before and after the opportunistic screening intervention, and to measure inequality in the distribution of newly diagnosed cases. We proxied socioeconomic status by a wealth index equal to the first principal component from analysis of a battery of household durable assets, housing quality, water and sanitation facilities, and other assets (Appendix Table A3). A concentration curve traced the cumulative proportion of undiagnosed cases, for example, against the cumulative proportion of the sample ranked from the poorest according to the wealth index to the richest. A concentration curve above (below) the 45-degree line of equality indicates a disproportionate concentration of cases among the poor (rich). We measured inequality using a concentration index appropriate for a binary outcome (18). A negative (positive) concentration index indicates inequality in the direction of the poor having more (less) of the outcome. We used a two-sample z-test to test a null hypothesis of equal proportions of newly diagnosed (or undiagnosed) between groups defined by the poorest and richest quintiles of the wealth index distribution.

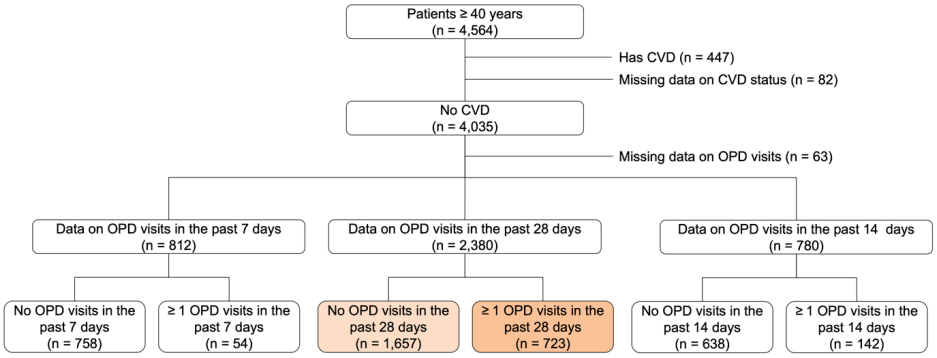
### 6.2.6 Sensitivity analysis

For both the 28-day and 1-year programs, we evaluated the impact of varying the assumed probability of follow-up from 60% to 80% and 40%. We also modeled a 1-year program that would have the same screening probabilities and so be as intensive as the 28-day program.

## 6.3 RESULTS

Out of 6,668 participants aged 18+, 4,564 were aged 40+, and 4,035 of those in this age group had no history of CVD (Figure 2). After the loss of 63 participants with no data on OP visits, there were 3,972 participants in the analysis sample. Of these, 2,380 had data on OP visits in the past 28 days and were used to model the 28-day program. In this sub-sample of 2,380 people, 730 (31%) had at least one chronic condition that was undiagnosed (Table 2). Among those with an undiagnosed chronic condition, around 63% (458/730) had undiagnosed hypertension, 31% (228/730) had diabetes, and 33% (241/730) had hypercholesterolemia or high CVD risk. Of these 730 participants, 176 (24.1%) had more than one undiagnosed condition.

*Figure 2 Participant flow*




Over 25% of those who had any undiagnosed chronic condition had an OP visit in the past 28 days (Table 2). Among participants with an undiagnosed chronic condition, higher percentages had visited public sector facilities.

***Table 2 Sample participants ≥ 40 years with an undiagnosed chronic condition, and percent with outpatient (OP) visits by sector***

| Undiagnosed condition | Number | Percent with any OP visit (%) | | |
|---|---|---|---|---|
| | | Public | Private | Any |
| 28-day period | | | | |
| Hypertension | 458 | 13.4 | 12.5 | 25.5 |
| Diabetes | 228 | 16.6 | 5.3 | 21.7 |
| Hypercholesterolemia or high CVD risk | 241 | 16.1 | 8.7 | 24.8 |
| Any | 730 | 15.0 | 10.7 | 25.4 |
| 1-year period | | | | |
| Hypertension | 749 | 40.2 | 30.5 | 58.5 |
| Diabetes | 368 | 40.1 | 30.6 | 58.5 |
| Hypercholesterolemia or high CVD risk | 398 | 40.6 | 30.2 | 58.6 |
| Any | 1,220 | 40.3 | 30.5 | 58.5 |

**Notes:** Percentages calculated from weighted sample.

Out of the 3,972 participants used to model the 1-year program – that is, people with no CVD and had data on whether they had a OP visit in the past 7, 14 or 28 days – 31% (1,220/3,972) had an undiagnosed chronic condition. From the model, over half (59%) of those with an undiagnosed chronic condition would have at least one OP visit in a year.

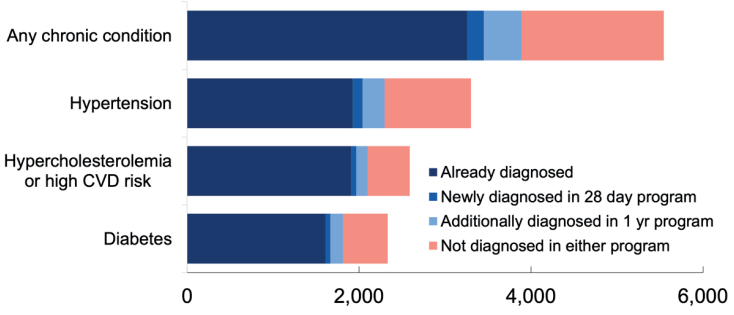
Scaled to the Sri Lankan population, we estimated that there would be 2.32 million people (95% CI: 2.317, 2.322) without a previous diagnosis of CVD with an OP visit within a 28day period that would be eligible for opportunistic screening (Table 3). Using the assumed

probabilities of undergoing opportunistic screening when attending public and private sector clinics, we estimated that 1.4 million people (95% CI: 1.29, 1.53) would be assessed in a 28-day screening program. Assuming that 60% of those assessed and requested to return for a follow-up visit would make that visit, 666 thousand (95% CI: 615, 718) would complete the screening process, and 192 thousand (95% CI: 167, 217) would be newly diagnosed with one or more of the chronic conditions. Of those assessed, 13.6% (191,959/1,411,970) (95 CI: 11.0, 16.2) would be newly diagnosed with at least one chronic condition.

With a less intensive 1-year program that would screen lower proportions of those with OP visits, we estimated that about 4.5 million (95% CI: 4.37, 4.60) patients would be eligible for screening, and 3.7 million (95% CI: 3.59, 3.78) of them would be assessed, with 17.0% (95% CI: 15.8, 18.2) of those assessed (627,531/3,682,674) being newly diagnosed with at least one chronic condition (Table 3).

The 28-day program would identify 8.0% (95% CI: 6.5, 9.4) of undiagnosed hypertensives, 7.4% (95% CI: 5.9, 8.9) of undiagnosed diabetics and 8.7% (95% CI: 6.8, 10.7) of those with undiagnosed hypercholesterolemia or high CVD risk, in the population aged 40 years or more (Figure 3, Appendix Table A4). Overall, 8.2% (191,959/2,331,756) (95% CI: 6.8, 9.6) of people with any undiagnosed chronic condition would be diagnosed. The 1-year program was estimated to detect 26.9% (627,531/2,331,756) (95% CI: 26.5, 27.4) of people with any undiagnosed chronic condition. Males would comprise 42% (279,634/666,493) (95% CI: 37, 47) of those screened and followed-up (Appendix Table A5).

***Figure 3 Population estimates of people with chronic conditions that are diagnosed before screening, diagnosed by screening and undiagnosed after screening in 28-day program and 1year program ('000s)***



With the 28-day program, the cost to the government per person screened in the public sector was estimated to be US$1.01 (95% CI:0.90, 1.13), and the cost per person diagnosed was US$7.05 (95% CI:6.24, 7.85) (Table 3). The costs in the 1-year program are similar, where the public cost per person screened is US$1.17 (95% CI: 1.13, 1.20) and cost per diagnosis is US$6.82 (95% CI: 6.61, 7.03). The estimated total cost to the government was US$867,000 with the 28-day program and US$2,555,000 with the 1-year program (Table 3), which is 0.07% and 0.21% of total public health expenditure in 2019, respectively (19). The out-of-pocket costs for patients in the private sector was estimated to be US$2.64 (95% CI: 2.32, 2.97) per person screened in the 28-day program and US$2.87 (95 CI: 2.78, 2.96) in the 1year program, with the total spent being the equivalent of 0.12% and 0.35% of total private health expenditure, respectively (19) (Appendix Table A6).

Table 4 shows the distributions of people eligible for screening, undiagnosed before and after screening, and newly diagnosed by screening by socioeconomic quintile, with estimated numbers shown in Appendix Table A7. Of the people eligible for screening, 59% (95% CI: 53, 64) of the poorest quintile and 70% (95% CI: 65, 76) of the richest quintile had at least one chronic condition. Point estimates indicate that the percentage with an undiagnosed chronic condition was higher in the poorest quintile than in the richest quintile, although this difference is not significant (32.5% vs 29.5%, p=0.4). The negative concentration index (C) (0.11; 95% CI: -0.16, -0.05; p<0.001) confirms that poorer individuals with a chronic condition were more likely to be undiagnosed before screening with the 28-day program, which is also demonstrated by a concentration curve that lies above the 45-degree line in Figure 4A. We estimated that after implementation of this program the distribution of undiagnosed chronic conditions amongst those with a chronic condition would become very slightly less concentrated on poorer individuals, which is indicated by a concentration index that is smaller in magnitude (C=-0.09; 95% CI: -0.14, -0.04; p=0.001) and less undiagnosed people in the poorer quintiles following the intervention (Figure 4B). However, neither the concentration indices nor the concentration curves are significantly different. We estimated that new diagnoses of any chronic condition identified through screening at public clinics would be slightly skewed toward the poor (C=-0.03; 95% CI: -0.04, -0.02; p<0.001), confirmed by the concentration curve above the 45-degree line in Figure 4C) while private clinics would make slightly more new diagnoses of richer individuals (C=0.01; 95% CI 0.002, 0.018; p=0.013, confirmed by the concentration curve below the 45-degree line in Figure 4D). Overall, considering both public and private sectors, new diagnoses would be slightly more concentrated among poorer individuals (C=-0.02; 95% CI: -0.03, -0.004; p=0.01).

Estimates for the sensitivity analyses are shown in Appendix Table A5 and A6. The cost per person diagnosed ranged from US$6.44 to US$7.73 in the public sector and US$15.03 to US$25.75 in the private sector. A more intensive 1-year program, where probability of

*Table 3 Population estimates of people aged ≥ 40 years without pre-existing CVD, who are assessed, followed-up and newly diagnosed in 28-day and 1-year opportunistic screening programs*

| | Eligible for screening with ≥ 1 OP visit† No. ('000s) (95% CI) | Assessed No. ('000s) (95% CI) | Followed-up No. ('000s) (95% CI) | Newly diagnosed | | Cost per person screened (USD) (95% CI) | Cost per person diagnosed (USD) (95% CI) | Total cost (USD '000) (95% CI) |
|---|---|---|---|---|---|---|---|---|
| | | | | No. ('000s) (95% CI) | As % of assessed ‡ No. ('000s) (95% CI) | | | |
| **28-day program** | | | | | | | | |
| Public | 1,400 (1,398, 1,402) | 857 (776, 939) | 396 (350, 441) | 123 (98, 148) | 14.3 (11.0, 17.7) | 1.01 (0.90, 1.13) | 7.05 (6.24, 7.85) | 867 (768, 966) |
| Private | 976 (974, 978) | 555 (483, 627) | 271 (230, 311) | 69 (49, 89) | 12.4 (8.6, 16.2) | 2.64 (2.32, 2.97) | 21.27 (18.67, 23.88) | 1,467 (1,288, 1,647) |
| All | 2,320 (2,317, 2,322) | 1,412 (1,292, 1,532) | 666 (615, 718) | 192 (167, 217) | 13.6 (11.0, 16.2) | 1.65 (1.52, 1.79) | 12.16 (11.16, 13.16) | 2,334 (2,141, 2,527) |
| **1-year program** | | | | | | | | |
| Public | 3,084 (3,007, 3,162) | 2,191 (2,13, 2,248) | 1,147 (1,112, 1,182) | 375 (348, 401) | 17.1 (15.9, 18.3) | 1.17 (1.13, 1.20) | 6.82 (6.61, 7.03) | 2,555 (2,476, 2,634) |
| Private | 2,336 (2,276, 2,396) | 1,492 (1,450, 1,535) | 770 (745, 796) | 253 (235, 271) | 17.0 (15.7, 18.2) | 2.87 (2.78, 2.96) | 16.92 (16.37, 17.47) | 4,281 (4,143, 4,419) |
| All | 4,483 (4,371, 4,596) | 3,683 (3,587, 3,778) | 1,918 (1,859, 1,976) | 628 (584, 671) | 17.0 (15.8, 18.2) | 1.86 (1.80, 1.91) | 10.89 (10.56, 11.23) | 6,836 (6,625, 7,047) |

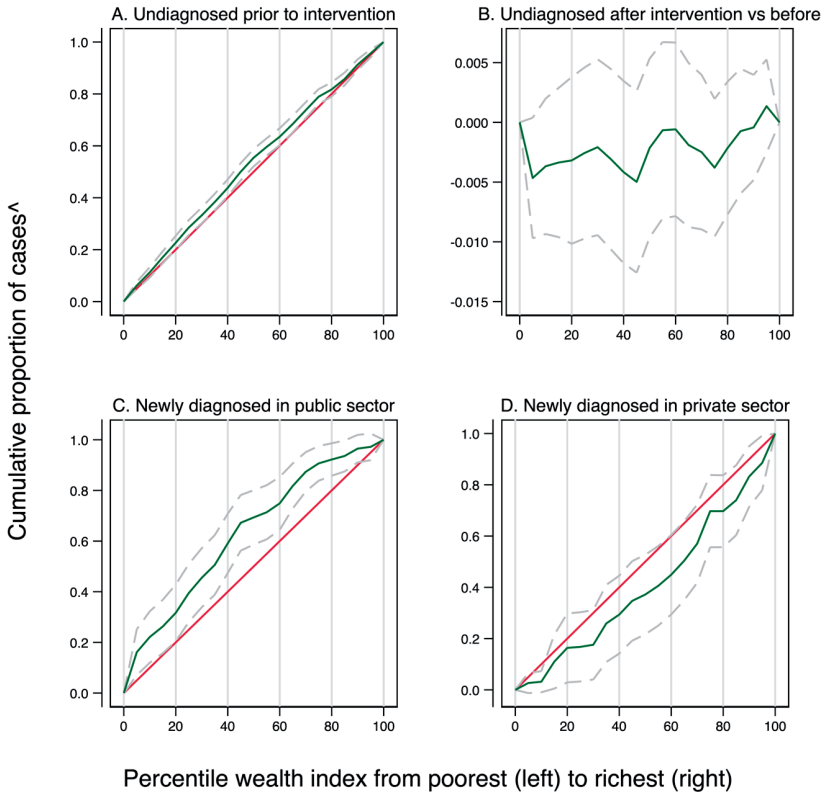
**Notes:** †People aged 40 years and over without pre-existing CVD are eligible for screening, regardless of chronic condition status. ‡Percentage of all people with an undiagnosed chronic condition, regardless of whether they reported an OP visit.

*Table 4 Distributions of screening eligible, undiagnosed and newly diagnosed individuals by socioeconomic status with 28-day screening program*

| SES quintile | Eligible for screening† No. ('000s) (95% CI) | Eligible for screening with ≥ 1 chronic condition % (95% CI) | Undiagnosed | | Newly diagnosed | | |
|---|---|---|---|---|---|---|---|
| | | | Before screening % (95% CI) | After screening % (95% CI) | Public % (95% CI) | Private % (95% CI) | Both % (95% CI) |
| 1 (poorest) | 1,536 (1,424, 1,647) | 58.7 (53.2, 64.2) | 32.5 (27.2, 37.8) | 29.2 (24.5, 34.0) | 2.5 (1.4, 3.7) | 0.7 (0.0, 1.4) | 3.3 (2.0, 4.5) |
| 2 | 1,533 (1,423, 1,642) | 58.8 (53.1, 64.4) | 29.1 (23.8, 34.3) | 26.9 (21.9, 32.0) | 1.6 (0.9, 2.3) | 0.5 (0.0, 1.0) | 2.1 (1.3, 3.0) |
| 3 | 1,528 (1,428, 1,628) | 62.9 (57.4, 68.4) | 31.3 (26.1, 36.5) | 29.0 (24.0, 33.9) | 1.6 (0.7, 2.6) | 0.7 (0.2, 1.2) | 2.3 (1.3, 3.4) |
| 4 | 1,531 (1,427, 1,636) | 65.4 (59.9, 70.9) | 29.9 (24.6, 35.2) | 27.1 (22.2, 32.0) | 1.6 (0.8, 2.5) | 1.2 (0.5, 1.9) | 2.8 (1.8, 3.9) |
| 5 (richest) | 1,532 (1,417, 1,647) | 70.1 (64.8, 75.5) | 29.5 (24.1, 34.8) | 27.5 (22.4, 32.5) | 0.6 (0.1, 1.2) | 1.4 (0.6, 2.1) | 2.0 (1.1, 2.9) |
| Total | 7,660 (7,418, 7,902) | 63.2 (60.7, 65.6) | 30.4 (28.1, 32.8) | 27.9 (25.7, 30.1) | 1.6 (1.2, 2.0) | 0.9 (0.6, 1.2) | 2.5 (2.0, 3.0) |
| **Concentration index (95% CI)** | | | | | | | |
| | Eligible with ≥ 1 chronic condition‡ | Not applicable | -0.106 (-0.164, -0.049) p<0.001 | -0.089 (-0.143, -0.035) p=0.001 | -0.027 (-0.038, -0.016) p<0.001 | 0.010 (0.002, 0.018) p=0.013 | -0.017 (-0.030, -0.004) p=0.010 |
| | Eligible* | 0.100 (0.055-0.145) p<0.001 | -0.019 (-0.062, 0.023) p=0.375 | -0.012 (-0.052, 0.027) p=0.541 | -0.014 (-0.021, -0.008) p<0.001 | 0.008 (0.003, 0.013) p=0.003 | -0.007 (-0.015, 0.002) p=0.111 |

**Notes:** †People aged 40 years and over without pre-existing CVD. ‡Concentration index calculated on all people aged 40 years and over without preexisting CVD, and with at least one chronic condition. *(remove space)Concentration index calculated on all people aged 40 years and over without preexisting CVD.
SES = socioeconomic status,

*Figure 4 Concentration curves for undiagnosed cases before and after screening and for newly diagnosed cases*




**Notes:** Concentration curves drawn for people aged 40 years and over without preexisting CVD, with at least one chronic condition. ^ y-axis for Figure B is the difference of the proportion undiagnosed after intervention and proportion undiagnosed before intervention. Grey dashed lines show the 95% confidence intervals of the concentration curves.

assessment was doubled to 60% in the public sector and 55% in the private sector, marginally increased the percentage of newly diagnosed cases from 27% to 32%, with the total cost to the government increasing by a similar amount (16%). The program with the most impact is a 1-year program with high probabilities of screening per encounter (60% in the public sector and 55% in the private sector), as well as a high follow-up rate of 80%. Such a program would newly diagnose 42% of undiagnosed cases; the costs per person diagnosed is similar to the 1-year base case, and the total cost for the public health sector would be 0.31% of the 2019 annual expenditure on health by the government. The cost per person diagnosed in the government sector reduced by 5% if the follow-up rate increased from 60% to 80%, and increased by about 10% if the follow-up rate reduced from 60% to 40% in both the

28-day and 1-year scenarios. For example, in the 1-year scenario where the probability of being screened is 30% in the public sector and 28% in the private sector, if the probability of follow-up was lowered from 60% to 40%, the proportion of undiagnosed people that would be newly diagnosed over the course of the year reduces from 27% to 18%, with a 10% increase in the cost per diagnosis from US$6.82 to US$7.53.

## 6.4 DISCUSSION

Opportunistic screening at healthcare encounters has been proposed to increase detection of chronic conditions in LMICs (3, 20). However, there was a lack of evidence on the effectiveness, cost, and distributional impact of such.

Our study finds that opportunistic screening could moderately increase the detection of people with undiagnosed chronic conditions. With a pragmatic 28-day program in which 60% of OP patients at public clinics and 55% of OP patients at private clinics would be assessed, and only 60% followed-up, we estimated that 8% of people with an undiagnosed chronic condition would be detected. With a 1-year program in which the probabilities of assessment on a single encounter were lowered to 30% and 20% for public and private clinics, respectively, 27% of those with an undiagnosed chronic condition would be detected. Furthermore, the distribution of new diagnoses was broadly distributionally neutral: overall, the distribution of people with an undiagnosed chronic condition would become slightly less skewed towards the poor. The detection of new diagnoses would be slightly pro-poor at public clinics and slightly pro-rich at private clinics. Whilst the government could introduce screening that is pro-poor in the public sector, it is likely that there will be spill-on effects in the private sector since most physicians in the private sector are government doctors engaged in dual practice (14).

A major advantage of opportunistic screening over community-based screening is that it makes use of doctors and facilities that are already available. Although such a screening program would require additional resources at several stages, most requirements are likely to be manageable. First, the initial assessment, which involves asking patients a simple set of questions, taking physical measurements, and arranging laboratory tests and follow-up, would require only a slight lengthening of the duration of existing consultations, and could potentially be carried out by several types of healthcare staff, particularly in the public sector (21). Furthermore, screening would take place in only 3.7% of all public OP visits (2.2 million out of 58.7 million visits in 2019 (9)) in the 1-year program. The private sector generally has longer consultation times, which may be compatible with a quick assessment (14). Whilst it is difficult to ascertain the burden on laboratory testing, the envisaged cost of laboratory supplies for the 1-year program in the government sector is 1% of the total government laboratory supplies expenditure

reported in 2019 (9), suggesting it would be feasible to absorb laboratory testing of publicly assessed participants in the public sector, with labour for testing costed as well. The number of visits required for follow-up in the public sector would represent, at most, a 2% increment to the total OP visits in 2019 (9), assuming that they cannot be absorbed into existing follow-up visits and the underutilized capacity of Healthy Lifestyle Centres of 200,000 patients a year. Though this may require extra planning prior to launching a large-scale screening program, given that there was a 2.4% annual increase in public OP visits between 2008 and 2019, it is possible the system would be able to absorb the additional follow-up visits needed (9, 22). Nevertheless, the cost of follow-up, including personnel, infrastructure and indirect costs, was included for both sectors.

Even in the intensive 1-year screening program, the total cost to the government was estimated at USD 3,745,000, which is 0.31% of the total annual public health expenditure for 2019 (19). A 1-year program with a modest screening probability can diagnose more people, at less cost per diagnosis, than a high-intensity one month program.

We modeled a uniform follow-up rate by disease condition because the conditions considered are largely asymptomatic, and there is no disease-based reason to expect a differential in follow-up visit rates. However, follow-up rates may vary, particularly by gender and socioeconomic status. In the sensitivity analysis, higher follow-up rates would reduce the cost per person diagnosed and proportionately increase the percentage of new diagnoses. However, even a 1-year program with a probability of screening of 30% and 28% per public and private sector encounter, and a low follow-up rate of 40%, would still newly diagnose 18% of undiagnosed people, with a marginal increase in cost per diagnosed person in the public sector compared to the base case. To increase the impact of the program, reduce cost per diagnosis, and ensure that any expansion of the health system is fully utilized, it is imperative the follow-up rates be increased as much as possible.

