



Hypertension in low- and middle-income countries

Burden, interventions, and potential for philanthropic funding

Global Health and
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Editorial note

This report is a “shallow” investigation, as described [here](#), and was commissioned by Open Philanthropy and produced by Rethink Priorities from October to November 2022. Open