Whilst richer people were more likely to have a chronic condition, poorer people were more likely be undiagnosed. This is similar to other LMICs (23, 24) with authors hypothesizing that higher diagnosis rates in the rich may be due to better access to screening (23). Diagnoses from opportunistic screening at public clinics would slightly more concentrated on poorer people. However, poorer people would predominate among those who remained undiagnosed after opportunistic screening, with the extent of this inequality depending on how intensive the screening programs in the public and private sectors would be and how much follow-up would be achieved in each sector and socioeconomic group. The opportunistic screening program would also likely diagnose a greater proportion of males than is currently the case at Healthy Lifestyle Centres. The projected reductions in inequalities in diagnosis are consistent with a

study which found opportunistic screening for hypertension in LMICs would reduce female-male and urban-rural differences in diagnosis of hypertension (10).

There are several limitations to this study. The estimates of doctor visits for the 1-year program relied on modeling, although a subanalysis suggests that our model gives a conservative estimate of the number of people who had an OP visit in the past year (Appendix Text A1). As Sri Lanka undergoes an economic crisis with a depreciating currency and foreign exchange shortage resulting in medicine shortages, advocating for screening programs may be challenging in the short-term (25), given that up to 86% of those assessed would not be ultimately diagnosed with chronic conditions, and the need for initiating longterm treatment for those who reach treatment thresholds. However, implementing cost-effective screening and treatment programs for those with chronic conditions will help reduce the long-term impact and costs of undiagnosed chronic disease (20). Lastly, this study does not assess treatment and control, which are imperative to reduce the burden of disease.

The current community-based screening program for chronic conditions is problematic with limited penetration and systematic difficulty in reaching men. A key strength of this study is that it demonstrates that in a country with relatively low health spending, and where each person on average visits a doctor seven to eight times a year (similar to the OECD average (26)), and 30% of people eligible for screening have at least one undiagnosed chronic condition, the use of opportunistic screening for the four chronic conditions could newly diagnose a sizeable number of people in an equitable way, for relatively low cost.

## 6.5 CONCLUSION

The modeling exercise showed that it would be affordable, likely feasible and effective to screen opportunistically for people at high-risk for CVD. Furthermore, such a screening program would address a gender disparity diagnosis by increasing the diagnosis of males disproportionately, and it would slightly reduce socioeconomic inequality in diagnosis. It is important to assess whether the public health system would be able to absorb an estimated 2% increase in outpatient visits arising from the program.

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# APPENDIX

## Text A1

### *Additional information on survey design and measurements*

Participants in the Sri Lankan Health and Ageing Study (SLHAS) were asked to fast for 10 to 12 hours, and venous samples were taken soon after clinic arrival. Those who did not report diabetes had an oral glucose tolerance test: after the fasting samples were taken, participants drank the equivalent of 75 grams of anhydrous glucose in solution, and a repeat venous sample was taken two hours later. Plasma and serum were extracted from the venous samples in the field and transported at -30 degrees Celsius to the study laboratory at the Medical Research Institute in Colombo, where they were analyzed, usually within two weeks of sample collection.

### *Additional information on intervention*

We modeled a screening program for people aged 40 years or older who did not have a self-reported or recorded history of CVD. A person was defined as eligible for screening following Figure 1. In more detail, they were defined as eligible for screening if they fulfilled any one of:

a) no reported or recorded diagnosis of hypertension, not taking antihypertensives in the past 14 days, and no measurement of blood pressure by a health worker in the past year;

b) no reported or recorded diagnosis of diabetes, not taking oral hypoglycemics or insulin in the past 14 days, and no fasting glucose test (irrespective of result) conducted in the past year;

c) no reported or recorded diagnosis of hypercholesterolemia, and not taking a statin in the past 14 days.

These selection criteria are consistent with how the MOH guidelines for CVD screening in Sri Lanka identifies the target population. There is a slight difference in criteria for selecting participants in our model for screening, versus the criteria for identifying if a patient "has condition" for diabetes in Table 1. We did not include a recent OGTT (oral glucose tolerance test) as part of the modeling criterion for diabetes as SLHAS did not collect data on pasthistory of an OGTT (OGTT was performed in the SLHAS study itself). Furthermore, we believe it is unlikely that large numbers of people will have recent OGTT results readily available. Similarly, a history of a cholesterol test in the past 12 months was also not available in the SLHAS dataset and a cholesterol test was performed in the SLHAS study itself. A person who had a cholesterol test in the previous year would not require another cholesterol test, however our dataset limited us from modeling this. Furthermore, as the actual cholesterol level is ideally needed for CVD risk calculation, we modeled cholesterol testing for all people who

did not report hypercholesterolemia and were not taking statins, even if some may have done cholesterol tests in the past 12 months. In reality, it is possible that only a small proportion of people would have recent cholesterol test results readily available.

Examples of people who would not qualify for screening in the model:

A 45-year-old with hypertension and taking a statin, but has no reported diagnosis of diabetes, is not on oral hypoglycemics or insulins, but had a blood glucose test in the past year does not qualify for screening.

A 50-year-old who reports having diabetes and is on a statin, but has no diagnosis of hypertension, and is not on an antihypertensive, but had a blood pressure measured in the past year does not qualify for screening.

*Using binomial probability to calculate probability of being screened*

We used binomial probabilities to calculate the probability that a participant would get the initial screen based on the number of OP visits reported over a 28-day period.

The formula used was

$$P_{assesed} = 1 - ((1 - P_{a\_pub})^{n_{pub}} \times (1 - P_{a\_priv})^{n_{priv}})$$

Where $P_{a\_pub}$ is the probability of being assessed in the public sector
$P_{a\_pri}$ is the probability of being assessed in the private sector
$n_{pub}$ is the number of visits to the public sector
$n_{priv}$ is the number of visits to the private sector

For example, in the case where $P_{a\_pub}$ = 0.6 and $P_{a\_pri}$ = 0.55, a participant who had one public sector visit was given a probability of 0.6 of being screened, whilst a person with two public sector visits was assigned a probability of $1 - \left((1 - 0.6)^2 \times (1 - 0.55)^0\right) = 0.84$.

## *Calculations for a yearly program*

The SLHAS dataset used three separate recall periods for outpatient visits: Of the people aged 40 years and over with no CVD, the number of OP visits was asked from 812 people for a 7-day recall period, 780 people for a 14-day recall period and 2,380 people for a 28 day-recall period. There is no obvious way identify which proportion of people had at least one public OP visit or one private OP visit during the previous year, and of those who had either a public or private OP visit, how many visits were made to each. Presumably a proportion of people

who reported zero visits in their respective recall period would have visited at least once over a 12-month period.

Given the lack of any other survey or administrative data available to i) estimate the proportion of people with at least one public or private OP visit in the past 12 months, and ii) the number of visits per person to each sector, we attempted to model this with our dataset.

We created a dataset of the proportion of people aged 40 years and over with zero public OP visits and zero private OP visits for each gender, sector (urban, rural, estate), socioeconomic quintile and recall period in days.

We then ran a regression:

$prop_h = ß_1.\ln(day) + ß_2.sector + ß_3.sex + ß_4.sesquintile$

Where *prop* is the proportion of the group that had no healthcare visits
*h* is the public or private health sector
*day* is the recall period in days
*sector* is urban, rural or estate/rural
*sesquintile* is the socioeconomic quintile.

Variables with coefficients with a p-value greater than 0.01 were dropped from the full model. The model confirmed an association of the proportion with no visits to the public sector with the number of days in the recall period and socioeconomic quintile (Appendix Table A1). For the private sector, there was an association between the number of days in the recall period, sector and socioeconomic quintile (Appendix Table A2).

From the proportion of people who were estimated to have no visits during the previous year, we estimated the proportions of people in each sex, socioeconomic quintile and sector group who had one or more visits. We calculated the total number of visits for each group over a year based on the mean visits per person in each group for the recall period, scaled to one year, and divided it by the number of people with one or more visit to estimate the mean number of visits for each group. We then applied a Poisson distribution bounded by one, using the method outlined by Cohen (1) using Molina's tables, to estimate the distribution of visits for each group given the calculated mean. The dataset was expanded so that one record was representative of one person, and the distribution of visits was randomly applied within each group.

***Table A1 Linear regression estimates of the proportion of people with no public outpatient visits with recall time period and sociodemographic factors***

| | Full model | | | Final model | | |
|---|---|---|---|---|---|---|
| | **Coefficient** | **95% CI** | **p** | **Coefficient** | **95% CI** | **p** |
| Days (log) | -0.10 | (-0.13, -0.08) | 0.000 | -0.10 | (-0.13, -0.08) | 0.000 |
| Sector | | | | | | |
| Rural | -0.02 | (-0.06, 0.01) | 0.196 | * | * | * |
| Rural / Estate | -0.01 | (-0.05, 0.02) | 0.535 | * | * | * |
| Female | -0.02 | (-0.04, 0.01) | 0.262 | * | * | * |
| SES quintile | | | | | | |
| 2 | 0.00 | (-0.04, 0.04) | 0.997 | 0.00 | (-0.04, 0.04) | 0.997 |
| 3 | 0.02 | (-0.02, 0.07) | 0.268 | 0.02 | (-0.02, 0.07) | 0.267 |
| 4 | 0.05 | (0.01, 0.10) | 0.021 | 0.05 | (0.01, 0.10) | 0.021 |
| 5 (richest) | 0.08 | (0.04, 0.13) | 0.000 | 0.08 | (0.04, 0.13) | 0.000 |
| Constant | 1.14 | (1.06, 1.22) | 0.000 | 1.12 | (1.05, 1.20) | 0.000 |
| n | 90 | | | 90 | | |
| Adj $R^2$ | 0.476 | | | 0.476 | | |

***Table A2 Linear regression estimates of the proportion of people with no private outpatient visits with recall time period and sociodemographic factors***

| | Full model | | | Final model | | |
|---|---|---|---|---|---|---|
| | **Coefficient** | **95% CI** | **p** | **Coefficient** | **95% CI** | **p** |
| Days (log) | -0.08 | (-0.09, -0.06) | 0.000 | -0.08 | (-0.09, -0.06) | 0.000 |
| Sector | | | | | | |
| Rural | -0.01 | (-0.03, 0.02) | 0.641 | -0.01 | (-0.03, 0.02) | 0.648 |
| Rural / Estate | 0.03 | (0.01, 0.06) | 0.017 | 0.03 | (0.01, 0.06) | 0.019 |
| Female | -0.02 | (-0.04, 0.00) | 0.034 | * | * | * |
| SES quintile | | | | | | |
| 2 | -0.01 | (-0.04, 0.03) | 0.651 | -0.01 | (-0.04, 0.03) | 0.658 |
| 3 | -0.01 | (-0.04, 0.03) | 0.728 | -0.01 | (-0.04, 0.03) | 0.734 |
| 4 | -0.02 | (-0.05, 0.01) | 0.184 | -0.02 | (-0.06, 0.01) | 0.193 |
| 5 | -0.04 | (-0.07, -0.01) | 0.018 | -0.04 | (-0.07, -0.01) | 0.021 |
| Constant | 1.15 | (1.10, 1.21) | 0.000 | 1.14 | (1.09, 1.20) | 0.000 |
| n | 90 | | | 90 | | |
| Adj $R^2$ | 0.479 | | | 0.456 | | |

Whilst recognizing that visits to a sector may cluster in individuals (for example, an individual may be more likely to have mostly private sector visits with minimal or no public sector visits), it is difficult to model how much overlap of public and private visits there would be over a course of a year. However, as visits were distributed within sector-SES or SES groups, with the chance of screening very similar in both sectors, and binomial probabilities resulting in a person with multiple visits having a high probability of being screened, the impact of the method of random distribution of visits used in this analysis is likely to be minimal.

The estimates generated are likely to be conservative, given that visits may cluster in time in individuals during a short recall period. Indeed, analysis of a weighted subsample of 131 people with an undiagnosed chronic condition, who were asked when they last had an OP visit, found that 66% of people had a public OP visit in the past year and 86% had a private OP visit (separate results, not shown), which is higher than the estimates generated from our model.

The remaining analysis for assessment, follow-up and diagnosis followed the same principles as the analysis using a 28-day timeframe.

## References

1. Cohen AC. Estimating the parameter in a conditional Poisson distribution. Biometrics. 1960;16(2):203-11.

***Table A3 Assets used to calculate wealth index***

| Category | Details of assets included | |
|---|---|---|
| Durable assets | TV | |
| | VCD/DVD player | |
| | Sewing machine | |
| | Washing machine | |
| | Electric fan | |
| | Domestic phone | |
| | Mobile phone | |
| | Computer | |
| | Camera/Video camera | |
| | Bicycle | |
| | Motorcycle/Scooter | |
| | Threewheeler | |
| | Motor car/Van | |
| | Bus, Lorry/Tipper | |
| Housing quality | Bedrooms in household | |
| | Main material used for floor | Cement, terrazzo or tile, concrete, mud, wood, sand, other |
| | Main material used for walls | Brick, cabok, cement block, pressed soil block, mud, wood or sheets, cadjan, palyrah or straw, other |

| Category | Details of assets included | |
|---|---|---|
| Water and sanitization facilities | Main source of drinking water | Protected well within premises, protected well outside premises, unprotected well, river, natural spring, reservoir, tank, tap inside home, tap within premises, tap outside premises, project in village, tube well, bowser, rain water, |
| | Toilet facility | Exclusive to household, shared with another household, public convenience, no toilet facility |
| | Garbage disposal | Collected by garbage truck, burned, dumped within premises, processed for fertilizer, dumped or thrown away outside premises, other |
| Food storage and cooking facilities | Cooking place | In the house, in a separate building, outdoors, other |
| | Cooking fuel | Electricity, LP gas, natural gas, biogas, kerosene, coal or lignite, charcoal, wood, straw, shrubs or grass, agricultural crops, animal dung, no food cooked in house, other |
| | Fridge | |
| Other items | Household tenure type | Constructed/purchased & owned by an occupant, inherited & owned by an occupant, freely received/received as a gift & owned by occupant, compensated, rent free (employer/other), relief payment (employer/other), rent - government owned, rent - privately owned, lease - government owned, lease -privately owned, encroached, other |
| | Principal type of lighting | Kerosene, electricity, solar energy, battery or generator, gas, other |
| | Internet | |

***Table A4 New diagnoses by program and chronic condition***

| | | Newly diagnosed in 28-day program | | Newly diagnosed in 1-year program | |
|---|---|---|---|---|---|
| **Chronic condition** | **Total undiagnosed No. ('000s) (95% CI)** | **No. ('000s) (95% CI)** | **as % of total undiagnosed (95% CI)** | **No. ('000s) (95% CI)** | **as % of total undiagnosed (95% CI)** |
| Any chronic condition | 2,332 (2,148, 2,515) | 192 (167, 217) | 8.2 (6.8, 9.6) | 628 (584, 671) | 26.9 (26.5, 27.4) |
| Hypertension | 1,413 (1,266, 1,559) | 112 (92, 133) | 8.0 (6.1, 9.8) | 370 (335, 404) | 26.2 (25.6, 26.8) |
| Hypercholesterolemia or high CVD risk | 708 (599, 817) | 62 (48, 75) | 8.7 (6.2, 11.3) | 195 (170, 221) | 27.6 (27.2, 28.1) |
| Diabetes | 770 (663, 877) | 57 (45, 68) | 7.4 (5.2, 9.6) | 204 (177, 230) | 26.5 (25.7, 27.2) |

*Table A5 Sensitivity analysis: Number of people assessed, followed-up, and diagnosed by probability of assessment and follow-up, 28day and 1-year program*

| Scenario | Probability of assessment (public %, private %) | Probability of follow-up (public %, private %) | Assessed No. ('000s) (95% CI) | Followed-up No. ('000s) (95% CI) | Males followed-up No. ('000s) (95% CI) | As % of followed-up group (95% CI) | Newly diagnosed cases No. ('000s) (95% CI) | As % of undiagnosed cases‡ (95% CI) |
|---|---|---|---|---|---|---|---|---|
| 28-day program | 60, 55 | 80, 80 | 1,412 (1,292, 1,532) | 889 (820, 957) | 373 (329, 417) | 42 (37, 47) | 256 (207, 304) | 11.0 (9.1, 12.8) |
| 28-day program * | 60, 55 | 60, 60 | 1,412 (1,292, 1,532) | 666 (615, 718) | 280 (247, 312) | 42 (37, 47) | 192 (156, 228) | 8.2 (6.8, 9.6) |
| 28-day program | 60, 55 | 40, 40 | 1,412 (1,292, 1,532) | 444 (410, 479) | 186 (165, 208) | 42 (37, 47) | 128 (104, 152) | 5.5 (4.6, 6.4) |
| 1-year program | 30, 28 | 80, 80 | 3,683 (3,587, 3,778) | 2,557 (2,479, 2,634) | 1,147 (1,098, 1,195) | 45 (43, 47) | 837 (778, 895) | 35.9 (35.3, 36.5) |
| 1-year program * | 30, 28 | 60, 60 | 3,683 (3,587, 3,778) | 1,918 (1,859, 1,976) | 860 (824, 896) | 45 (43, 47) | 628 (584, 671) | 26.9 (26.5, 27.4) |
| 1-year program | 30, 28 | 40, 40 | 3,683 (3,587, 3,778) | 1,278 (1,240, 1,317) | 573 (549, 598) | 45 (43, 47) | 418 (389, 448) | 17.9 (17.6, 18.2) |
| 1-year program | 60, 55 | 80, 80 | 4,279 (4,170, 4,387) | 2,972 (2,883, 3,060) | 1,391 (1,333, 1,449) | 47 (45, 49) | 976 (909, 1,043) | 41.9 (41.2, 42.5) |
| 1-year program | 60, 55 | 60, 60 | 4,279 (4,170, 4,387) | 2,229 (2,162, 2,295) | 1,043 (1,000, 1,087) | 47 (45, 49) | 732 (681, 783) | 31.4 (30.9, 31.9) |
| 1-year program | 60, 55 | 40, 40 | 4,279 (4,170, 4,387) | 1,486 (1,441, 1,530) | 696 (667, 725) | 47 (45, 49) | 488 (454, 522) | 20.9 (20.6, 21.2) |

**Notes:**

* Base-case 28-day program and 1-year program

‡ Reported as a percentage of all people with an undiagnosed chronic condition, regardless of whether they reported an OP visit (2,331,757 people).

*Table A6 Sensitivity Analysis: Costs of screening program by probability of assessment and follow-up, 28-day and 1-year program*

| Scenario | Probability of assessment (public %, private %) | Probability of follow-up (public %, private %) | Cost per person screened (USD) (95% CI) | | Cost per person diagnosed (USD) (95% CI) | | Total cost ('000 USD) (95% CI) | | Cost as % of annual expenditure (%) (95% CI) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Public | Private | Public | Private | Public | Private | Public | Private |
| 28-day program | 60, 55 | 80, 80 | 1.28 (1.14, 1.43) | 3.15 (2.76, 3.55) | 6.71 (5.94, 7.47) | 19.04 (16.63, 21.44) | 1,100 (974, 1,226) | 1,751 (1,530, 1,972) | 0.09 (0.08, 0.10) | 0.14 (0.12, 0.16) |
| 28-day program * | 60, 55 | 60, 60 | 1.01 (0.90, 1.13) | 2.64 (2.32, 2.97) | 7.05 (6.24, 7.85) | 21.27 (18.67, 23.88) | 867 (768, 966) | 1,467 (1,288, 1,647) | 0.07 (0.06, 0.08) | 0.12 (0.10, 0.13) |
| 28-day program | 60, 55 | 40, 40 | 0.74 (0.65, 0.82) | 2.13 (1.88, 2.38) | 7.73 (6.84, 8.61) | 25.75 (22.73, 28.76) | 634 (561, 706) | 1,184 (1,045, 1,323) | 0.05 (0.05, 0.06) | 0.10 (0.09, 0.11) |
| 1year program | 30, 28 | 80, 80 | 1.47 (1.43, 1.52) | 3.41 (3.30, 3.52) | 6.47 (6.27, 6.67) | 15.08 (14.59, 15.57) | 3,231 (3,131, 3,331) | 5,087 (4,923, 5,251) | 0.27 (0.26, 0.28) | 0.41 (0.40, 0.43) |
| 1year program * | 30, 28 | 60, 60 | 1.17 (1.13, 1.20) | 2.87 (2.78, 2.96) | 6.82 (6.61, 7.03) | 16.92 (16.37, 17.47) | 2,555 (2,476, 2,634) | 4,281 (4,143, 4,419) | 0.21 (0.21, 0.22) | 0.35 (0.34, 0.36) |
| 1year program | 30, 28 | 40, 40 | 0.86 (0.83, 0.88) | 2.33 (2.25, 2.40) | 7.53 (7.29, 7.76) | 20.60 (19.94, 21.26) | 1,879 (1,821, 1,938) | 3,475 (3,363, 3,587) | 0.16 (0.15, 0.16) | 0.28 (0.27, 0.29) |
| 1year program | 60, 55 | 80, 80 | 1.47 (1.43, 1.52) | 3.41 (3.31, 3.52) | 6.44 (6.25, 6.63) | 15.03 (14.56, 15.50) | 3,745 (3,632, 3,857) | 5,930 (5,744, 6,116) | 0.31 (0.30, 0.32) | 0.48 (0.47, 0.50) |
| 1year program | 60, 55 | 60, 60 | 1.17 (1.13, 1.20) | 2.87 (2.78, 2.96) | 6.79 (6.59, 6.99) | 16.86 (16.33, 17.39) | 2,961 (2,872, 3,050) | 4,989 (4,833, 5,145) | 0.25 (0.24, 0.26) | 0.41 (0.39, 0.42) |
| 1year program | 60, 55 | 40, 40 | 0.86 (0.83, 0.88) | 2.33 (2.26, 2.40) | 7.49 (7.26, 7.72) | 20.52 (19.87, 21.16) | 2,177 (2,112, 2,243) | 4,048 (3,921, 4,175) | 0.18 (0.18, 0.19) | 0.33 (0.32, 0.34) |

**Notes:** Annual Health Expenditure in 2019 estimated at USD 1,195 million in the public sector and USD 1,228 million in the private sector converted to December 2021 US dollars (US$1=LKR 201.40).

Source: Amarasinghe S, Dalpatadu K, Rannan-Eliya R. Sri Lanka Health Accounts: National Health Expenditure 1990-2019. Colombo: Institute for Health Policy; 2021.

*Table A7 Distributions of screening eligible, undiagnosed and newly diagnosed individuals by socioeconomic status with 28-day screening program (number of participants)*

| SES quintile | Eligible for screening† No. ('000s) (95% CI) | Eligible for screening with ≥ 1 chronic condition | Undiagnosed | | Newly diagnosed | | |
|---|---|---|---|---|---|---|---|
| | | | Before screening | After screening | Public | Private | Both |
| | | No. ('000s) (95% CI) | No. ('000s) (95% CI) | No. ('000s) (95% CI) | No. ('000s) (95% CI) | No. ('000s) (95% CI) | No. ('000s) (95% CI) |
| 1 (poorest) | 1,536 (1,424, 1,647) | 901 (794, 1,009) | 499 (409, 589) | 449 (375, 523) | 39 (21, 57) | 11 (1, 22) | 50 (29, 71) |
| 2 | 1,533 (1,423, 1,642) | 901 (795, 1,007) | 446 (358, 533) | 413 (334, 492) | 25 (14, 36) | 8 (0, 15) | 33 (20, 46) |
| 3 | 1,528 (1,428, 1,628) | 961 (858, 1,065) | 478 (392, 564) | 443 (367, 519) | 25 (11, 39) | 11 (3, 18) | 36 (20, 52) |
| 4 | 1,531 (1,427, 1,636) | 1,002 (892, 1,111) | 458 (370, 545) | 414 (338, 491) | 25 (11, 38) | 18 (8, 28) | 43 (27, 60) |
| 5 (richest) | 1,532 (1,417, 1,647) | 1,074 (958, 1,191) | 451 (363, 539) | 421 (341, 500) | 10 (1, 18) | 21 (9, 33) | 30 (16, 45) |
| Total | 7,660 (7,418, 7,902) | 4,840 (4,596, 5,083) | 2,332 (2,136, 2,528) | 2,140 (1,968, 2,311) | 123 (93, 153) | 69 (47, 91) | 192 (156, 228) |
| **Concentration index (95% CI)** | | | | | | | |
| | Eligible with ≥ 1 chronic condition‡ | Not applicable | -0.106 (-0.164, -0.049) p<0.001 | -0.089 (-0.143, -0.035) p=0.001 | -0.027 (-0.038, -0.016) p<0.001 | 0.010 (0.002, 0.018) p=0.013 | -0.017 (-0.030, -0.004) p=0.010 |
| | Eligible* | 0.100 (0.055, 0.145) p<0.001 | -0.019 (-0.062, 0.023) p=0.375 | -0.012 (-0.052, 0.027) p=0.541 | -0.014 (-0.021, -0.008) p<0.001 | 0.008 (0.003, 0.013) p=0.003 | -0.007 (-0.015, 0.002) p=0.111 |

**Notes:** †People aged 40 years and over without pre-existing CVD. ‡Concentration index calculated on all people aged 40 years and over without preexisting CVD, and with at least one chronic condition. *Concentration index calculated on all people aged 40 years and over without preexisting CVD.
SES = socioeconomic status.

# Chapter 1

# Optimizing screening for cardiovascular disease risk in Sri Lanka with respect to equity and efficiency: Distributional cost-effectiveness analysis with stochastic dominance

With Pieter van Baal, Ravindra Rannan-Eliya, and Owen O'Donnell

# ABSTRACT


## Objectives

Screening for cardiovascular disease (CVD) risk is potentially cost-effective but its impact across socioeconomic groups likely depends on a) who is screened, b) what criteria are used to prescribe preventive treatment, and c) how health opportunity costs are distributed. We conducted a distributional cost-effectiveness analysis (DCEA) to identify the CVD risk screening strategy for Sri Lanka offering the best equity-efficiency trade-off.

## Methods

Using nationally representative data, we modelled four strategies of opportunistic CVD risk screening at public outpatient clinics compared with the current screening program. We measured socioeconomic status (SES) with an assets index. For each strategy, we simulated costs and quality-adjusted life years (QALYs), as well as the distribution of QALYs net of health opportunity costs by SES. We used stochastic dominance to rank strategies by impact on net QALYs over the SES distribution.

## Results

Within the current budget, total QALYs increased by raising the age for screening from ≥ 35 years to ≥ 40, prescribing statins at lower CVD risks (≥ 10% vs ≥ 20%) and to all with diabetes, and prescribing antihypertensives at lower blood pressure (130/80 vs 140/90) to all with diabetes or those at high CVD risk. These strategies coupled with opportunistic screening would generate more net QALYs across SES percentiles than the current strategy. However, the findings were sensitive to the assumed value and distribution of health opportunity costs.

## Conclusions

Stochastic dominance-based DCEA identified modifications to CVD risk screening in Sri Lanka that would improve both equity and efficiency.

# 7.1 INTRODUCTION

Cardiovascular disease (CVD) risk screening is a key component of the World Health Organization's Package of Essential Noncommunicable Disease Interventions (1). Evidence suggests it may be cost-effective when tailored to local context (2), but little is known about the socioeconomic distribution of the health impact. This limits assessment of the potential for CVD risk screening to advance progress toward Health For All, a component of the Sustainable Development Goals (3) that many health systems, including in Sri Lanka (4), strive to achieve.

Sri Lanka established a CVD risk screening program in 2011 (5). A previous study identified cost-effective modifications to the program (6) but confined attention to routine screening at designated clinics where uptake is low among males (5), and it did not examine distributional impact. Given the high frequency and pro-poor pattern of outpatient visits to public clinics (7, 8), opportunistic screening of all patients presenting at these clinics could potentially increase screening substantially and reduce inequality in its uptake (9).

Within opportunistic screening, parameters of program design can affect equity impact as well as efficiency. Setting a lower age threshold increases coverage but extends screening to many low-risk individuals for whom health gains may be less than opportunity costs falling on potential users of public healthcare with a different socioeconomic profile. The equity and efficiency consequences of prescribing preventive medications (antihypertensives and statins) based on risk factors and global CVD risk depend on the socioeconomic distributions of the risk factors as well as medicine effectiveness. In Sri Lanka, other low- and middle-income countries (LMICs) and even high-income countries, there is scant knowledge of the distributional consequences of alternative CVD risk screening strategies.

Distributional cost-effectiveness analysis (DCEA)(10, 11) can address the evidence gap but is still rarely performed (12, 13), particularly in LMICs (13-17), and has been used to evaluate CVD risk screening only once in a high-income country setting (18). DCEA applications (12, 16, 17, 19-21) usually capture the equity-efficiency trade-off in an inequality aversion parameter. Consensus on its value is unlikely and there is limited evidence to guide the choice (22, 23). An alternative is to compare health distributions using dominance analysis, which requires taking a position on the existence and direction of inequality aversion and, possibly, the range in which it lies, but avoids specification of its precise value (24, 25). This approach has not been applied in DCEA, except for one textbook illustration (24).

This study used dominance-based DCEA to evaluate strategies of CVD risk screening differing in target screening age and criteria for prescribing antihypertensives and statins with the aim of optimizing the program in Sri Lanka with respect to equity and efficiency.

# 7.2 METHODS

## 7.2.1 Screening strategies

We modelled the long-term consequences of a one-year CVD risk screening program under five strategies (Table 1). The comparator was defined by current Sri Lankan guidelines: screening people invited to attend one of 1000 Healthy Lifestyle Centres (HLCs) without a previous history of CVD and aged 35 years and older (35+) using the WHO 2019 office screening tool to calculate the 10-year risk of a CVD event (CVD risk, hereafter) (26), prescribing antihypertensives to those with blood pressure (BP) ≥ 140/90 mm Hg, antidiabetics to those with fasting blood glucose ≥ 126 mg/dL or a random blood glucose ≥ 200 mg/dL, and statins to those with a CVD risk of ≥ 20% (27, 28). We assumed the HLCs would operate at 70% capacity for 48 weeks of the year to screen 672,000 adults, which is close to the number screened in 2019 (29). Consistent with the guidelines, we assumed all individuals in the target population have an equal probability of being screened.

***Table 1 Modelled strategies of CVD risk screening***

| Treatment | Screening | Setting | Age threshold | High CVD risk | Antihypertensives at BP 130/80 mm Hg if high CVD risk or diabetes | Statins to all with diabetes |
|---|---|---|---|---|---|---|
| Current program (comparator) | Routine | Healthy Lifestyle Centre | 35+ | ≥ 20% | NO | NO |
| A | Opportunistic | Any public outpatient clinic | 35+ | ≥ 20% | NO | NO |
| B | Opportunistic | Any public outpatient clinic | 40+ | ≥ 10% | NO | NO |
| C | Opportunistic | Any public outpatient clinic | 40+ | ≥ 10% | YES | NO |
| D | Opportunistic | Any public outpatient clinic | 40+ | ≥ 10% | YES | YES |

The other modelled strategies all involved opportunistic screening at any visit to a public outpatient clinic. We assumed a 30% probability of being screened on each visit (9). In strategy A, there were no other differences from the comparator. In strategies B, C and D, the age threshold for screening was raised to 40+ and the CVD risk threshold for prescribing statins was lowered from ≥ 20% to ≥ 10% (30). Additionally, in C and D, the BP threshold for prescribing antihypertensives was lowered to 130/80 mm Hg for all people with diabetes or CVD risk ≥ 10% (31, 32). Strategy D added prescription of statins to all people with diabetes (31).

Strategies B–D were modelled because versions of them, but with routine screening at HLCs rather than opportunistic screening, were previously found cost-effective (6).

### 7.2.2 Data

We used data from Wave 1 (November 2018 – November 2019) of the Sri Lanka Health and Ageing Study (SLHAS) (33). A sample of 6,665 adults aged 18+ was selected by stratified, multi-stage cluster random sampling that, with weights applied, is representative of the age, sex and ethnicity distribution of the adult population of Sri Lanka in 2019 (Appendix A1) (33). These data were used to estimate CVD risk of each participant, identify those who would qualify for treatment in each strategy, measure socioeconomic status (SES) and healthcare use, and evaluate quality of life (QOL).

### 7.2.3 Model structure

We adapted a Markov model previously used to evaluate cost-effectiveness of CVD risk screening in Sri Lanka (9). It has an initial state of no CVD diagnosis and five nodes: fatal and non-fatal coronary heart disease (CHD) and stroke (CVD events), and death from any other cause (Appendix Figure A1). We used a one-year cycle for ten years, with transition to death thereafter determined by age-specific mortality rates until age 100. While recognizing potential health gains from medical advice on lifestyle and prevention of microvascular complications of diabetes, screening was assumed to lower risks of CVD events primarily through prescription of antihypertensives and statins (34, 35). Risk reductions were assumed to be immediate but modelled to last for only 10 years.

### 7.2.4 Model inputs

Model parameter values are in Appendix Table A2. To estimate probabilities of opportunistically screening simulated individuals distinguished by sex and SES, we used data on outpatient visits to public clinics (SM Appendix A7) (33). For each participant, BP was measured and a blood sample taken to measure blood glucose and cholesterol. Current smoking status was reported. We used these risk factors, as well as age and sex, to calculate CVD risk with the WHO-2019 CVD risk tool (26). We used all these data to determine whether screened individuals would be prescribed antihypertensives, statins and diabetes medication under each strategy. We used metanalyses estimates of the effects of antihypertensives (36) and statins (37) on probabilities of CVD events and deaths (Appendix Table A2).

### 7.2.5 Model outputs

The model simulated CVD events and deaths due to other causes (6). QALYs generated by strategies A–D and the comparator were calculated by aggregating the QOL score in the initial state and each subsequent year of survival. Initial QOL scores were calculated using a Sri Lankan valuation of EQ-5D-5L responses (38). For each subsequent year in the cycle, adjustments were made using age, stroke and CHD values from a Sri Lanka-specific catalogue based on EQ-5D-5L (SM Appendix A8.1) (39). We calculated total lifetime QALYs under

each strategy by assuming full health until the age of 18, adjusting QOL for each year lived from 18 to age at entry to the model, and QOL consistent with the modelled state thereafter.

For each strategy, we calculated costs of a) screening (glucose test and consultation time), b) lifetime follow-up (glucose test and consultation time), c) lifetime treatment with antihypertensives, statins and antidiabetics, d) cost of inpatient and outpatient public medical care (usual care), and e) costs of treating any CVD event.

Taking a public health system perspective, we used local data to calculate values used for costing (SM Appendix A8.2) (6) and converted them to December 2019 US dollars (US$) (1 US$ = 181.63 Sri Lankan Rupees). We used a lifetime horizon as the costs and impacts of CVD preventative treatment and follow-up is long-term. We discounted all costs and QALYs at 3% per year (2).

### 7.2.6 Cost-effectiveness analysis

We calculated the Incremental Cost-Effectiveness Ratio (ICER) for each of strategies A-D with respect to the comparator. Incremental costs were plotted against incremental QALYs and a cost-effectiveness frontier drawn. An ICER was calculated for each pair of consecutive strategies along the frontier. Since Sri Lanka has no official cost--effectiveness threshold (CET), we used a benchmark of 0.5×Gross Domestic Product (GDP) per capita (pc) and 0.3×GDP pc per QALY, based on estimates for LMICs (40-42).

### *7.2.7* Distributional analysis

We proxied SES by an assets index – the first principal component of an analysis of household durable assets, water and sanitation facilities and other housing conditions (SM Appendix A9) (43). We used the index to categorize participants into SES quintile and percentile groups.

In order to compare socioeconomic distributions of net effects of the strategies, we used the 0.5×GDP pc CET to transform the estimated monetary cost of each strategy into a health opportunity cost (44, 45)—QALYs foregone from reduced spending on other public healthcare under a fixed budget—and assigned this cost over the SES distribution proportionate to utilization of public outpatient care (SM Appendix B). We subtracted these health opportunity costs from the QALYs generated by each strategy to get net QALYs over the SES distribution.

To compare distributional impacts, for each strategy we first calculated by SES quintile group (for easier visualization) the number of individuals screened and the percentage prescribed preventive medications. Then, we calculated the difference between each strategy and the comparator in the net QALYs generated at all SES percentiles. If, for a strategy, this difference were non-negative at all percentiles, then that Pareto dominant strategy would be preferred

to the comparator provided it were judged an improvement to generate more QALYs at least at one percentile without generating less at any other. To rank strategies between which there was no Pareto dominance, we compared cumulative means of net QALYs along the SES distribution from the poorest to richest percentile. If a strategy generated a higher (or the same) cumulative mean at all percentiles, then that Generalized Concentration Curve (GCC) dominant strategy would be judged an improvement by any decision maker with aversion to socioeconomic health inequality (24). When there was no GCC dominance, we compared weighted cumulative mean net QALYs with weights that declined linearly (at any rate) on moving from poorer to richer percentiles. If, at all percentiles, a strategy generated a higher (or the same) weighted cumulative mean, then that second-order GCC dominant strategy would be judged an improvement by a decision maker with stronger aversion to inequality at the bottom of the SES distribution than at the top (24). Finally, we compared weighted cumulative means with weights declining at any decreasing rate on moving from poorer to richer percentiles. If, with these weights, a strategy always generated a higher, or the same, weighted cumulative mean, then that third-order GCC dominant strategy would be judged an improvement under even greater inequality aversion, while still avoiding specification of its precise intensity (24). We continued up to and including fourth-order GCC dominance: we classified a strategy as having no dominance over another strategy if dominance could not be established after using fourth-order dominance.

For each strategy and the comparator, we calculated inequality-penalized net QALYs: the level of QALYs that if distributed equally by SES would be judged as good as the unequal QALY distribution generated by the strategy (46). This was calculated as $\mu(1-I)$, where $\mu$ is mean net QALYs and $-1 \leq I \leq 1$ is an index of socioeconomic inequality analogous to the extended Gini family, with the concentration index as a special case (47, 48). A larger positive value of I indicates greater inequality disadvantaging poorer individuals. We calculated inequality-penalized net QALYs for different intensities of inequality aversion representing willingness to accept lower mean QALYs for less pro-rich inequality. Appendix C in the SM gives details of the distributional analysis.

### 7.2.8 Sensitivity analysis

We performed deterministic sensitivity analyses of ICERs to key parameters for strategies on or close the cost-effectiveness frontier (Appendix Figure E2). Probabilistic sensitivity analysis was performed for strategies A–D, with 1,000 simulations and random draws from the distributions in Appendix Table A2, and the ranking of strategies based on the probability of being cost-effective at various CETs (0.3, 0.5 and 1.0×GDP pc per QALY) were determined.

We performed a sensitivity analysis in which health opportunity costs were assumed to be distributed uniformly across the SES distribution rather than proportionate to outpatient utilization (SM Appendix B). We also tested sensitivity to different values for converting monetary costs to health (QALY) opportunity costs: 0.3 and 1.0×GDP pc vs 0.5×GDP pc for main estimates, based on the CETs used in the probabilistic sensitivity analysis. We calculated inequality-penalized QALYs using inequality indices consistent with the Kolm (49) and Atkinson (50) social welfare functions, in addition to the extended Gini family.

We reported using the Consolidated Health Economic Evaluation Reporting Standard (CHEERS) checklist (51) (SM Appendix D). All analyses were done in Stata V17.0 using weighted data (52).

## 7.3 RESULTS

### 7.3.1 Screens and medication

We used data on 4,745 participants aged 35+ without a previous history of CVD to simulate screening of a population of 9.7 million. In this population, we estimated that mean CVD risk was higher and use of antihypertensive, statin or antidiabetic medication was lower in poorer quintile groups that were slightly older and had lower mean QALYs (Appendix Figure E1).

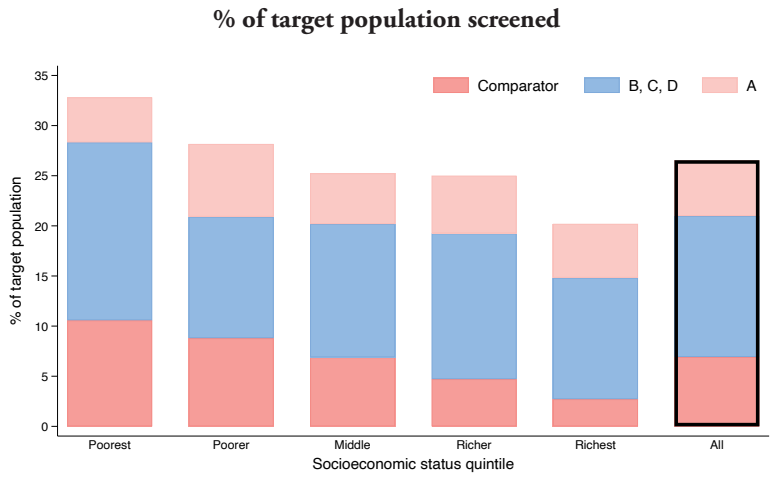
We calculated that the number screened would be 672,000 in the comparator program, 2.0 million with strategies B–D, and 2.6 million with strategy A. With all strategies, the percentage of the target population screened would be higher in poorer groups (Figure 1A). The percentage newly prescribed antihypertensive, statin or antidiabetic medication would be 1.7% with the comparator, 6.8% with strategy A and 9.1% with D (Figure 1B). With all strategies, the percentage medicated would be higher in the poorest quintile than in the richest quintile, although it would not always decrease monotonically across quintiles.

### 7.3.2 Cost-effectiveness

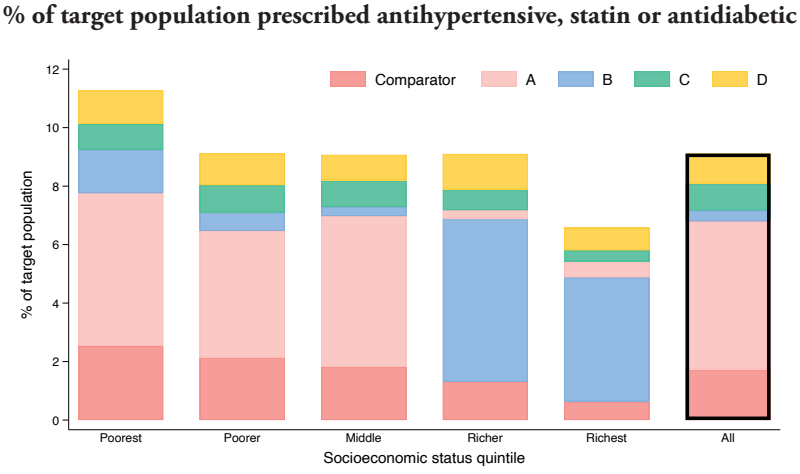
Costs, QALYs and ICERs for each strategy are in Appendix Table E1. Relative to the comparator, strategies B–D each have an ICER below 0.5×GDP pc. Strategy A does not, but its ICER is below 1×GDP pc. Strategies C (ICER US$ 1,714/QALY) and D (ICER US$1,789/QALY) lie on the cost-effectiveness frontier, while B (ICER US$ 1,769/QALY) is close to it (Appendix Figure E2). None of strategies A–D have an ICER below 0.3×GDP pc.

***Figure 1 Percentages of target population screened and prescribed medications by strategy and socioeconomic status***

**A**




**B**



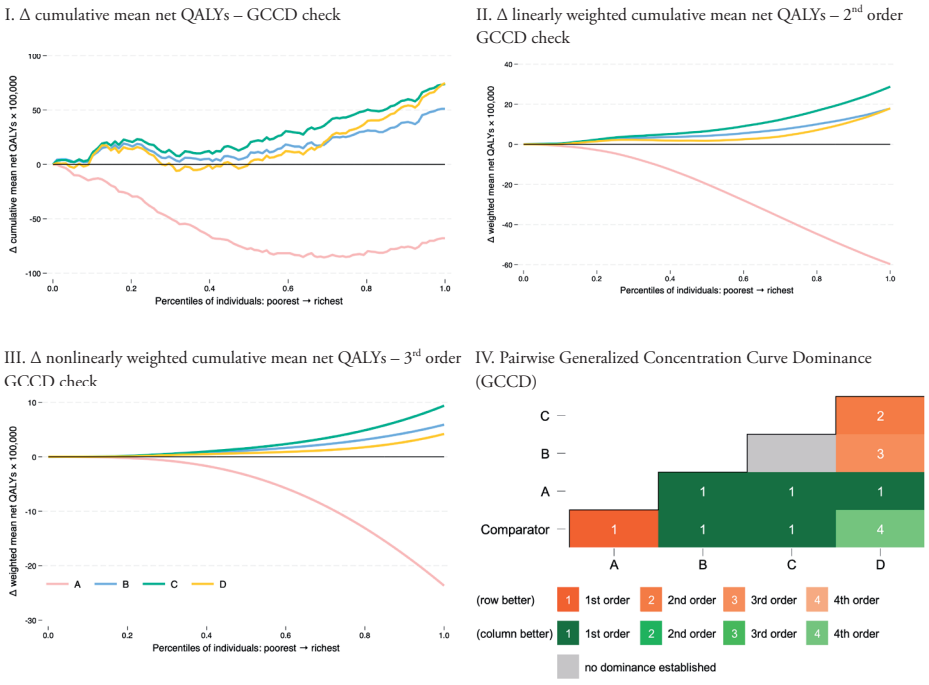

**Notes:** Target population aged 35+ with no previous history of CVD. Bars for A-D indicate additional percentage screened/prescribed medication with the respective strategy.

### 7.3.3 Distributional analysis using stochastic dominance

No strategy generated at least as many net QALYs as the comparator at all SES percentiles (Appendix Figure E3), and so no strategy Pareto dominated the comparator. Neither was there Pareto dominance of the comparator over any strategy.

Figure 2 Panels I-III show differences (multiplied by 100,000) between each strategy and the comparator in (weighted) cumulative means of net QALYs generated at SES percentiles from poorest (left) to richest (right). Panel IV summarizes the respective dominance results. In Panel I, which shows differences in cumulative mean net QALYs, the difference between strategy A and the comparator is negative at every percentile, indicating that the comparator GCC dominates A. For B and C, the respective differences are all positive, and so each of these strategies GCC dominates the comparator. Hence, an inequality averse decision maker would

***Figure 2 Differences between each strategy and comparator (Δ) in (weighted) cumulative means of net QALYs over distribution of socioeconomic status and Generalized Concentration Curve dominance***




**Notes:** Δ indicates a difference: strategy X – comparator. GCCD = Generalized Concentration Curve Dominance. Each of panels I–III show differences in cumulative (weighted) means of net QALYs at each of 100 percentiles in the distribution of socioeconomic status (SES). The differences at the percentiles are connected with a line to make comparison with the horizontal at 0 (no difference from the comparator) and between strategies easier. Panel II shows differences in weighted cumulative means with weights linearly decreasing from low to high SES. In Panel III, weights are decreasing at a decreasing rate. In panel IV, the numbers in each shaded box indicate the order at which one strategy dominates the other.

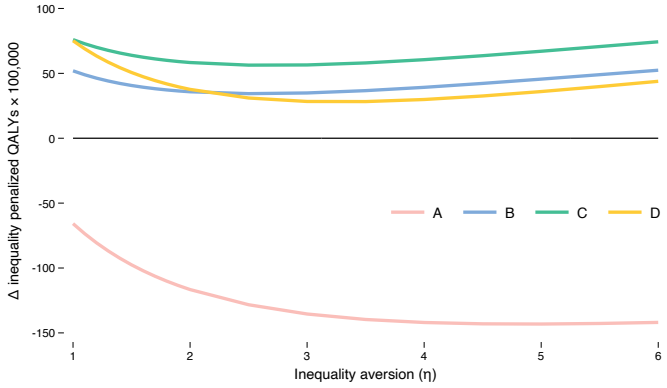
judge the comparator to be better than A and worse than each of B and C. The differences cross for C vs B, D vs the comparator, D vs B, and D vs C.

In Panel II, the differences in linearly weighted cumulative mean net QALYs between C and the comparator are all greater than the respective differences for D, indicating that C second-order GCC dominates D and implying that greater aversion to inequality towards the bottom of the SES distribution (along with preference for more QALYs and less inequality) is sufficient to prefer C to D. The differences between C and B, D and B, and D and the comparator, still cross. In Panel III, the difference between B and the comparator in the nonlinearly weighted cumulative means of net QALYs is greater than the respective difference for D at all percentiles. This means that B third-order GCC dominates D and implies that B would be preferred to D with sufficiently strong aversion to inequality to the disadvantage of the poor. In a similar manner, D fourth-order GCC dominates the comparator (not shown). A preference cannot be established between strategies B and C, as the lines cross.

### 7.3.4 Inequality-penalized QALYs

Figure 3 shows, for different degrees of inequality aversion, the difference between inequality-penalized net QALYs generated by each of strategies A–D and those generated by the comparator. With no inequality aversion ($\eta = 1$), mean net QALYs are compared. In this case, positive differences for B–D confirm that these strategies are more cost-effective than the comparator, while the negative difference for A signals that it is less cost-effective. Irrespective of the degree of inequality aversion, strategy C generated more inequality-penalized net QALYs

***Figure 3 Difference between each strategy and the comparator (Δ) in inequality-penalized net QALYs calculated at different degrees of inequality aversion***




Notes: Δ indicates a difference: strategy X – comparator. Inequality-penalized net QALYs calculated for a social welfare function analogous to the extended Gini family (47, 48). There is no inequality aversion at $\eta = 1$ and it increases with the value of this parameter. Differences are multiplied by 100,000.

than all other strategies. Strategy D generated more inequality-penalized net QALYs than B only at lower aversion to inequality ($\eta < 2.2$), which corresponds to the finding that B GCC dominates D only on reaching the third order.

### 7.3.5 Sensitivity analysis

ICERs were sensitive to the discount rate (r), increasing by 22–25% at r = 0% and decreasing by 18–20% at r = 6% (Appendix Figure F1, Appendix Figure F2). At r = 6%, strategy D had a lower ICER than strategy B. The probability of having an ICER below the cost-effectiveness threshold (CET) of 0.5×GDP pc per QALY or less is 67.1%, 65.4%, 65.0%, 25.4% (strategies ranked C ≻ B ≻ D ≻ A). However, using a higher CET of 1.0×GDP pc per QALY or less, the strategies ranked D ≻ B ≻ C ≻ A (99.2%, 98.4%, 97.3%, 79%) while at a lower CET of 0.3×GDP pc per QALY the strategies ranked C ≻ B ≻ D ≻ A (9.2%, 6.5%, 5.4%, 1.4%), with a similar ranking seen as with a CET of 0.3×GDP pc per QALY (Appendix Figure F3). The low probabilities of cost-effectiveness for the latter is also consistent with the finding that none of strategies A–D were under the CET of 0.3×GDP pc per QALY.

Similarly, DCEA results were sensitive to the value used to convert monetary costs to health opportunity costs. When a low opportunity cost of 0.3×GDP pc per QALY was used instead of the baseline 0.5×GDP pc per QALY, the comparator first-order GCC dominated most other strategies (Appendix Figure F4, Appendix Figure F5). When a higher opportunity cost of 1.0×GDP pc per QALY was used, both A and D first-order GCC dominated the comparator, and a preference could not be determined between B, C and D.

When health opportunity costs were assigned uniformly over the SES distribution instead of proportionately to the utilization of public clinics, no dominance could be established between strategies B, C and D using lower-orders of GCC dominance.

When health opportunity costs were assigned uniformly over the SES distribution instead of proportionately to the utilization of public clinics, some changes in ranking were seen where strategy C second-order GCC dominates strategy B, and no dominance could be established between strategies B and D, or C and D (Appendix Figure F6).

Superiority of strategy C and inferiority of A compared with all other strategies are both robust to using Kolm and Atkinson (instead of extended Gini-type) social welfare functions irrespective of the degree of inequality aversion. With Kolm, D is preferred to B, though they converge at a high inequality aversion. With Atkinson, D ranks above B irrespective of the degree of inequality aversion (Appendix Figure F7).

## 7.4 DISCUSSION

Moving to opportunistic CVD risk screening at public clinics in Sri Lanka and modifying protocols for prescribing preventive medication to at-risk patients would likely be cost-effective and equitable if there is aversion to pro-rich inequality in the distribution of QALYs.

The cost-effectiveness analysis shows that in combination with opportunistic screening, each of these incremental changes have an ICER of less than 0.5×GDP pc/QALY: i) targeting people aged 40 years and over and reducing the CVD-risk threshold for statin treatment to 10%, ii) prescribing people antihypertensives at a lower BP threshold of 130/80 if they have a CVD risk of 10% or diabetes, and iii) prescribing a statin to all with diabetes. The strategy which includes both (i) and (ii) only has the smallest ICER of all strategies modelled and would be prioritized if maximizing efficiency. However, adding statins to all people with diabetes (iii) has a slightly higher ICER and results in a higher number of QALYs gained. Since it expands treatment, it costs more. However, the additional cost of treating all people with diabetes for a cohort aged 40+, including a lifetime of follow-up, is equivalent to only 2% of the government's annual health expenditure (US$1.3 billion in 2019)—highlighting its likely affordability. Therefore, a decision maker only prioritizing efficiency may opt for the strategy that prescribes antihypertensives at a lower threshold, but may also consider including statin prescription for diabetes with a small loss of efficiency, for a larger impact.

The DCEA introduces an equity consideration to strategy prioritization. Here, using stochastic dominance after factoring in health opportunity costs, we confirm that the strategies that were identified as cost-effective also provide better health across SES percentiles. Additionally, we find that a decision maker who is averse to some inequality at the poorer end of the wealth distribution would opt not to prescribe statins to all with diabetes. They may choose to prescribe antihypertensives at a lower threshold, as this strategy neither dominates nor is dominated by the strategy that does not.

DCEA with methods that parametrizes the degree of aversion also finds that with some degree of aversion ($\eta \geq 2.2$), statin prescription produces lower health than the other strategies. Unlike stochastic dominance however, it finds that the strategy that includes antihypertensives prescription at a lower threshold produces the highest amount of inequality-penalized health. The contrasting result is due to the differences in the underlying method. In the parametric method used, the overall inequality-penalized health is compared, whereas in stochastic dominance, even if there is higher mean overall health in a strategy being tested, if any wealth percentile is worse off, that strategy cannot dominate. Given that the parametric method selects prescription of antihypertensives, and the stochastic dominance analysis does not identify whether this

would be preferred or not, a decision maker with some aversion to inequality could most likely opt for using this strategy.

This study demonstrates that dominance analysis can be used to analyse health inequalities and establish preferences for programs without utilizing parametric methods, which require choices to be made on the functional form of the social welfare function, and parametrization of the degree of aversion. The findings from the dominance analysis closely follow those from calculating inequality-penalised average health with the extended generalised extended Gini index. For example, in the dominance analysis, the strategy that prescribed antihypertensives at a lower threshold, as well as statins to all people with diabetes was 3rd order GCC dominated by the strategy that only prescribed antihypertensives, which is consistent with the parametric method where the former strategy resulted in lower inequality-penalized health than the latter at higher degrees of aversion ($\eta \geq 2.2$).

The findings were highly sensitive to the opportunity cost of health. When the conversion rate for opportunity cost was low (e.g. 0.3×GDP pc per QALY), the screening program currently at place at HLCs provided equal or better mean health across the SES gradient than all other modifications. Conversely, when the opportunity cost was high at 1.0×GDP pc per QALY, strategies with higher QALY gains on the cost-effectiveness frontier also provided greater health across SES groups compared to the current strategy. The distribution of health opportunity costs, that is, whether opportunity costs are uniform across the population or if they are a function of healthcare utilization, also impacts the dominance of strategies. The sensitivity of the results to the opportunity cost value is consistent with findings in the UK (18) and further highlights the importance of producing countryspecific costs of health production to carry out DCEA effectively.

There are several limitations to this study. For the comparator, we modelled an idealistic version of the current screening program, where all eligible individuals have an equal chance of being screened regardless of sex and SES. However, it is likely if we were able to model likely patterns in the current screening program, such as screening a higher proportion of females—who are at lower risk of CVD— that ICERs of the modelled strategies will be even lower, as the comparator strategy will screen and treat less at-risk individuals and have a lower impact than currently modelled. Furthermore, we assume 100% adherence and an equal risk reduction from medications across all individuals. Lower rates of adherence could increase the ICERs of all strategies, particularly those involving the use of more medications. Non-uniform risk-reduction or adherence rates, especially across the SES gradient could produce different results in DHEA. Adherence rates could well differ by SES, and can become more pronounced as each success strategy treats a larger percentage of individuals, and non-representative studies suggest that pressures in medicine cost and availability with the economic crisis may lead

to poorer individuals omitting or reducing their medication intake (53). The opportunistic screening modelling is difficult to validate due to a lack of Sri Lankan data on the number of public outpatient visits per year per person. Furthermore, we do not know the distribution of opportunity costs by wealth gradient and assumed that it would be proportionate to outpatient healthcare use.

## 7.5 CONCLUSIONS

Strategies that used opportunistic screening instead of screening at HLCs, screening people at 40+ years instead of 35+, along with lowering the CVD risk threshold from 20% to 10% to initiate statin treatment and reducing the blood pressure threshold for antihypertensive treatment for those with a CVD-risk of 10% or diabetes, produced better health across SES percentiles than the current strategy when aversion to worse health outcomes in the poor was accounted for. Additionally, prescribing statins to all with diabetes also achieved better health across all SES percentiles than the current strategy if there is sufficiently strong aversion to inequality to the disadvantage of the poor. However, the findings of the CEA and DCEA are highly sensitive to the opportunity cost of health, where cheaper strategies dominated the DCEA when the rate of conversion to opportunity costs was low.

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# Appendix A Methodology

## A1 Sri Lanka Health and Ageing Study Methodology

The SLHAS is a longitudinal cohort study that recruited its first participants using a nationally representative survey of 6,665 adults aged 18 years and over. A multi-stage cluster random sampling design, stratified by district, residential sector and area socioeconomic status (SES) was used to collect data in 297 sampling units selected by probability-proportionate-to-size sampling in all 25 districts of Sri Lanka (1). Within each sampling unit (smallest administrative division), households were randomly selected and one adult (18 years and older) was randomly chosen from each household roster, with oversampling of those aged ≥70 years. Consenting participants attended a survey field clinic held nearby in a single visit, where a questionnaire was completed, blood samples were taken and measurements such as blood pressure were taken. Data were collected from 9 November 2018 to 14 November 2019. After application of sampling weights, the sample was representative of the adult population of Sri Lanka in 2019 by gender, age, geographical region, area SES and ethnicity.

## A2 Questionnaire and medical records

The questionnaire included modules such as demographics (age, sex), behavioural risk factors (smoking history), past medical history, medicines use in the past 2 weeks, the EQ-5D-5L questionnaire, and household assets. In addition to completing a questionnaire, each respondent was asked to bring their medical records to the interview and asked for consent for the enumerator to consult these records. These were used to collect additional data on diabetes and CVD diagnoses, and add to the list of medicines used in the past 2 weeks. A participant was classified as a smoker if they reported being a current smoker.

Participants were asked how many outpatient visits they made to various types of facilities in the past 7, 14 or 28 days. Participants were randomly assigned to one of the three recall periods, although most were assigned to 28 days. We identified visits to public specialist clinics, public general clinics, public Medical Officer of Health clinics, and public HLCs as those at which opportunistic screening could potentially be initiated.

## A3 Measurements and blood tests

Blood pressure was measured twice using an OMRON HEM-7320 Automatic BP Monitor. The readings were taken 10 minutes apart, with the first reading taken after five minutes of rest, and the mean of the readings was calculated. Weight without shoes, heavy clothing or jewellery, was measured using an OMRON BF511 body composition monitor, and height without shoes was measured using a seca 240 mechanical measuring rod (stadiometer).

Participants were asked to fast for 12 hours, and a venous sample was taken soon after the participant arrived at the clinic to determine fasting (or random, if the participant had not fasted) blood glucose and lipid profiles. Those who did not report diabetes, and had fasted for 12 hours, had an oral glucose tolerance test: after the fasting samples were taken, participants drank the equivalent of 75 grams of anhydrous glucose in solution, and a repeat venous sample was taken two hours later. Plasma and serum were extracted from the venous samples in the field, stored within 6-10 hours of initial collection in a field freezer (TwinBird Freezer SC-DF25 and Glacio 55L Portable Cooler Fridge PFN-E-WEA-L-GR) at -40oC to -20oC and transported to the study laboratory at the Medical Research Institute in Colombo, where they were analyzed, usually within two weeks of sample collection.

## A4 Data collection platform and validity checks

Data were collected using a computer-assisted personal interviewing platform, iFormBuilder (Zerion Software Inc., Herndon, VA, USA), with built-in skip logic and checks for unlikely values during data entry. During data cleaning, less likely values were cross-checked using manually recorded clinic checklists.

## A5 Constructed variables

A respondent was defined as diagnosed with pre-existing CVD (and thus ineligible for screening) if they reported ever being diagnosed with angina, myocardial infarction or coronary artery disease, or their medical records indicated such a diagnosis.

For the Markov model, to estimate CVD events and deaths, we utilized the WHO 2019 laboratory-based tool, which uses the fasting total cholesterol value. For determining who would be prescribed statins and antihypertensives based on CVD risk, we utilised the WHO 2019 office-based tool which substitutes body mass index for total cholesterol. Body mass index was calculated using the standard formula of weight ÷ height2.

The WHO 2019 CVD risk tool requires an individual's diabetes status as an input variable. We identified individuals as having diabetes if a) they reported having been diagnosed with diabetes or their medical records showed this, or b) they had a fasting blood glucose ≥ 126 mg/dL, a random glucose ≥ 200 mg/dL, or an oral glucose tolerance test (OGTT) result ≥ 200 mg/dL, or c) they reported taking oral hypoglycemics or insulin in the past 14 days.

To estimate quality of life (QOL), data from the EQ-5D-5L questionnaire were used, where respondents were asked to grade their health status in five dimensions (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression) from one to five, where one is the best health state and five is the worst (2). This instrument can define 3,125 health states, where 11111 represents full health and 55555 represents the poorest health state. We used a Sri

Lankan valuation of each EQ-5D-5L state (3) to map each response to a quality of life, where 1 represents "perfect health", 0 represents death, and negative values were worse than death.

## A6 Study weights

Sample weights which represent the national population were used, with calibration to address the observed skewed representation of different ethnic groups, as described previously (4). In short, SLHAS provides non-response weights which modelled the propensity of participation based on characteristics collected at recruitment, and produced weights that are adjusted to the age-sex population structure of strata (the primary sampling units were categorized into 57 strata based on district and sector of residence), districts and provinces. These weights were then calibrated to match the strata, age-sex, ethnic and sector population structure at district, province and national levels using iterative proportional fitting, an additional step that was required due to some under-representation of Muslim people in the sample (5).

## A7 Modelling the number of annua clinic visits per individual

The SLHAS dataset used three separate recall periods for outpatient visits: Of the people aged 35 years and over with no CVD, the number of OP visits was asked from 950 people for a 7-day recall period, 903 people for a 14-day recall period and 2,817 people for a 28 day-recall period. There is no obvious way identify which proportion of people had at least one public OP visit during the previous year, and of those who had a public OP visit, how many visits were made. Furthermore, presumably a proportion of people who reported zero visits in their respective recall period would have visited at least once over a 12-month period.

Given the lack of any other survey or administrative data available to i) estimate the proportion of people with at least one public OP visit in the past 12 months, and ii) the number of visits per person, we attempted to model this with our dataset.

*Step 1: Calculate the proportion of people with 0 visits to the public sector in 1 year*

We created a dataset of the proportion of people aged 35 years and over with zero public OP visits for each gender, sector (urban, rural, estate), socioeconomic quintile and recall period in days (3) group (total of $2 \times 3 \times 5 \times 3 = 90$ groups).

We then ran a regression:

$prop = ß_1.\ln(day) + ß_2.sector + ß_3.sex + ß_4.sesquintile$

where *prop* is the proportion of the group that had no public healthcare visits
*day* is the recall period in days
*sector* is urban, rural or estate/rural
*sesquintile* is the socioeconomic quintile.

Variables with coefficients with a p-value greater than 0.01 were dropped from the full model. The model confirmed an association of the proportion with no visits to the public sector with the number of days in the recall period and socioeconomic quintile.

***Table A1 Linear regression estimates of the proportion of people with no public outpatient visits with recall time period and sociodemographic factors***

| | Full model | | | Final model | | |
|---|---|---|---|---|---|---|
| | **Coefficient** | **95% CI** | **p** | **Coefficient** | **95% CI** | **p** |
| Days (log) | -0.08 | (-0.10, -0.05) | 0.000 | -0.08 | (-0.10, -0.05) | 0.000 |
| Sector | | | | | | |
| Rural | -0.01 | (-0.05, 0.02) | 0.413 | * | * | * |
| Rural / Estate | -0.02 | (-0.05, 0.02) | 0.290 | * | * | * |
| Female | -0.01 | (-0.04, 0.01) | 0.361 | * | * | * |
| SES quintile | | | | | | |
| 2 | 0.03 | (-0.01, 0.07) | 0.166 | 0.03 | (-0.01, 0.07) | 0.163 |
| 3 | 0.04 | (0.00, 0.08) | 0.052 | 0.04 | (0.00, 0.08) | 0.051 |
| 4 | 0.05 | (0.01, 0.09) | 0.019 | 0.05 | (0.01, 0.09) | 0.018 |
| 5 (richest) | 0.09 | (0.05, 0.13) | 0.000 | 0.09 | (0.05, 0.13) | 0.000 |
| Constant | 1.09 | (1.02, 1.16) | 0.000 | 1.07 | (1.00, 1.14) | 0.000 |
| n | 90 | | | 90 | | |
| Adj $R^2$ | 0.386 | | | 0.393 | | |

We then used predict in Stata to predict the proportion of each group that would have no visits for a recall period of 365 days.

*Step 2: Model the number of visits for individuals*
We categorised the sample into unique groups based on sex (2), socioeconomic quintile (5) and sector (3), giving a total of 30 (2 × 5 × 3) groups. We estimated the proportions of people in each group who had one or more visits (1 – proportion of people who had 0 visits).

We calculated the total number of visits for each of these groups over a year based on the mean visits per person in each group for the recall period, scaled to one year, and divided it by the number of people who we modelled to have one or more visit, to estimate the mean number of visits for each group. We then applied a Poisson distribution bounded by one, using the method outlined by Cohen (6) using Molina's tables, to estimate the distribution of visits for each group given the calculated mean. The dataset was expanded so that one record was representative of one person, and the distribution of visits was randomly applied within each group.

The estimates generated are likely to be conservative, given that visits may cluster in time in individuals during a short recall period. Indeed, analysis of a weighted subsample of 131 people with an undiagnosed chronic condition, who were asked when they last had an OP visit, found that 66% of people had a public OP visit in the past year (separate results, not shown), which is higher than the estimates (35%) generated from our model.

*Step 3: Use binomial probability to calculate the probability of being screened*
We used binomial probabilities to calculate the probability that a participant would be screened in a one-year period.

First, we calculated the probability. The formula used was:

$$P_{assessed} = 1 - (1 - P_{a\_pub})^{n_{pub}}$$

where $P_{a\_pub}$ is the probability of being assessed in the public sector
$n_{pub}$ is the number of visits to the public sector.

For example, in the case where $P_{a\_pub}$ = 0.3, a participant who had one public sector visit was given a probability of 0.3 of being screened, whilst a person with two public sector visits was assigned a probability of $1 - (1 - 0.6)^2 = 0.84$.

Adapted with permission from:

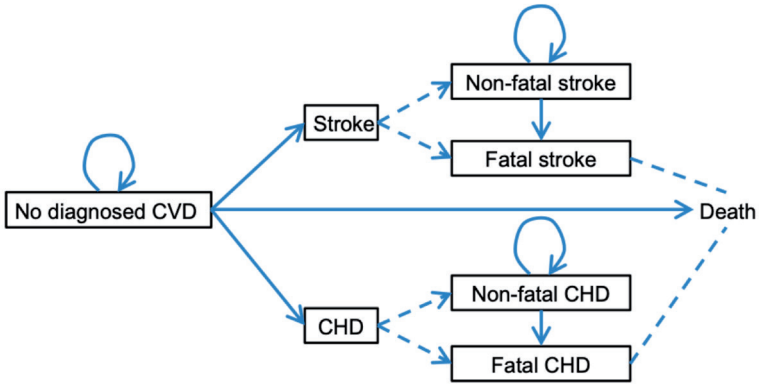
Wijemunige N, Rannan-Eliya RP, Maurer J, O'Donnell O. Cost-effectiveness and distributional impact of opportunistic screening for people at high-risk of cardiovascular disease in Sri Lanka: a modelling study. Global Heart. 2022;17(1).

## A8 Modelling of outcomes and costs

### *A8.1 Modelling outcomes*

We utilised a Markov model developed previously to model CVD risk screening scenarios (Figure A1) (7). This model used a 1-year cycle for the first 10 years of modelling. All individuals started in a state of no diagnosed CVD, could either remain in that state or transition to developing a stroke, coronary heart disease (non-fatal or fatal) or death from other causes. After 10 years, we assumed that all individuals who were still alive would transition to death using the probability of natural death for that age group. Cycles continued for each participant until death or until the participant reached the age of 100 years.

***Figure A1 Markov model of population with no known history of CVD.***




**Notes:** Reproduced with permission from Wijemunige N, Rannan-Eliya RP, Van Baal P, O'Donnell O. Optimizing cardiovascular disease risk screening in a low-resource setting: cost-effectiveness of program modifications in Sri Lanka modelled with nationally representative survey data. BMC Public Health. 2023 Sep 15;23(1):1792. Available at: https://link.springer.com/article/10.1186/s12889-023-16640-5

For all scenarios, we fed each individual's risk factor data into the WHO-2019 laboratory risk tool to estimate the 10-year probability of developing each of coronary heart disease (CHD) and stroke assuming that this tool would be the most accurate for the Sri Lankan population (7). We converted the 10-year probabilities to 1-year probabilities. The WHO-2019 screening

*Table A2 Input parameters*

| Parameter | Value (95% CI) | Distribution | Source |
|---|---|---|---|
| **Events** | | | |
| 10-year probability of CHD / stroke event | Risk factor specific rates | | WHO CVD Risk Chart Working Group (14) |
| 10-year probability of death from CVD event | Age-sex specific proportion applied to CHD events and stroke events | ± 10% (uniform) | Global Burden of Disease Collaborative Network (15) |
| 1-year probability of death without previous CVD event | Age-sex specific natural mortality from life-tables. | | World Health Organization (16) |
| 1-year probability of dying after non-fatal CHD event | 0.03 (0.01, 0.04) | limits of 95% CI (β) | Velagaleti, Pencina, Murabito Velagaleti, Pencina (17) |
| 1-year probability of dying after non-fatal stroke event | 0.10 | ± 20% (uniform) | Sun, Lee, Heng (18) |
| **Statin treatment** | | | |
| Cost for one year of treatment of atorvastatin 20 mg per day (USD) | 3.98 | ± 10% (uniform) | IHP analysis (19) |
| RR of non-fatal MI | 0.74 (0.67, 0.81) | 95% CI (log normal) | Mills, Wu, Chong (10) |
| RR of non-fatal stroke | 0.86 (0.78, 0.95) | 95% CI (log normal) | Mills, Wu, Chong (10) |
| RR of fatal MI | 0.82 (0.75, 0.91) | 95% CI (log normal) | Mills, Wu, Chong (10) |
| RR of fatal stroke | 0.92 (0.80, 1.07) | 95% CI (log normal) | Mills, Wu, Chong (10) |
| **Antihypertensive treatment** | | | |
| Cost for one year of treatment of enalapril 5 mg per day (USD) | 2.21 | Gamma distribution, assuming 10% standard deviation | IHP analysis (19) |
| Cost for one year of treatment of nifedipine SR 20 mg per day (USD) | 0.78 | Gamma distribution, assuming 10% standard deviation | IHP analysis (19) |
| RR of non-fatal MI | 0.86 (0.76, 0.96) | 95% CI (log normal) | Brunstrom and Carlberg (9) |
| RR of non-fatal stroke | 0.86 (0.72, 1.01) | 95% CI (log normal) | Brunstrom and Carlberg (9) |
| RR of fatal MI | 0.86 (0.65, 1.14) | 95% CI (log normal) | Brunstrom and Carlberg (9) |
| RR of fatal stroke | 0.86 (0.65, 1.14) | 95% CI (log normal) | Brunstrom and Carlberg (9) |
| **Anti-diabetic treatment** | | | |
| Cost of one year of treatment with metformin 500 mg three times a day (USD) | 6.27 | Gamma distribution, assuming 10% standard deviation | IHP analysis (19) |

| Parameter | Value (95% CI) | Distribution | Source |
|---|---|---|---|
| **Screening costs (USD)** | | | |
| Glucose test | 0.17 | Gamma distribution, assuming 10% standard deviation | IHP analysis (19) |
| Total cholesterol test | 0.19 | Gamma distribution, assuming 10% standard deviation | IHP analysis (19) |
| Consultation | 1.96 | Gamma distribution, assuming 10% standard deviation | Amarasinghe, Dalpatadu and Rannan-Eliya [20], Ministry of Health (21) |
| **Adjustment of annual usual care costs** | | | |
| Inflation of usual inpatient and outpatient care costs for general public | 1.00 | ± 20% (uniform) | Authors' analysis (Additional file 1: Text S1) |
| Inflation of usual inpatient care costs for people with CHD | 2.85 (1.79, 4.54) | 95% CI (log normal) | Authors' analysis (Additional file 1: Text S1) |
| Inflation of usual inpatient care costs for people with stroke | 1.09 (0.53, 2.26) | 95% CI (log normal) | Authors' analysis (Additional file 1: Text S1) |
| Inflation of usual outpatient care costs for people with CHD | 1.95 (1.45, 2.61) | 95% CI (log normal) | Authors' analysis (Additional file 1: Text S1) |
| Inflation of usual outpatient care costs for people with stroke | 1.97 (0.83, 4.69) | 95% CI (log normal) | Authors' analysis (Additional file 1: Text S1) |
| **Event costs (USD)** | | | |
| Cost of myocardial infarction admission | 318 | ± 10% (uniform) | Perera, Rannan-Eliya, Senanayake (22), Amarasinghe, Dalpatadu and Rannan-Eliya (20) |
| Cost of stroke admission | 241 | ± 10% (uniform) | Perera, Rannan-Eliya, Senanayake (22), Amarasinghe, Dalpatadu and Rannan-Eliya (20) |
| **Disutilities** | | | |
| Non-fatal MI | -0.0210 (-0.066, 0.024) | 95% CI (log normal) | Wijemunige, Gamage, Rannan-Eliya (12) |
| Non-fatal stroke | -0.2493 (-0.340, -0.158) | 95% CI (log normal) | Wijemunige, Gamage, Rannan-Eliya (12) |
| 1 year increase in age | -0.0066 (-0.007, -0.006) | 95% CI (log normal) | Wijemunige, Gamage, Rannan-Eliya (12) |

**Notes:** Reproduced with permission from Wijemunige N, Rannan-Eliya RP, Van Baal P, O'Donnell O. Optimizing cardiovascular disease risk screening in a low-resource setting: cost-effectiveness of program modifications in Sri Lanka modelled with nationally representative survey data. BMC Public Health. 2023 Sep 15;23(1):1792. Available at: https://link.springer.com/article/10.1186/s12889-023-16640-5.

tool is accompanied by a Stata program whocvdrisk (8) which can calculate 1-year, 5-year and 10-year probabilities of events and deaths for each of CHD, stroke and CVD. For each participant, we calculated 1, 5 and 10-year probabilities of events and deaths for each condition. We fitted quadratic equations to predict the 2, 3, 4, 6, 7, 8, and 9-year probabilities of events and deaths for each participant for each condition, then used the difference between the probabilities of neighbouring years to obtain the probability of each event/death by year (e.g. 10-year probability – 9-year probability = probability of dying in year 9). This method was used so that the full spectrum of data available (1, 5 and 10-year probabilities) could be utilised.

We used estimates from metanalyses to model the reduction of CVD events by treating individuals with antihypertensives (9) and statins (10) (Table A2). These risk reductions were assumed to be immediate but to only last for 10 years, though treatment would continue for the individual's lifetime. Although we modelled the costs of providing treatment for people with diabetes, we did not model potential health gains from managing diabetes, such as a reduced burden from diabetic retinopathy, nephropathy and neuropathy, expecting that most of the health gains would come from preventing cardiovascular disease (11).

We calculated the baseline utility at the start of the screening program for each individual using the Sri Lanka valuation of responses to the EQ-5D-5L questionnaire (3). For each subsequent year in the cycle that each individual was alive, we applied the marginal disutility of a one-year increase in age, as well as stroke and coronary heart disease for those who transitioned to these states, using a Sri Lanka-specific disutility catalogue, (12) following the method described by Sullivan (13). For distributional analysis, lifetime QALYs were calculated by adding utility for each year of life lived between 18 years and the current age (maximum utility allowable was 1), and assuming that the utility from each year of life from birth to 18 years of age was 1.

### *A8.2 Measurements of costs*

Costs were calculated for screening (glucose test and consultation costs), follow-up costs, a lifetime treatment with statins, antihypertensives and antidiabetics, usual inpatient and outpatient medical care, and CVD events, using the same methods as in our previous study (7). These costs were calculated using locally available data, and converted to December 2019 US dollars (1 US dollar = 181.63 Sri Lankan Rupees), which was the time that SLHAS was completed, and an effective way to handle fluctuating inflation (23).

Costs of medicines were calculated from data obtained from the Medical Supplies Division of the Ministry of Health (24). Laboratory costs were based on prices for reagents, consumables, and labour cost in the public sector in 2019. The cost of a consultation was calculating by dividing total public expenditure on outpatient care by the number of outpatient visits in 2019 (20, 21). We obtained the cost per hospital admission for each of CHD and stroke from

a 2005 Sri Lanka public hospital survey of condition-specific costs and admissions (20, 22). We inflated these costs to 2019 values using the 2019:2005 ratio of total public inpatient expenditures.

*Costs of usual care*

We also allocated a cost of usual medical care to all individuals based on an estimated average cost of inpatient and outpatient care by 10-year age groups using data from multiple sources (20-22). Usual costs for people with incident CHD or stroke in the first 10 years were increased by factors based on analysis of inpatient and outpatient contacts in people with CHD and stroke compared to those without.

*Outpatient care*

The total current expenditure on public outpatient care was calculated by applying the share of outpatient expenditure that is public (36%) to the total outpatient expenditure (Rs. 89,242 million) in 2019 (20, 21). Since some of this expenditure would be on people less than 18 years old, we adjusted the expenditure by the ratio of non-paediatric clinic visits to all clinic visits (0.98).

We used SLHAS Wave 1 data to estimate the weighted distribution of outpatient visits to the public sector by 10-year age groups (Appendix Table A3). The adult public expenditure on outpatient care was distributed amongst each age group based on each age group's proportion of outpatient visits. The total cost of each age group was divided by the estimated population of that age group to estimate an average annual cost for outpatient care per person of that age group (25).

*Inpatient care*

The total current expenditure on public inpatient care was calculated by applying the share of inpatient expenditure that is public (74%) to the total inpatient expenditure (Rs. 207,258 million) in 2019 (20, 21). To exclude expenditures on people less than 18 years old, we used the percentage of bed-days used by people aged 18 years and over from the Public Hospital Inpatient Discharge Survey (PHIDS) (77%) (22).

Similar to the technique used for outpatient care, we used SLHAS Wave 1 data to estimate the weighted distribution of inpatient visits to the public sector by 10year age group, allocated total costs for each age group, and used the estimated population for each age group to estimate an average annual cost for inpatient care (25) (Appendix Table A3).

***Table A3 Distribution of inpatient and outpatient encounters, costs, and cost per capita***

| Age group | Distribution of visits | Total costs (million LKR) | Cost per capita (LKR) | Cost per capita (USD) |
|---|---|---|---|---|
| **Outpatient** | | | | |
| 18-24 | 12.49 | 3,920 | 1,748 | 9.6 |
| 25-34 | 10.04 | 3,151 | 1,064 | 5.9 |
| 35-44 | 17.47 | 5,483 | 1,786 | 9.8 |
| 45-54 | 16.13 | 5,063 | 1,938 | 10.7 |
| 55-64 | 20.67 | 6,488 | 2,853 | 15.7 |
| 65-74 | 17.33 | 5,440 | 3,544 | 19.5 |
| ≥ 75 | 5.88 | 1,846 | 2,537 | 14.0 |
| **Inpatient** | | | | |
| 18-24 | 12.03 | 14,295 | 6,373 | 35.1 |
| 25-34 | 15.08 | 17,919 | 6,051 | 33.3 |
| 35-44 | 16.4 | 19,487 | 6,348 | 34.9 |
| 45-54 | 18.79 | 22,327 | 8,547 | 47.1 |
| 55-64 | 16.52 | 19,630 | 8,631 | 47.5 |
| 65-74 | 13.83 | 16,433 | 10,707 | 58.9 |
| >=75 | 7.35 | 8,734 | 12,007 | 66.1 |

*Adjusting costs for people with CHD and stroke*

The SLHAS Wave 1 data collected information on number of inpatient and outpatient visits based on patient recall (26). Data were also collected on whether participants had CHD and stroke based on self-report and medical records. Annualised inpatient and outpatient numbers were calculated for all participants.

Negative binomial regressions were run for inpatient and outpatient encounters respectively, to determine the impact of having CHD and stroke on number of encounters, after controlling for age, gender and socioeconomic quintile. The coefficients were exponentiated to produce factors to increase annual usual inpatient and outpatient costs for individuals with CHD or stroke. The exponentiated values are also presented in Appendix Table A4.

***Table A4 Coefficients and 95% confidence intervals of negative binomial regression to assess the impact of CHD and stroke on inpatient and outpatient encounter numbers***

| | Log values | | Exponentiated values | |
|---|---|---|---|---|
| | **Coefficient** | **95% CI** | **Coefficient** | **95% CI** |
| **Inpatient** | | | | |
| CHD | 1.05 | (0.58 - 1.51) | 2.85 | (1.79 - 4.54) |
| Stroke | 0.09 | (-0.64 - 0.82) | 1.09 | (0.53 - 2.26) |
| | | | | |
| **Outpatient** | | | | |
| CHD | 0.67 | (0.37 - 0.96) | 1.95 | (1.45 - 2.61) |
| Stroke | 0.68 | (-0.19 - 1.54) | 1.97 | (0.83 - 4.69) |

## *A8.3 Modelling follow-up*

We modelled follow-up based on the Sri Lankan screening guidelines. Those classified as high CVD risk were assumed to be both followed-up and have a glucose test twice a year, whilst those who were not high CVD risk but qualified for any medication were assumed to be both followed-up and have a glucose test annually, with an additional follow-up in the initial year. We assumed that all individuals that qualified for medications would continue to need the medications after the first year. For people with diabetes, we only modelled follow-up of CVD risk and not for diabetes management.

*Adapted and reproduced with permission from:*

Wijemunige N, Rannan-Eliya RP, Van Baal P, O'Donnell O. Optimizing cardiovascular disease risk screening in a low-resource setting: cost-effectiveness of program modifications in Sri Lanka modelled with nationally representative survey data. BMC Public Health. 2023 Sep 15;23(1):1792.

Wijemunige N, Gamage A, Rannan-Eliya RP, Kularatna S. Population Norms and Disutility Catalog for Chronic Conditions in Sri Lanka. Value in Health Regional Issues. 2025 Jan 1;45:101033.

Wijemunige N, van Baal P, Rannan-Eliya RP, O'Donnell O. Health outcomes and healthcare utilization associated with four undiagnosed chronic conditions: evidence from nationally representative survey data in Sri Lanka. BMC Global and Public Health. 2024 Jul 8;2(1):45.

## A9 Estimation of household socioeconomic status using principal components analysis

The SLHAS Wave 1 uses an asset index approach to generate a proxy measure of each household's living standard. The index was computed by using principal components analysis (PCA) of a set of householdlevel variables relating to asset ownership or household characteristics. Variables were selected from those used in recent Sri Lanka Household Income and Expenditure Surveys conducted by the Department of Census and Statistics, selecting those with most predictive performance, and excluding some assets that are only relevant to agricultural households (e.g., tractor, thresher, fishing equipment). Variables were either dichotomous (e.g., household has a car) or categorical (e.g., type of drinking water source), apart from one ordinal variable (number of bedrooms). Dichotomous variables consisted of whether the household possessed each of the following items: radio/cassette player, television, VCD/DVD player, washing machine, fridge, electric fan, domestic phone, mobile phone, computer, internet access, camera/video camera, bicycle, motorcycle/scooter, three-wheeler, motor car/van, and bus/lorry/tipper.

Categorical variables were transformed into dichotomous indicators by creating separate dummy variables for each category. They consisted of the following (numbers in parentheses indicates number of categories in each): flooring material (5), material of wall (7), type of housing tenure (12), drinking water source (16), type of toilet (4), method of household garbage disposal (6), lighting power source (5), cooking fuel (13), and type of cooking place (3).

There was a small percentage of missing values in each variable (2–3%). These were imputed with either the PSU or stratum level mean of the variable or failing those the district/sector or national means. The principal component factor or index obtained by PCA after combining all these variables was then used to divide the sample into population weighted quantiles of equal size. Separate indices were not estimated for urban or rural sectors, but analysis indicates little difference between sectors in how the national index performs.

*Reproduced with permission from:*

Rannan-Eliya RP, Wijemunige N, Perera P, Kapuge Y, Gunawardana N, Sigera C, Jayatissa R, Herath HM, Gamage A, Weerawardena N, Sivagnanam I. Prevalence of diabetes and prediabetes in Sri Lanka: a new global hotspot–estimates from the Sri Lanka Health and Ageing Survey 2018/2019. BMJ Open Diabetes Research and Care. 2023 Feb 1;11(1):e003160.

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## Appendix B Estimating the distribution of opportunity costs

In a fixed health budget, additional money spent on a proposed scenario would result in an opportunity cost, where reduced expenditures elsewhere in the health system would lead to QALYs lost in those areas. Distributional analysis looks at the net health benefit: it is important to transform the costs incurred by each scenario into health opportunity costs to ensure that resource allocation maximizes health benefits.

For use in a distributional analysis, net health benefit can be calculated by socioeconomic status (1):

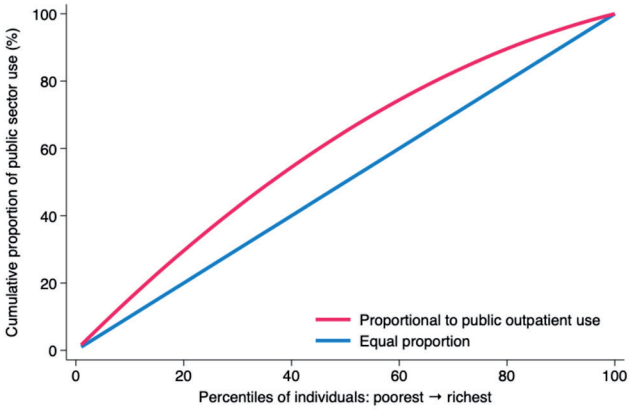
$$n_j = h_j - \frac{c}{k} p_j$$

Where
$n_j$ = net health benefit for group j
$h_j$ = health benefit for group j
$c$ = programme cost
$k$ = conversion rate of costs to foregone health (cost per QALY of foregone alternatives)
$p_j$ = proportion of opportunity costs that will fall onto group j

The values for and are not known for most low- and middle-income countries, including Sri Lanka. Estimates for have been attempted in multi-country studies using the elasticity of a change in health resulting in a change in expenditure, with estimates for Sri Lanka ranging from USD 453–USD 1,686 per QALY (2) (2013 USD) and USD1,281–USD 2,090 per QALY (3) (2015 USD). This translates to 12–46% and 32–52% of Sri Lanka's GDP per capita in those respective years (4).

The value of by socioeconomic status is not directly known. We used two methods to estimate . For the main study, we calculated the proportion of public outpatient use by SES percentile and applied regression smoothing to reduce fluctuations. For the sensitivity analysis, we allocated equal proportions to each percentile group (Figure B1).

*Figure B1 Cumulative values of used in analysis and sensitivity analysis*

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# Appendix C Distributional cost-effectiveness analysis (DCEA)

### Weighting functions and social welfare indices

We used four different weighting functions based on established social welfare indices (SWI). These include the generalised extended Gini SWI and Atkinson SWI which indicate relative inequality aversion, as well as the generalised extended Gini SWI and Kolm SWI which indicate absolute relative inequality aversion.

For the general extended Gini index, we used the weighting function $1-\eta(1-p)^{\eta-1}$ where p is a quantile and for $\eta \geq 1$. However, due to small-sample and grouping bias, estimators from Errygers et al. (1), equation A9 (shown in equation 1) were used:

$$w_{j,n} = \frac{n_j}{N} - \left[\left(1-\frac{I_{j-1}}{N}\right)^{\eta} - \left(1-\frac{I_j}{N}\right)^{\eta}\right]; \eta \geq 1 \quad (1)$$

where $n_j$ is the number of people in the jth decile, $I_j$ is the number of people in all deciles up to and including decile j, N is the population size, and $\eta$ is the degree of aversion in inequality. Where there is no aversion to inequality, $\eta = 1$ (1). When $\eta = 2$, the weighting is a linear function from -1 for the poorest person to +1 to the richest person. As $\eta$ increases above 2, there is more aversion to inequality, with larger negative weights placed on poorer people. Using this weighting, the extended Gini index $I_\omega$, which measures relative inequality, and general extended Gini index $I_G$, which measures absolute inequality, are given by:

$$I_\omega = \frac{1}{\bar{H}} \sum_{j=1}^{J} \left(\bar{h}_j \times w_{J,n}\right) \quad (2)$$

$$I_G = \bar{H} \times I_\omega \quad (3)$$

where $\bar{H}$ is the mean population health, there are J deciles, and $\bar{h}_j$ is the mean health of decile j. The extended Gini index $I_\omega$, ranges from -1 to +1, where -1 signifies inequality concentrated on the lower end of the distribution (poorest deciles) and +1 signifies inequality concentrated on the higher end of the distribution, and 0 represents no inequality.

Atkinson's Index, $I_A$, which measures relative inequality, and Kolm's index, $I_K$, which measures absolute inequality are given by:

$$I_A = 1 - \left[\sum_{j=1}^{J} \left(\frac{\bar{h}_j}{\bar{H}}\right)^{1-\varepsilon} \times \frac{n_j}{N}\right]^{\frac{1}{1-\varepsilon}} ; \varepsilon \neq 1 \quad (4)$$

$$I_A = 1 - exp\left[\sum_{j=1}^{J} \log_e \frac{\bar{h}_j}{\bar{H}} \times \frac{n_j}{N}\right]; \varepsilon = 1$$

$$I_K = \left(\tfrac{1}{\alpha}\right) LOG\left(\sum_{j=1}^{J} e^{\alpha\left(\bar{H}-\bar{h}_j\right)} \times \frac{n_j}{N}\right); \alpha > 0 \quad (5)$$

where $\varepsilon$ and $\alpha$ are quantify constant relative and absolute risk aversion, with higher values representing greater aversion to equality (2). For the Atkinson index, $\varepsilon$ can be any value between 0 to infinity, and the index value $I_A$ is 0 if there is no inequality, and can increase to maximum of 1 as $\varepsilon$ increases. In the Kolm Index $I_K$ converges to the mean for high values of $\alpha$, so $\alpha$ is generally set at low levels, such as 0.025–1 (3).

We then calculated Gini, Atkinson and Kolm EDEH for each scenario.

**EDEH equations**

$$EDEH_{Gini} = \bar{H} - I_G \quad (6)$$

$$EDEH_{Atkinson} = \bar{H}(1 - I_A) \quad (7)$$

$$EDEH_{Kolm} = \bar{H} - I_K \quad (8)$$

**References**

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# Appendix D CHEERS checklist

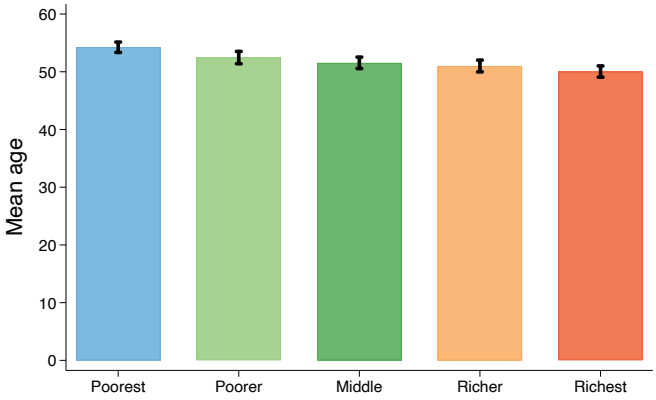
| Topic | No. | Item | Location where item is reported |
|---|---|---|---|
| **Title** | | | |
| | 1 | Identify the study as an economic evaluation and specify the interventions being compared. | Title |
| **Abstract** | | | |
| | 2 | Provide a structured summary that highlights context, key methods, results, and alternative analyses. | Abstract |
| **Introduction** | | | |
| **Background and objectives** | 3 | Give the context for the study, the study question, and its practical relevance for decision making in policy or practice. | Context (local): Introduction, Paragraph 2<br>Context (general): Introduction, Paragraph 3<br>Study question, practical relevance - Introduction, Paragraph 4, 5 |
| **Methods** | | | |
| **Health economic analysis plan** | 4 | Indicate whether a health economic analysis plan was developed and where available. | Not applicable |
| **Study population** | 5 | Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics). | Methods: Data |
| **Setting and location** | 6 | Provide relevant contextual information that may influence findings. | Methods: Screening strategies |
| **Comparators** | 7 | Describe the interventions or strategies being compared and why chosen. | Methods: Screening strategies |
| **Perspective** | 8 | State the perspective(s) adopted by the study and why chosen. | Methods: Model inputs |
| **Time horizon** | 9 | State the time horizon for the study and why appropriate. | Methods: Model outputs |
| **Discount rate** | 10 | Report the discount rate(s) and reason chosen. | Methods: Model outputs, Appendix F1 |
| **Selection of outcomes** | 11 | Describe what outcomes were used as the measure(s) of benefit(s) and harm(s). | Methods: Model outputs |
| **Measurement of outcomes** | 12 | Describe how outcomes used to capture benefit(s) and harm(s) were measured. | Methods: Model outputs |
| **Valuation of outcomes** | 13 | Describe the population and methods used to measure and value outcomes. | Methods: Model outputs |
| **Measurement and valuation of resources and costs** | 14 | Describe how costs were valued. | Methods: Model outputs |
| **Currency, price date, and conversion** | 15 | Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion. | Methods: Model outputs |
| **Rationale and description of model** | 16 | If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed. | Methods: Model structure, Appendix A8 |

| Topic | No. | Item | Location where item is reported |
|---|---|---|---|
| **Title** | | | |
| **Analytics and assumptions** | 17 | Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used. | Appendix A5 (Constructed variables)<br>Appendix A7 (Modelling annual clinic visits)<br>Appendix A8.2 (Calculating costs) |
| **Characterising heterogeneity** | 18 | Describe any methods used for estimating how the results of the study vary for subgroups. | Methods: Distributional analysis |
| **Characterising distributional effects** | 19 | Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations. | Methods: Distributional analysis |
| **Characterising uncertainty** | 20 | Describe methods to characterise any sources of uncertainty in the analysis. | Methods: Scenario analysis<br>Methods: Sensitivity analysis |
| **Approach to engagement with patients and others affected by the study** | 21 | Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study. | Not applicable |
| **Results** | | | |
| **Study parameters** | 22 | Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions. | Appendix Table A2 |
| **Summary of main results** | 23 | Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure. | Appendix Table E1, Figure E2 |
| **Effect of uncertainty** | 24 | Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable. | Results: Sensitivity analysis<br>Appendix F |
| **Effect of engagement with patients and others affected by the study** | 25 | Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study | Not applicable |
| **Discussion** | | | |
| **Study findings, limitations, generalisability, and current knowledge** | 26 | Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice. | Discussion |
| **Other relevant information** | | | |
| **Source of funding** | 27 | Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis | Funding/Support |
| **Conflicts of interest** | 28 | Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements. | Author Disclosures |

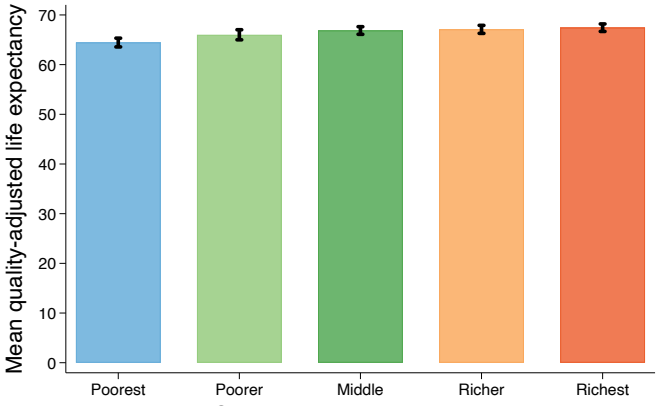
# Appendix E Further results

*Figure E1 Mean characteristics of the target population*

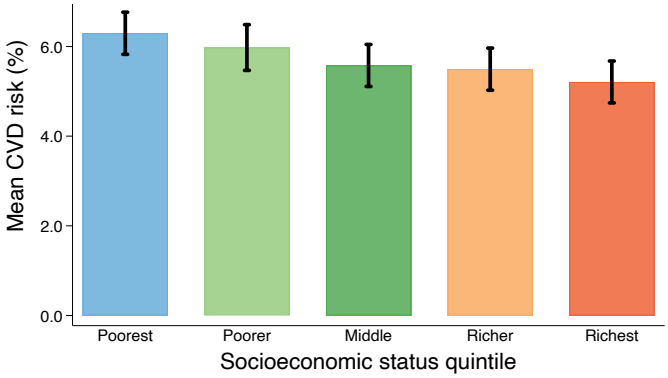
**A. Mean age**



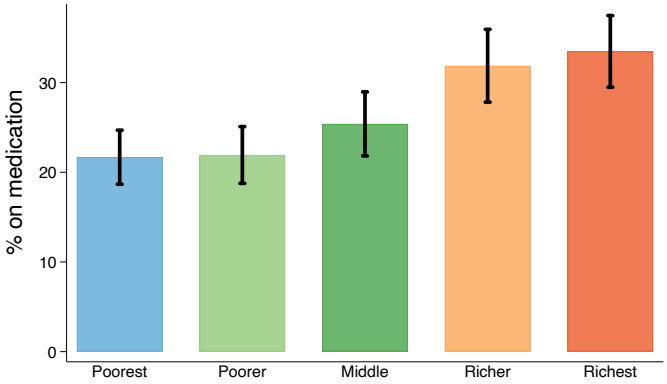

**B. Mean quality-adjusted life expectancy**



**C. Mean 10-year risk of CVD event (%)**




**D. Already using antihypertensive, statin or antidiabetic medication (%)**



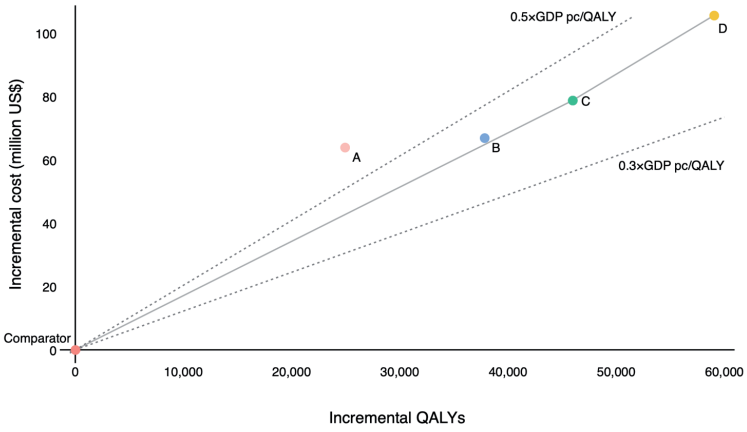

**Notes:** CVD = cardiovascular disease. Estimates for target population aged 35+ with no previous history of CVD from sample of 4,745 individuals. CVD event is fatal or non-fatal coronary heart disease or stroke. Panel B shows percentage using any of the three medications. Interval lines show cluster-adjusted 95% confidence intervals. P-values for tests of equal means across quintile groups: (A) ANOVA P<0.001; (B) ANOVA P<0.001; (C) ANOVA P = 0.014; (D) Wald test P <0.001.

*Table E1 Incremental costs, QALYs, ICERs, QALYs net of opportunity cost by scenario*

| Treatment | Screening | Setting | Age threshold | High CVD risk | Antihyperten-sives at BP 130/80 mm Hg if high CVD risk or has diabetes | Statins to all people with dia-betes | Incremental costs (mil-lion US$) | Incremental QALYs | ICER (US$/ QALY) | ICER from previous scenario on CEF[a] (US$/ QALY) | Difference in mean QALYs × 100,000 net of op-portunity cost |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Current program (comparator) | Routine | Healthy Lifestyle Centre | 35+ | ≥ 20% | NO | NO | Comparator | Comparator | Comparator | Comparator | Comparator |
| A | Opportunistic | Any public outpatient clinic | 35+ | ≥ 20% | NO | NO | 63.9 | 24,922 | 2,565 | - | -66 |
| B | Opportunistic | Any public outpatient clinic | 40+ | ≥ 10% | NO | NO | 66.9 | 37,819 | 1,769 | - | 52 |
| C | Opportunistic | Any public outpatient clinic | 40+ | ≥ 10% | YES | NO | 78.8 | 45,963 | 1,714 | 1,714 | 76 |
| D | Opportunistic | Any public outpatient clinic | 40+ | ≥ 10% | YES | YES | 105.6 | 59,025 | 1,789 | 1,789 | 75 |

**Notes:** CVD = cardiovascular diseases, BP = blood pressure, US$ = US dollars, QALY = Quality-Adjusted Life Year, ICER = incremental cost-effectiveness ratio, CEF = cost-effectiveness frontier.
a ICERs are calculated from the closest least costly scenario on the CEF.

***Figure E2 Cost-effectiveness frontier***




**Notes:** US$ = US dollars, GDP = Gross Domestic Product, QALY = Quality-adjusted life years. Points A, B, C and D show incremental costs and QALYs for the respective strategies with respect to the comparator (origin) of the current CVD risk screening program. The line connecting the origin with points C and D is the cost-effectiveness frontier. Dashed lines show thresholds at 0.3 (US$ 1,225) and 0.5×GDP (US$2,041) pc per QALY.

***Figure E3 Differences between each strategy and comparator (Δ) in mean QALYs over distribution of socioeconomic status – Pareto dominance check***

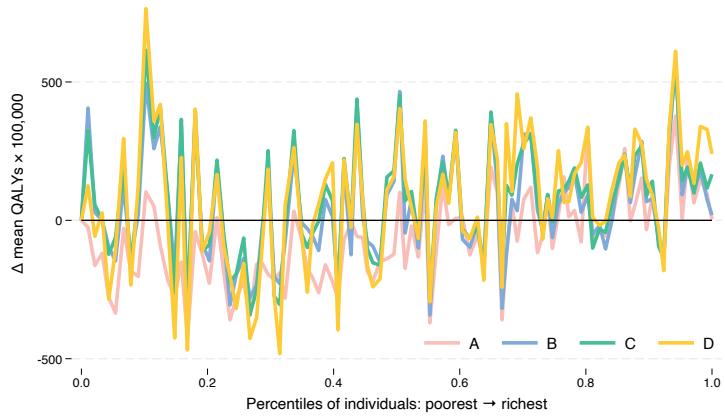


*Figure E4 Differences between each strategy (Δ) in mean QALYs by economics status quintile*


# Appendix F Sensitivity analysis

## F1 Deterministic sensitivity analysis

We tested the sensitivity of the modelled ICERs in strategies B, C and D to the following changes in key parameters.

(1) Increasing the effect of antihypertensives on the risk of non-fatal stroke, with the risk reduction changed from 0.86 to 0.69, as seen in individuals with systolic blood pressures at 160 mmHg and above (1).

(2) Altering the discount rate from 3% to 0% and 6%, as there is no consensus on the discount rate for Sri Lanka, and these are common values used in cost-effectiveness analyses (2).

(3) Effect of reducing the quality of life weight following a myocardial infarction from 0.02 to 0.25, similar to that of stroke.

(4) Cost of usual non-CHD and non-stroke inpatient and outpatient care to 80% and 120% of the values used.

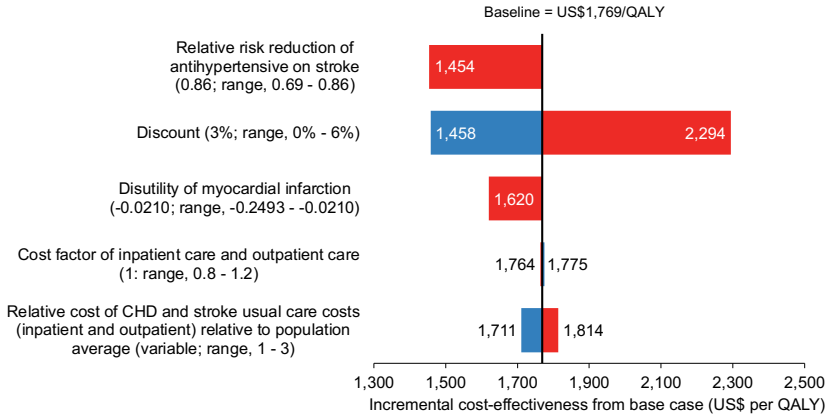
(5) Inflation of cost of CHD and stroke inpatient and outpatient care reduced to 100% of usual costs and increased to 300%, instead of 109 – 285%

(6) C and D following changes We modelled two discount values (0% and 6%), increased the impact of antihypertensive on stroke (relative risk reduced from 0.86 to 0.69, as seen in people with a systolic blood pressure ≥ 160 mmHg), reduced the quality of life weight after a myocardial infarction to be on par with that of a stroke, and varied costs for inpatient and outpatient care.

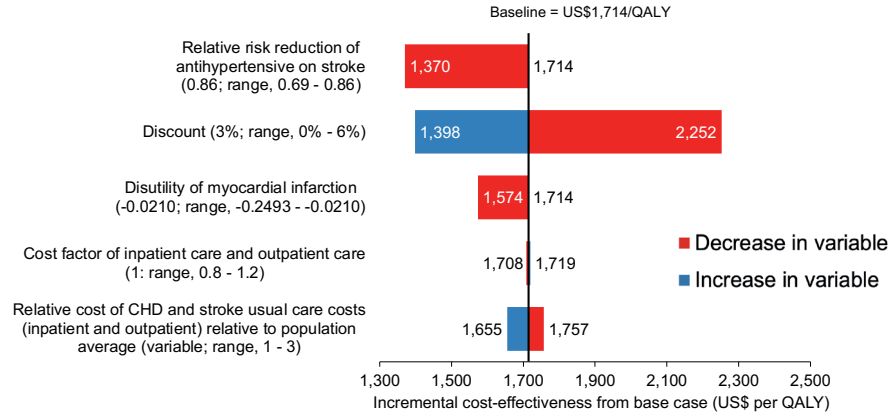
Tornado diagrams with the results are shown below for each scenario.

*Figure F1 Deterministic sensitivity analysis*

**Scenario B**




**Scenario C**




**Scenario D**

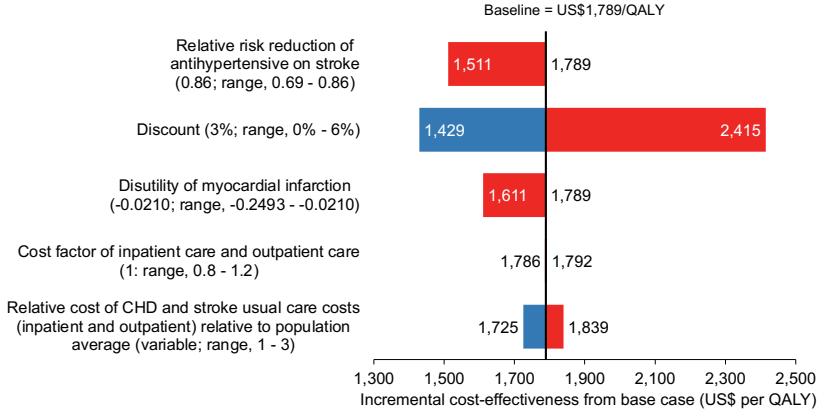
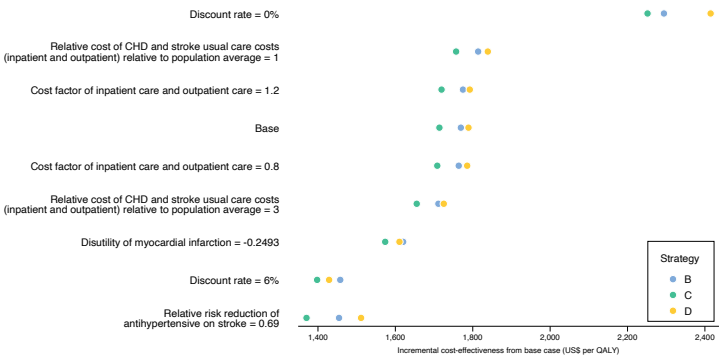


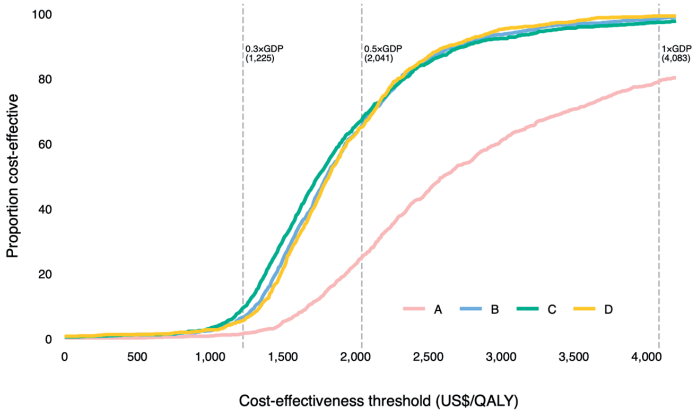
Figure F2 shows the ICER for each strategy for each change in parameter. For most scenarios the ICER is lowest for strategy C, followed by B, then D. There are two exceptions: 1) when the disutility of myocardial infarction is similar to that of stroke (-0.2493), and 2) when the discount rate is 6%, strategy D has a slightly lower ICER than strategy B.

***Figure F2 Comparison of ICERs of strategies B, C and D for each parameter in DSA***




## F2 Probabilistic sensitivity analysis

***Figure F3 Probabilistic sensitivity analysis***

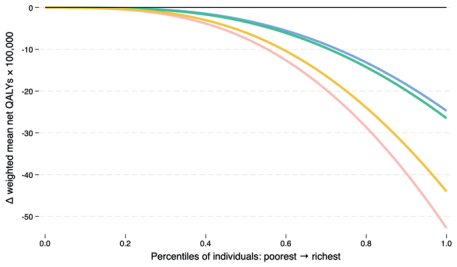



**Notes:** The probabilistic sensitivity traces are show for strategies A, B, C, and D. Dotted vertical lines show cost-effectiveness thresholds (CET) for 1 QALY at 0.3 (US$ 1,225), 0.5 (US$2,041) and 1 (US$ 4,083) × GDP per capita.
US$ = US dollar, QALY = Quality-adjusted life year.

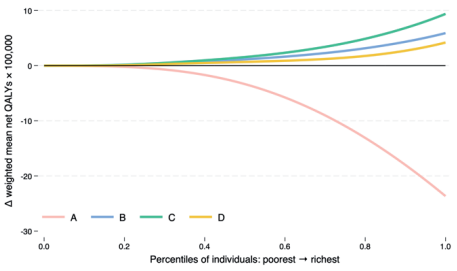
## F3 Health opportunity costs

***Figure F4 Difference between each strategy and comparator (Δ) in QALY means using 3rd order GCC check and alternative conversion rates to estimate health opportunity costs (graphs)***

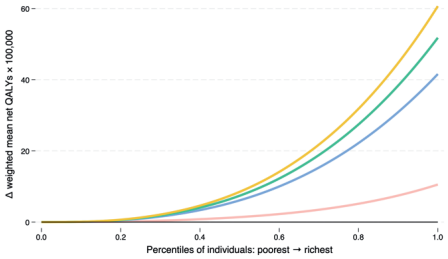
I. Opportunity cost is 0.3×GDP pc/QALY




II. Opportunity cost is 0.5×GDP pc/QALY



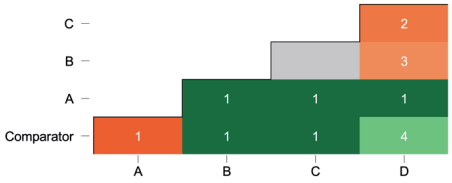

III. Opportunity cost is 1.0×GDP pc/QALY



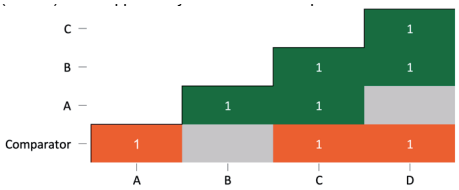

**Notes**: GCC = generalized concentration curve. The monetary costs of each scenario are converted to QALYs foregone, using alternative conversion rates of 0.3, 0.5 and 1×GDP pc per QALY.

***Figure F5 Generalized concentration curve dominance (GCCD), using alternative conversion rates to estimate health opportunity costs***

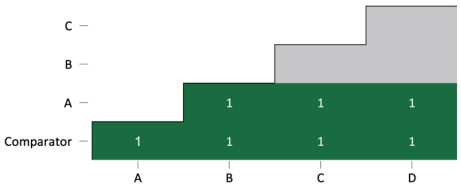
I. Pairwise Generalized Concentration Curve Dominance (GCCD) when opportunity cost is 0.3×GDP pc/QALY




II. Pairwise Generalized Concentration Curve Dominance (GCCD) when opportunity cost is 0.5×GDP pc/QALY




III. Pairwise Generalized Concentration Curve Dominance (GCCD) when opportunity cost is 1.0×GDP pc/QALY

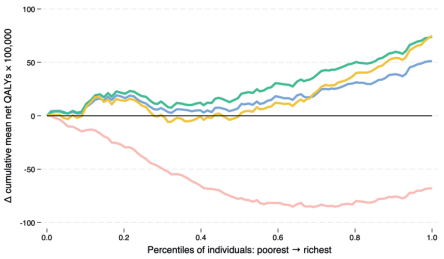




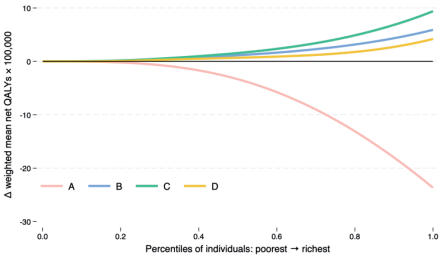
**Notes:** The monetary costs of each scenario are converted to QALYs foregone, using alternative conversion rates of 0.3, 0.5 and 1×GDP pc per QALY.

***Figure F6 Differences between each strategy and comparator (Δ) in QALY means over distribution of socioeconomic status and summary of dominance results, using uniform distribution of health opportunity costs***

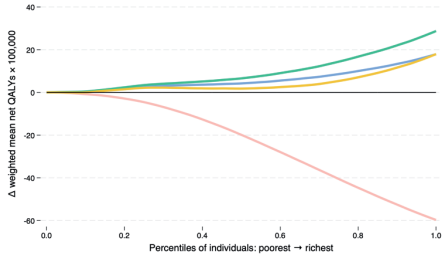
I. Δ cumulative mean net QALYs – GCCD check




II. Δ linearly weighted cumulative mean net QALYs – 2nd order GCCD check



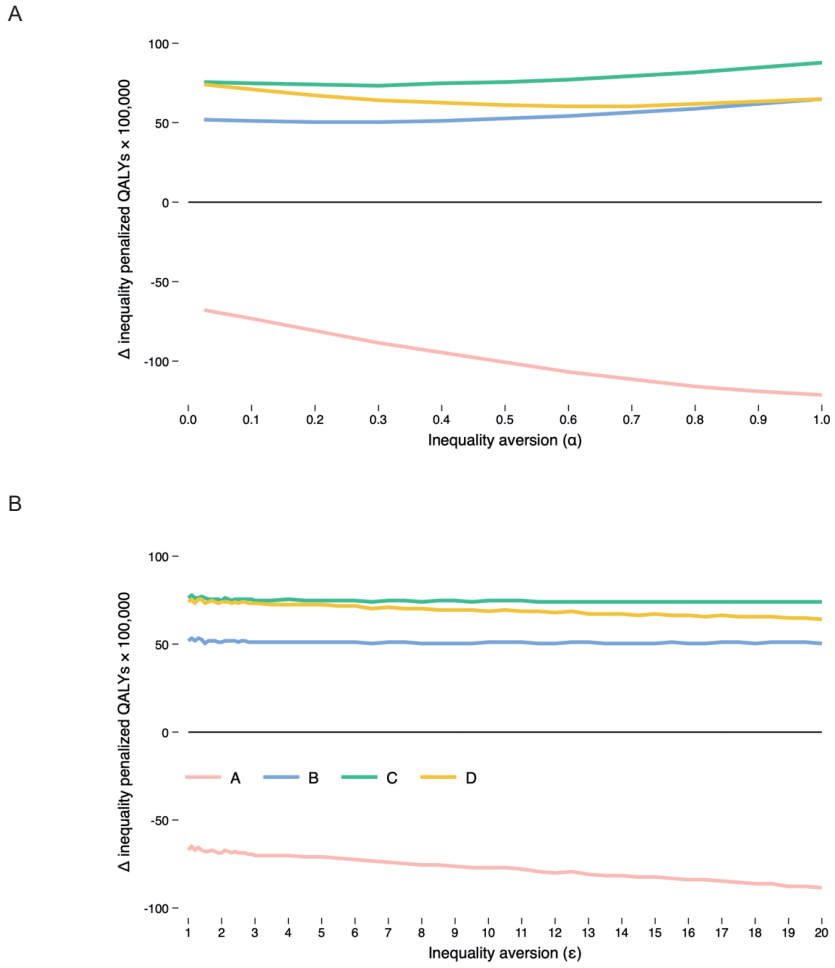

III. Δ nonlinearly weighted cumulative mean net QALYs – 3rd order GCCD check




IV. Pairwise Generalized Concentration Curve Dominance (GCCD)

## F4 Inequality penalized QALYs using alternative social welfare functions

***Figure F7 Difference between each strategy and the comparator (Δ) in inequality-penalized QALYs at different degrees of inequality using Kolm and Atkinson social welfare functions***




**Notes:** Δ indicates a difference: strategy X – comparator. Inequality-penalized QALYs calculated for the A) Kolm (3) and B) Atkinson (4) social welfare functions. Differences are multiplied by 100,000.

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# Chapter ∞

# Conclusion

# CONCLUSION

As low- and middle-income countries (LMICs) progress in their epidemiological transition, many face ageing populations and are making inadequate progress, compared to high-income countries, in reducing key metabolic risk factors for cardiovascular diseases (CVDs), the leading cause of both overall mortality and premature morality in working-age populations. In Sri Lanka, while key health indicators are above the LMIC average, the burden of disease of CVDs has resulted in slow improvements in male life expectancy.

Several LMICs have introduced programs to screen for CVD and associated conditions, and to improve their management. However, refinement of such screening and management programs requires evidence on how the burden of these conditions varies across sociodemographic groups, which is lacking in many LMICs. Furthermore, there is only limited LMIC evidence on the potential to improve the effectiveness, efficiency and equity impact of screening and management programs through modifications to their design.

This thesis uses Sri Lanka as a case study to look at these two aspects of CVD and its associated conditions. Firstly, it quantifies the burden of these conditions and describes their sociodemographic profile, and then estimates the costs, effectiveness and distributional impacts of modifications of screening and management programs that are tailored to the needs of the population.

# 8.1 RESEARCH FINDINGS

## 8.1.1 Cardiovascular disease burden

Chapter 2 finds 4% of Sri Lankan adults report a history of ischaemic heart disease—henceforth referred to in this chapter as coronary heart disease (CHD)—and 3% report symptoms consistent with angina. This is the first estimate on the prevalence of CHD using nationally representative data in Sri Lanka, and one of the few estimates in any LMIC. Using similar definitions, the prevalence is 70% higher (3.8% versus 2.2% of the total population) than that estimated for Sri Lanka by the Global Burden of Disease (GBD) Study. Even after excluding participants that only reported symptoms consistent with angina (the Rose Angina questionnaire is not highly sensitive or specific), the prevalence is still higher (2.5%). Given the data constraints on the CHD incidence, prevalence and mortality in many LMICs, the GBD study relies on extensive modelling, transforming and adjusting data from vital registration systems with mean values for physical and biochemical measurements, behavioural and sociodemographic covariates such as fasting plasma glucose. My findings of a likely underestimation of CHD prevalence align with similar findings for diabetes, where prevalence estimates from global studies by the International Diabetes Federation and Non-Communicable Disease Risk Factor Collaboration (7–11%) appear to have significantly underestimated the prevalence determined by the Sri Lanka Health and Ageing Study (23%) (1). Whilst the GBD study acknowledges limitations in its estimates, primarily due to data gaps (2), my findings underline the importance of improving and prioritising high-quality primary data collection in LMICs. Not only could local data provide more robust prevalence estimates, simple survey data, most of which is collected in frequent STEPwise approach to surveillance (STEPS) surveys in LMICs, can be used for detailed health-economics and equity analyses to inform the design of CVD-risk screening strategies. The addition to surveys of the EQ-5D-5L, a multi-attribute utility instrument with five quick questions, could potentially help countries move to calculating Quality-Adjusted Life Years (QALYs), particularly if country- or region-specific mapping of utility scores are produced. Alternatively, responses to the EQ-5D-5L can also be used to produce disability weights to calculate Disability-Adjusted Life Years (DALYs) for the local context.

Of note, I find that the odds of CHD were higher in the urban sector, in people with less education, and in poorer areas, although no association was found with poorer households. There is also a possible element of underdiagnosis in women, a pattern reported globally, as women had higher odds of angina than men, yet lower odds of being diagnosed with CHD. There is a higher prevalence of CHD, more pronounced in women, in the 50–70-year age group than that estimated by the GBD study. This has implications for the CVD risk prediction tool published by the World Health Organization (WHO) in 2019. Since the GBD prevalence estimates were used to recalibrate the WHO-2019 CVD risk tool, it is possible that the risk tool underestimates true risk. This should be considered when setting CVD risk thresholds,

with an inclination towards lower thresholds to identify high-risk individuals. When more follow-up data is available for the Sri Lanka Health and Ageing Study, efforts should be made to validate the WHO-2019 risk tool, as well as produce a Sri Lankan-specific CVD risk tool using these local data.

The analysis in Chapter 3 finds that people with chronic diseases have higher odds of issues across domains covered by the EQ-5D: namely mobility, self-care, usual activities, pain/discomfort and anxiety/depression, even after controlling for gender, age, ethnicity, education category, sector of residence and other common chronic conditions. The patterns of problems vary by type of CVD. People with CHD have higher odds of difficulties in self-care, while those with angina symptoms have higher odds of pain/discomfort and anxiety/depression. People with stroke have significantly higher odds (2.4–7.0) of difficulties across multiple domains including mobility, self-care, usual activities, and anxiety/depression. Additionally, hypertension and diabetes increase the odds of mobility and activity limitations, with diabetes also associated with challenges in self-care and pain/discomfort. The reduction in quality of life (QOL) (disutility) due to having stroke is large and is just behind the disutility of cancer. Diabetes also results in a sizeable disutility, whilst CHD and angina have smaller disutilities.

Though the disutilities of CHD may be somewhat small in magnitude, Chapter 4 finds that CHD is associated with significant impacts on physical and mental functioning, as well as on outpatient use. Furthermore, people with indications of CHD but no diagnosis (that is, they fulfill the criteria for angina) have reduced physical functioning, to the same level as those with diagnosed CHD. Furthermore, those with undiagnosed CHD experience a significant psychological and physical burden, utilize more healthcare services and incur higher out-of-pocket expenses, likely for symptomatic relief, compared to those that have been diagnosed. Additionally, those with diagnosed hypertension and diabetes, had poorer physical and mental functioning, and had more outpatient visits and out-of-pocket expenditures than those without these conditions. People who had undiagnosed hypertension and diabetes had minimal health impacts and healthcare use. The differences in impacts seen between CHD, and hypertension and diabetes may be related to undiagnosed CHD being symptomatic, whilst undiagnosed hypertension and diabetes may be asymptomatic until they progress further. I also found that a significant proportion of people with CHD (12%) had comorbid depression. Both undiagnosed and diagnosed depression was associated with poor physical and mental functioning, and reduced health-related QOL.

### 8.1.2 Modifications to CVD-risk screening strategies can result in substantial health gains

The Sri Lankan CVD screening program, though evolving, is very much in line with the basic package of recommendations in the WHO Package of Essential Noncommunicable Disease Interventions (PEN) from 2010 and 2020. Furthermore, it relies on screening individuals in separate clinics called "Healthy Lifestyle Centres", and additional programs such as workplace screening, in a country where there are already a high number of healthcare encounters per individual. Indeed, I estimate that 26% of individuals aged 40 years and over who would have been eligible for treatment under the Sri Lankan CVD-risk screening strategy and yet were undiagnosed had an outpatient visit with a healthcare provider (more than half of them in the public sector) in the previous month (Chapter 6). Up to 59% of undiagnosed individuals may have had an outpatient visit over a year and yet remained untreated for CVD. Through modelling, I estimate that even a 1-month opportunistic screening program which would screen at only 60% of visits to the public sector and 55% of visits to the private sector would identify 8% of individuals who were undiagnosed for CVD and would benefit from statin, antihypertensive or antidiabetic treatment. A less intensive year-long opportunistic screening program would detect 27% of undiagnosed individuals. Furthermore, this analysis demonstrated that poorer people with high CVD risk, hypertension, diabetes or hypercholesterolemia were more likely to be undiagnosed and that an opportunistic screening program at existing healthcare visits would treat slightly more poor people in the public sector and slightly more rich people in the private sector. Overall, it would reduce socioeconomic inequality in untreated high CVD risk.

My research identifies other modifications of the CVD screening programme in Sri Lanka that would make it more cost-effective (Chapter 5). These include, changing the risk tool used to assess CVD risk, raising the age threshold for screening, reducing the risk threshold for high CVD risk and consequent prescription of statins, providing antihypertensive treatment at a lower blood pressure threshold for people with diabetes or high CVD risk, and providing statins to all people with diabetes. Specifically, compared with the current program, changing to the WHO-2019 risk tool would be cost-saving, and raising the minimum age for screening from 35 to 40 would produce an additional 1,007 QALYS at a minimal 113 US dollars (USD) per QALY. Lowering the CVD risk threshold at which statins are prescribed from 20% to 10% would make a significant impact, producing more than 6,000 QALYs at an incremental cost of USD 1,009 per QALY. Finally, incorporating a lower blood pressure threshold for those with a CVD-risk of 10% or more, or diabetes, as well as providing statins to all people with diabetes can produce an additional 13,010 QALYs. All these potential modifications cost between a quarter to a half of the gross domestic product (GDP) per capita per QALY compared to the current screening strategy.

### 8.1.3 The distribution of health gains over socioeconomic groups

Chapter 7 examines CVD risk screening through an equity lens, analysing the distributional impact of combining cost-effective modifications to the current strategy (Chapter 5) with opportunistic screening (Chapter 6). I model the distribution of QALYs (net of health opportunity costs) under various screening scenarios across individuals ranked by socioeconomic status (SES).

While using the same screening guidelines and switching to opportunistic screening would likely greatly increasing the QALYs gained, it is not a given that it would improve equity, as opportunistic screening would screen a far larger number of people, thereby costing more and potentially resulting in health foregone elsewhere in the system, possibly to the disadvantage of poorer people. Nevertheless, I find that an opportunistic screening strategy that also raises the screening age from 35 to 40 years, and reduces the CVD risk threshold for prescription of statins to ≥ 10%, will generate more QALYs net of opportunity costs than the current strategy, but there would be a decrease in QALYs gained by the second poorest economic quintile. Using a stochastic dominance technique in a distributional cost-effectiveness analysis (DCEA), I find that that a strategy with opportunistic screening at an age threshold of 40 years and above, which prescribes statins for people with a CVD risk ≥ 10%, and also provides antihypertensives at a lower blood pressure threshold for people with diabetes or a CVD risk ≥ 10% provides higher mean health net of opportunity costs across economic percentiles after applying linearly decreasing weights when moving from poorest to richest percentiles. A decision maker with some aversion to inequality may choose this strategy over a strategy that additionally prescribes statins to all diabetics but achieves less net health.

While I demonstrate that there is scope for DCEA using stochastic dominance analysis, the application of this type of analysis in an LMIC-setting is new, and challenging. DCEA is very sensitive to the rate of converting the monetary costs of a program to health opportunity costs (e.g. measured in QALYs), to account for potential loss of health due to diversion of money from other areas of the health system. However, the rate of this conversion, and distribution of health-opportunity costs across the economic gradient is needed but not available in LMICs; only a few estimates exist, primarily for the UK in cost of "health production" studies.

## 8.2 FUTURE RESEARCH

Several chapters reveal key areas that require further research. More research is needed on the possibility of underdiagnosis of CHD in women in Sri Lanka, preferably using longitudinal data which will become available with the SLHAS cohort, or cross-linking SLHAS participants with national deaths data or electronic medical records in the future.

In Chapter 3, I find that the Sri Lankan EQ-5D-5L value set, which is mapped from an EQ-5D-3L valuation, has lower utility values than a directly valued EQ-5D-5L value set from India. Further research is needed to determine whether this is due to a cultural norm, where Sri Lankans value some health states less, or rather, due to methodological differences in eliciting the value sets. Such research would be informative in determining whether further work to produce a directly valued ED-5D-5L would be worth investing in for Sri Lanka.

This thesis is very much focussed on economic analysis of pharmacological management of CVD risk. Nevertheless, control of other risk factors, such as smoking, physical activity, poor diet, and exposure to air pollution are important aspects of primary prevention that influence CVD risk as well as the risk on other chronic diseases. Health economic analyses of acceptable and impactful interventions that can manage these risk factors, using similar parameters on horizon, perspective and discounting would be useful, will be useful in expanding the options available to policy makers and facilitating the prioritization of strategies.

As discussed previously, while cost-effectiveness analyses can present the incremental cost-effectiveness ratios (ICERs) of new strategies (Chapters 5 and 7), there is a lack of information on how much policy makers are willing to pay for health gains, or a "cost-effectiveness threshold" below which a strategy could be considered cost-effective. Whilst thresholds based on international modelling studies are available, there is no consensus locally on what the appropriate threshold is. Research to determine such a threshold would be valuable to interpret the ICERs calculated in health-economic studies.

For DCEA (Chapter 7), which incorporates opportunity costs, local studies are needed to determine the marginal cost of "health production", or the cost per QALY of alternatives that are foregone due to diversion of money to the strategy under consideration. Ideally, these opportunity cost conversion rates should be determined for each sociodemographic group. Whilst this ideally requires an analysis of the health system's outputs, it could initially begin with an analysis of local policy makers' expert views. Although the Sri Lankan health system has typically achieved equitable health outcomes over several domains, without utilising extensive distributional analysis prior to implementing strategies, DCEA can play an important role at present. From 2020, Sri Lanka has faced unprecedented challenges following a collapse in

government revenue, which lead to defaulting foreign debt repayments and high inflation. The economic crisis placed serious acute pressures on the public health system (3, 4), and though the economy is somewhat stabilised, immense fiscal pressures continue. As others have noted, the economic pressures on the health system has highlighted the importance of cost-effective interventions (5). Whilst the Sri Lankan Ministry of Health does not explicitly target the poor, it has achieved pro-poor outcomes over public healthcare utilisation, out-of-pocket spending and financial protection, with quality of care in the public sector often on-par with that of the private sector (6, 7). The pro-poor achievements are mainly through individuals self-selecting more "consumer-convenient" private healthcare if they can afford it, and through maintaining free, quality healthcare in the public sector. However, some studies, along with anecdotal evidence suggests that with the economic crisis, poorer individuals have changed medication patterns, reducing intake or stopping entirely, due to the rising costs of medications (8), and there is increasing utilisation of the public health system (9). Though not an explicit goal of the Ministry of Health, DCEA can provide confirmation that strategies under consideration are likely to maintain equitable health outcomes across socioeconomic strata.

## 8.3 IMPLICATIONS FOR POLICY

Chapter 2 demonstrates that people with CVD risk factors—hypertension, diabetes and high waist-to-hip ratio—also had higher odds of a diagnosis of CHD. Additionally, demographic factors such as age, residing in urban areas and middle and most developed areas, and lower education levels were associated with higher odds of CHD. A resource-constrained screening program may consider prioritizing these groups to optimize its impact.

The findings for females raise the possibility of underdiagnosis. Not only do females have a higher prevalence of angina than men, particularly in rural and estate areas, and more developed areas, they have far higher odds of reporting symptoms consistent with angina than men, even after adjusting for other risk factors[1], yet have similar odds of a CHD diagnosis. Given that there is a global pattern of underdiagnosis of CHD in females, it is important to ensure healthcare workers and policy makers are aware of the possibility of underdiagnosis in females, particularly in the groups (rural and estate areas, and more developed areas) where the prevalence of angina is higher than that in men. Although this may require further investigation to confirm, it is important in the meantime to increase awareness amongst healthcare workers of the possibility of underdiagnosis of CHD in females.

1 Adjusted for age, gender, ethnicity, sector of residence, education level, household SES, area SES, and risk factors include hypertension, diabetes, smoking status, total cholesterol and BMI.

The findings of Chapter 4 further motivate screening for high-risk of CVD. Chapter 4 shows that CHD poses a significant burden to physical and mental functioning, lowers health-related QOL, increases outpatient visits and out-of-pocket spending on healthcare. An effective CVD-risk screening strategy, by managing individuals who are at high-risk of developing CVD, will reduce the number individuals without CVD from developing CHD along with its associated adverse health and healthcare outcomes.

Interestingly, I also find that individuals with symptoms of CHD but are undiagnosed, have similar levels of poor physical functioning, poorer mental functioning, more outpatient visits and higher out-of-pocket spending on healthcare than people with diagnosed CHD. Whilst identifying individuals who have already developed CHD is not the aim of CVD-risk screening, they likely could be identified through such screening as they fit the criteria for it (that is, no known pre-existing diagnosis of CVD), then put on a different management pathway for investigation and management of CHD.

A CVD-risk screening strategy also identifies and manages individuals with hypertension and diabetes, as risk factors for CVD. I find that undiagnosed hypertension and diabetes on their own do not appear to be associated with poorer physical or mental functioning or QOL, nor are they associated with more healthcare use or healthcare expenditures. Nevertheless, early diagnosis and management of these conditions are still important to slow disease progression and reduce sequelae from these conditions, including CVD.

Chapter 5 demonstrates that several changes to the CVD screening program could greatly increase the impact of it in a way that is likely to be cost-effective in Sri Lanka. Firstly, there is a strong argument that in a money-constrained health system, that screening a slightly older age group (40 years and above instead of 35) could be more cost-effective. The counter argument is that lifetime exposure to risk factors increases CVD risk, and so interventions should include younger people. However, where there are limited resources and system constraints, it should be recognized that the incremental cost per QALY gained is higher when screening younger individuals who have a lower risk.

Secondly, it evaluates and confirms that moving from the older WHO International Society of Hypertension (WHO-ISH) CVD-risk tool to the WHO-2019 CVD-risk tool is indeed likely to be cost-effective. The change in risk tools will result in a far higher impact if combined with lowering the threshold for high CVD risk from 20% to 10%. Though the PEN guidelines imply a 20% risk threshold as high CVD risk, several countries, particularly high-income countries, opt for lower thresholds ranging from 7.5–10%. The threshold set can depend on the ability of the health system to pay for increased preventative treatment and follow-up. It can also be shaped by considerations to minimize the potential adverse health effects of placing

a higher proportion of the population on treatment, which could diminish the QOL improvements achieved by the program. However, the findings from Chapter 5 suggest that moving to a 10% CVD risk threshold, which has large impact in QOL gains, is likely cost-effective and even after accounting for some loss in QOL from taking additional medications, would still be cost-effective. In addition to these changes, prescribing antihypertensives at a lower blood pressure threshold (≥ 130/80) for those at high CVD risk or diabetes, and prescribing statins to all people with diabetes each increases impact and is likely to be cost-effective.

These findings suggest that implementing four key modifications to the current screening program—1) using the WHO-2019 risk tool, 2) setting a 10% CVD risk threshold for statin treatment, 3) prescribing antihypertensives at a lower blood pressure threshold (≥ 130/80) for those at 10% CVD risk or diabetes, and 4) prescribing statins to all individuals with diabetes—could substantially increase impact in a cost-effective manner. These changes could generate over 13,000 QALYs at a cost of USD 1,464 per QALY, which would likely be within accepted cost-effectiveness thresholds, being one-third of Sri Lanka's GDP per capita. For policymakers, this more intensive screening and treatment protocol likely represents a high-value, affordable investment that is cost-efficient and achieves significant health gains.

In terms of maximizing the impact of CVD-risk screening programs, Chapter 6 shows how, in a country such as Sri Lanka, where there is high rate of doctor-patient contacts, opportunistic screening may be a potential mechanism to increase CVD risk screening rates, increasing diagnoses in an equitable manner. Such a program would cost a fraction of a percentage of the annual health budget, and result in a 2% increase in patient contacts for follow-up, both of which are likely to be manageable with some planning.

There is increasing recognition of considering program impacts on health equity in addition to efficiency. Chapter 7 demonstrates that although opportunistic CVD risk screening with the additional four modifications would have the highest health impact and is likely to be cost-effective, a decision maker who is concerned with the distribution of health impacts through the economic gradient may wish to opt for a program with less features (in this case, a scenario with three of the four modifications which is less costly than all four modifications) in order to compromise some of the overall health impact for greater equity in the distribution of health gains.

Utilising outputs from health-economics analysis in Sri Lanka for decision making is not well-established, nor necessarily required. Though Sri Lanka lacks "economic evaluation guidelines" which outline a local consensus for key parameters needed in health-economic analyses, such as the time-horizon, perspective, discount rates, and a cost-effectiveness threshold, the studies in the thesis transparently describe what parameters have been used. Further, I have presented

the actual ICERs and compared it to various potential cost-effectiveness thresholds, leaving room for decision makers to determine whether these values are acceptable. As such, the recommendations presented can be seriously considered for implementation, and also form the basis of future discussions to better integrate cost-effectiveness and distributional analyses into health strategy design.

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# SUMMARY

Cardiovascular disease, in particular coronary heart disease (CHD) and stroke, is the leading cause of mortality worldwide, with a complex and evolving trajectory. While ageing populations and rising prevalences of risk factors such as sedentary lifestyles, hypertension and diabetes drive the CVD burden up, concurrent improvements in the medical management of people at high risk of CVD, along with effective treatment of CVD events, counterbalances this upward trend. Low- and middle-income countries (LMICs) face a dual challenge with rapidly ageing populations and likely inadequate levels of medical treatment for risk factors of CVD such as hypertension, diabetes and hypercholesterolemia. Indeed, while high-income countries have seen a 60% decline in the age-standardized burden (which accounts for ageing populations) of CVD from 1990–2021, LMICs have seen only a 14-16% decline in the same period. Sri Lanka, a lower-middle income country, is an interesting case study as a country that has outperformed many of its lower-middle income peers in indicators related to maternal health, child health and life expectancy yet faces significant challenges from CVD, which is believed to have contributed to the slowing in male life expectancy improvements. It has taken significant steps to counter the CVD burden through prevention, particularly by introducing a strategy to screen individuals for high CVD risk, hypertension, diabetes and hypercholesterolemia, and treat eligible individuals with antihypertensives, antidiabetics and statins as appropriate. This strategy is based on the World Health Organization's package of essential noncommunicable disease interventions (known commonly as PEN) and relies on a CVD-risk screening tool that estimates an individual's risk of having a CVD event over 10 years.

This thesis aims in its first part, to establish the burden of CVD, in particular CHD, in terms of prevalence (there is limited primary prevalence data in low- and middle-income countries), loss in quality of life, and impacts on physical and mental functioning as well as healthcare use and healthcare costs for individuals. It uses primary data from Sri Lanka, and presents some of the first findings on these aspects in an LMIC. The second part of the thesis aims to assess how the CVD-risk screening strategy in Sri Lanka can be modified to improve impact and equitability while maintaining cost-effectiveness.

Chapter 2 estimates the prevalence of CHD in Sri Lanka and looks at associations with sociodemographic and risk factors, which may help focus CVD-risk screening strategies. It finds that the prevalence of CHD may be higher than previously thought (3.8% versus an estimate of 2.2% in the Global Burden of Disease (GBD) Study). It also finds that there may be an element of underdiagnosis of CHD in women, who have higher odds of reporting symptoms consistent with CHD, but have similar odds of having a CHD diagnosis as men. This chapter underscores the importance of locally derived data and has implications for the accuracy of

the CVD-risk tool developed by the World Health Organization (WHO) in 2019, which is calibrated using data from the GBD study.

Chapter 3 reveals that quality of life is diminished in CVD, more so for stroke than for CHD. On a scale where 1 is the best possible health, and 0 is equivalent to death, a person with CHD rates his or her quality of life at 0.02 points less than a person with the same sociodemographic characteristics and chronic diseases, with the corresponding value for stroke being significantly worse at 0.25 points less. This chapter also presents the first published "disutility catalogue" for a South Asian country, which can be used in health-economic modelling that utilises Quality Adjusted Life Years (QALYs) as an outcome measure.

Chapter 4 provides a strong motivation for CVD-risk screening: it finds that the health and healthcare burden faced by individuals with CHD is high. The burdens of CHD are magnified for individuals with symptoms consistent with CHD, but who have not been diagnosed with CHD. Both diagnosed and undiagnosed individuals with CHD had poor physical functioning, while those with symptoms consistent with CHD but were not diagnosed had worse mental functioning, more outpatient healthcare visits and more out-of-pocket spending on health than individuals without CHD, as well as individuals with a CHD diagnosis. It also reveals that there is significant comorbidity of CHD and depression, and that individuals with depression also have poorer health outcomes and higher healthcare use. This chapter also analyses the same outcomes for people with hypertension and diabetes, both conditions that are screened and treated in CVD-risk screening strategies. It finds no significant differences in health and healthcare outcomes for individuals with undiagnosed hypertension and diabetes, compared to people without these conditions. Nevertheless, screening for these conditions is important to prevent their progression and reduce the incidence of CHD.

Chapter 5 does a cost-effectiveness analysis of alternatives to the current CVD-risk screening strategy in Sri Lanka. It finds that modifications to technical components of this strategy, such as switching from older CVD-risk charts to the WHO-2019 CVD-risk tool; increasing the age screened from 35 years to 40 years and above; lowering the CVD risk threshold for initiating statin treatment from 20% to 10%, prescribing antihypertensives at a lower blood pressure (≥130/80 mmHg) for people with diabetes, or a CVD risk of 10% or more; and prescribing statins to all people with diabetes, would provide large health gains at a likely affordable cost, and that each of these modifications are likely to be either "cost-saving" or "cost-effective".

Chapter 6 looks at an alternative setting for CVD risk screening, that is currently done in dedicated "Healthy Lifestyle Centres". Noting that 26% of individuals who are eligible for treatment under the current screening strategy had visited an outpatient healthcare provider in the previous month and yet remained untreated, this chapter looks at shifting screening to

existing healthcare encounters, thereby increasing coverage. It finds that a year-long opportunistic screening program could detect up to 27% of undiagnosed individuals, even if an eligible individual had only approximately a 30% chance of being screened at any visit. Further, it found that an opportunistic screening program would treat slightly more poor people in the public sector and slightly more rich people in the private sector, reducing the socioeconomic inequality seen in untreated high CVD risk.

Chapter 7 combines the concepts from Chapters 5 and 6, assessing the cost-effectiveness of moving to opportunistic screening, along with each of the technical modifications that were found to be cost-effective in Chapter 5. It also shows results of a distributional cost-effectiveness analysis (DCEA) using stochastic dominance, extending the cost-effectiveness analysis to assess the distribution of the impact of each strategy across the socioeconomic gradient. It finds that an opportunistic strategy screening people aged 40 years and above, which prescribes statins at a CVD risk ≥10%, and antihypertensives at a lower blood pressure (≥ 130/80 mmHg) to people with diabetes or a CVD risk of ≥ 10% would be preferred to the current strategy, if there is aversion to the poor experiencing worse health outcomes. With such aversion to health inequality, the same strategy may be preferred to another that additionally prescribes statins to all people with diabetes.

The findings from the six studies are synthesised in Chapter 8, highlighting the importance of CVD risk screening and identifying several key changes to the PEN-based screening strategy that could greatly increase impact, while remaining cost-effective and equitable. This work underlines the importance of collecting local data in LMICs that can be used to establish health burdens more accurately, as well as for high-quality modelling. Using survey data collected in an LMIC setting, these studies also demonstrate the potential for other LMICs to model and design evidence-based, cost-effective and equitable CVD risk screening strategies tailored to their specific contexts.

# SAMENVATTING

Hart- en vaatziekten, in het bijzonder coronaire hartziekten (CHD) en beroertes, zijn wereldwijd de belangrijkste doodsoorzaak, met een complex en evoluerend traject. Terwijl de vergrijzing van de bevolking en de toenemende prevalentie van risicofactoren zoals een gebrek aan lichamelijke beweging, hoge bloeddruk en diabetes de ziektelast van hart- en vaatziekten verhogen, hebben verbeteringen in de medische behandeling van mensen met een hoog risico op hart- en vaatziekten en effectievere behandelingen van hart- en vaatziekten gezorgd voor een tegenwicht van deze trend. Lage- en middeninkomenslanden (LMIL) zijn geconfronteerd met een dubbele uitdaging: een snel vergrijzende bevolking en een onderbehandeling van risicofactoren voor CVD zoals hypertensie, diabetes en hypercholesterolemie. Terwijl in landen met een hoog inkomen de ziektelast (rekening houdend met de vergrijzing) van CVD tussen 1990-2021 met 60% is gedaald, is in LMIL in dezelfde periode slechts sprake van een daling van 14-16%. Sri Lanka is een interessante casestudy als een land dat het beter heeft gedaan dan veel andere LIML op het gebied van indicatoren met betrekking tot de gezondheid van moeders, de gezondheid van kinderen en de levensverwachting, maar dat toch wordt geconfronteerd met aanzienlijke uitdagingen als gevolg van CVD. Het land heeft belangrijke stappen ondernomen om de ziektelast van hart- en vaatziekten tegen te gaan door middel van preventie, met name door een strategie in te voeren om mensen te screenen op een hoog risico op hart- en vaatziekten, hypertensie, diabetes en hypercholesterolemie, en mensen die hiervoor in aanmerking komen te behandelen met antihypertensiva, antidiabetica en statines. Deze strategie is gebaseerd op het pakket essentiële interventies voor chronische ziekten van de Wereldgezondheidsorganisatie (algemeen bekend als PEN) en is gebaseerd op een screeninginstrument voor het risico op hart- en vaatziekten dat het risico van een individu op het krijgen van een hart- en vaatziektegebeurtenis over een periode van 10 jaar schat.

Het eerste deel van deze dissertatie is gericht op het vaststellen van de ziektelast als gevolg van CVD in termen van prevalentie, verlies aan kwaliteit van leven en gevolgen voor het fysiek en mentaal functioneren, evenals zorggebruik en de kosten hiervan die voor eigen rekening vallen. Hiervoor wordt gebruik gemaakt van primaire gegevens uit Sri Lanka. Het tweede deel van het proefschrift heeft als doel te onderzoeken hoe, met behoud van kosteneffectiviteit, de screening op hart- en vaatziekten in Sri Lanka zou kunnen worden aangepast als er meer expliciet rekening wordt gehouden met sociaaleconomische gezondheidsverschillen.

Hoofdstuk 2 geeft een schatting van de prevalentie van hart- en vaatziekten in Sri Lanka en kijkt naar de associaties met sociaal-demografische kenmerken en risicofactoren, die kunnen helpen bij het verbeteren van de screeningstrategieën voor het risico op hart- en vaatziekten. Er wordt geschat dat de prevalentie van hart- en vaatziekten hoger is dan eerder werd gedacht (3,8% tegenover een schatting van 2,2% in de Global Burden of Disease (GBD) studie). Er

wordt ook vastgesteld dat er een element van onderdiagnose van hartinsufficiëntie kan zijn bij vrouwen. Dit hoofdstuk onderstreept het belang van lokale data en heeft implicaties voor de nauwkeurigheid van het predictiemodel op het risico van hart- en vaatziekten dat in 2019 werd ontwikkeld door de Wereldgezondheidsorganisatie (WHO) en dat is gekalibreerd met behulp van gegevens uit het GBD-onderzoek.

Hoofdstuk 3 laat zien dat de kwaliteit van leven afneemt als gevolg van CVD, meer voor beroerte dan voor hart- en vaatziekten. Op een schaal waarbij 1 staat voor de best mogelijke gezondheid en 0 gelijk staat aan dood, beoordeelt een persoon met hart- en vaatziekten zijn of haar kwaliteit van leven met 0,02 punten lager dan een persoon met dezelfde sociaal demografische kenmerken en chronische ziekten, terwijl de overeenkomstige waarde voor beroerte significant slechter is met 0,25 punten minder. Dit hoofdstuk presenteert ook de eerste gepubliceerde "disutility catalogus" voor een Zuid-Aziatisch land, die kan worden gebruikt in gezondheidseconomische modellering.

Hoofdstuk 4 biedt een sterke motivatie voor het screenen op het risico op hart- en vaatziekten: het stelt vast dat de ziektelast en zorggebruik bij mensen met hart- en vaatziekten hoog is. Zowel gediagnosticeerde als ongediagnosticeerde personen met CHD hadden een slecht lichamelijk functioneren, terwijl personen met symptomen die overeenkomen met CHD maar niet zijn gediagnosticeerd een slechter geestelijk functioneren, meer bezoeken aan de polikliniek en meer zorguitgaven hadden dan personen zonder CHD en personen met een CHD-diagnose. Het laat ook zien dat er een significante co-morbiditeit is van hartinsufficiëntie en depressie, en dat mensen met depressie ook slechtere gezondheidsuitkomsten hebben en meer zorg gebruiken. Dit hoofdstuk analyseert ook dezelfde uitkomsten voor mensen met hypertensie en diabetes, beide aandoeningen die worden gescreend en behandeld in CVD-risicoscreeningsstrategieën. Er worden geen significante verschillen gevonden in gezondheid en zorggebruik voor mensen met ongediagnosticeerde hypertensie en diabetes, vergeleken met mensen zonder deze aandoeningen. Toch is screening op deze aandoeningen belangrijk om de progressie ervan te voorkomen en de incidentie van hart- en vaatziekten te verminderen.

Hoofdstuk 5 beschrijft een kosteneffectiviteitsanalyse van diverse alternatieven voor de huidige screeningstrategie op het risico op hart- en vaatziekten in Sri Lanka. De conclusie is dat wijzigingen in de huidige strategie, zoals het gebruik van een ander predictiemodel om het risico op CVD in te schatten; het verhogen van de leeftijd waarop gescreend wordt; het verlagen van de drempel voor het CVD-risico voor het starten van een statinebehandeling en/of het voorschrijven van antihypertensiva; en het voorschrijven van statines aan alle mensen met diabetes, grote gezondheidswinst opleveren en dat elk van deze wijzigingen waarschijnlijk kosteneffectief of zelfs kostenbesparend zijn.

Hoofdstuk 6 kijkt naar een alternatieve setting voor het screenen op het risico op hart- en vaatziekten, die momenteel worden uitgevoerd in speciale "centra voor een gezonde levensstijl". Aangezien 26% van de personen die in aanmerking komen voor behandeling in het kader van de huidige screeningstrategie in de voorgaande maand een poliklinische zorgverlener heeft bezocht en toch onbehandeld is gebleven, wordt in dit hoofdstuk gekeken naar het verplaatsen van de screening naar poliklinische zorgverleners, waardoor de dekking wordt vergroot. Er wordt vastgesteld dat een opportunistisch screeningsprogramma dat een jaar duurt tot 27% van de niet gediagnosticeerde personen kan opsporen. Verder bleek dat een opportunistisch screeningsprogramma ervoor zorgt dat iets meer arme mensen in de publieke sector en iets meer rijke mensen in de private sector worden behandeld, waardoor de sociaaleconomische ongelijkheid in onbehandelde hoge CVD-risico's zou afnemen.

Hoofdstuk 7 combineert de concepten uit hoofdstuk 5 en 6 en schat de kosteneffectiviteit van de overgang naar opportunistische screening, samen met elk van de aanpassingen die in hoofdstuk 5 kosteneffectief werden bevonden. Het toont ook de resultaten van een distributieve kosteneffectiviteitsanalyse met behulp van stochastische dominantie, waarmee de kosteneffectiviteitsanalyse wordt uitgebreid om de verdeling van het effect van elke strategie over de economische gradiënt te beoordelen. De conclusie is dat een opportunistische strategie die mensen van 40 jaar en ouder screent, statines voorschrijft bij een CVD-risico ≥10%, en antihypertensiva bij een lagere bloeddruk (≥ 130/80 mmHg) aan mensen met diabetes of een CVD-risico ≥ 10%, de voorkeur zou hebben boven de huidige strategie, als er een afkeer is van slechtere gezondheidsuitkomsten voor de armen. Met een dergelijke afkeer van gezondheidsongelijkheid kan dezelfde strategie de voorkeur genieten boven een andere strategie die daarnaast statines voorschrijft aan alle mensen met diabetes.

De bevindingen van de zes onderzoeken worden samengevat in hoofdstuk 8, waarbij het belang van screening op het risico op hart- en vaatziekten wordt benadrukt en verschillende belangrijke wijzigingen in de screeningstrategie op basis van PEN worden geïdentificeerd die de volksgezondheid aanzienlijk zouden kunnen verbeteren, terwijl ze kosteneffectief en betaalbaar blijven. De onderzoeken gepresenteerd in deze PhD-thesis onderstrepen het belang van het verzamelen van lokale gegevens in LMIL die kunnen worden gebruikt om de ziektelast nauwkeuriger vast te stellen en voor gezondheidseconomische modellering. Door gebruik te maken van onderzoeksgegevens die zijn verzameld in een LMIL-setting, tonen deze studies ook het potentieel aan voor andere LMIL om op beter wetenschappelijk bewijs gebaseerde screeningstrategieën voor het risico op hart- en vaatziekten te ontwikkelen die zijn toegesneden op hun specifieke context.

# PORTFOLIO

## PhD publications

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# TRAINING

**2023** Health intervention technology assessment for decision making | The George Institute for Global Health
**2021** Inequalities in Health and Healthcare Summer School | Tingbergen Institute
**2021** Multilevel modelling 2: multilevel structural equation modelling (SEM) | Erasmus University Rotterdam
**2021** Multilevel modelling 1: an introduction | Erasmus University Rotterdam
**2019** Economic Evaluation | London School of Hygiene and Tropical Medicine via University of London
**2018** Healthcare Market Place | University of Minnesota
**2017** Basics of Health Economics (Facilitated) | World Bank Group – The Open Learning Campus
**2017** Mathematical Biostatistics Boot Camp 1 | Johns Hopkins University
**2017** Econometrics: Methods and Applications | Erasmus University Rotterdam
**2017** Practical Machine Learning| Johns Hopkins University
**2017** The Data Scientist's Toolbox | Johns Hopkins University
**2017** Getting and Cleaning Data | Johns Hopkins University
**2017** Exploratory Data Analysis | Johns Hopkins University
**2017** Regression Models | Johns Hopkins University
**2017** Developing Data Products | Johns Hopkins University
**2017** Reproducible Research | Johns Hopkins University
**2017** Statistical Inference | Johns Hopkins University
**2017** R Programming | Johns Hopkins University
**2017** Data Science Capstone | Johns Hopkins University
**2016** 14.100x Microeconomics | MITx

# CONFERENCES AND MEETINGS

**2023** SLHAS 1st Conference. Colombo, Sri Lanka. June 23, 2023. 8 presentations covering SLHAS Study Design, Quality of Life and Physical Functioning, Cardiovascular Disease, Availability of SLHAS Data.

**2022** Research Policy Workshop on Meeting Needs for Non-Communicable Disease Healthcare in LMICs, sponsored by University of Lausanne, Erasmus University Rotterdam, World Health Organisation. Lausanne, Switzerland. November 19, 2022. Cost-effectiveness of CVD screening programs in Sri Lanka.

**2021** iHEA World Congress Poster Presentation. Virtual. July 13, 2021. Opportunistic Screening for Cardiovascular and Metabolic Diseases in Outpatient Settings in Sri Lanka: Effectiveness, Cost and Distributional Impact.

**2019** iHEA World Congress. Basel, Switzerland. July 16, 2019. Equity implications of expansion of CVD screening and preventative treatment in Sri Lanka.

**2018** Improving coverage for Chronic Disease in Aging Populations – Evidence from Emerging Research sponsored by Institute for Health Policy, Swiss Agency for Development Cooperation (SDC) and the Swiss National Science Foundation (SNSF). February 12, 2018. Colombo, Sri Lanka. Two presentations: 1) A validation of CVD predictors using Sri Lankan mortality data, 2) Findings from Sri Lanka CVD intervention evaluation model.

**2017** iHEA Pre-Congress Session Poster Presentation. Boston. July 7, 2017. Wijemunige N, Rannan-Eliya RP, Modeling of cost-effectiveness, costs and impact of WHO PEN and alternative cardiovascular disease prevention protocols in Sri Lanka.

# TEACHING

**2024** Lecturer for Post-Graduate Diploma in Gender and Health on "Gender and health policy: From past to present" at the University of Colombo.

**2023** Lecturer for Post-Graduate Diploma in Gender and Health on "Gender and health policy: From past to present" at the University of Colombo.

**2023** Guest talk on HTA, cost-effectiveness analysis and benefits package design with examples for Global Health Economics (MSc), ESHPM

**2022** Lecturer for Post-Graduate Diploma in Gender and Health on "Gender and health policy: From past to present" at the University of Colombo.

# ABOUT THE AUTHOR

Nilmini Wijemunige was born in Colombo in 1986. She completed her Bachelor of Medicine and Bachelor of Surgery with Honours, along with a Bachelor of Medical Science in 2009 at the University of Melbourne, Australia. During her undergraduate studies, she travelled to Sri Lanka frequently, completing a year of research based at the Epidemiology Unit, and a 2-month elective at the National Cancer Hospital, Sri Lanka.

She worked as an intern at Austin and Northern Health in Melbourne in 2011, and as a Resident Medical Officer at the Princess Alexandra Hospital in Brisbane in 2012, and completed a Master of Public Health at the University of Sydney in 2013. She then relocated to Sri Lanka in 2013, where she commenced as a Research Associate at the Institute for Health Policy (IHP), an independent, non-profit Sri Lankan research institute which aims to improve health and social systems in Sri Lanka and beyond. During her time there, she worked on disease-based health accounts, assessing the process quality of clinical care in Sri Lanka and Malaysia, and analysing data from Afghanistan on out-of-pocket expenditures, and maternal and child health services. She worked in 2014–2015 with the Non-communicable Diseases (NCD) Unit in the Ministry of Health to finetune a national action plan for NCDs. As a Co-Investigator in the Sri Lanka Health and Ageing Study (SLHAS), she is an integral part of the team that established the first ever national cohort to study the health and ageing of Sri Lankan adults.

She started her PhD as an external student at the Erasmus School of Health Policy and Management at Erasmus University Rotterdam, the Netherlands. During her PhD, she utilised the data from the SLHAS to understand the burden presented by cardiovascular disease and its risk factors on health, quality of life and healthcare use, and used modelling to design better screening strategies to reduce this burden. She presented her findings at several academic events, including iHEA and workshops organised in Sri Lanka and Switzerland, and published studies in BMC Public Health, Global Heart, Value in Health Regional Issues, and BMC Global and Public Health.

Nilmini started work as a short-term consultant in the Service Delivery Indicators (SDI) team in the World Bank's Health, Nutrition and Population Global Practice, focusing on utilizing SDI data to analyse cross-country patterns in NCD care.

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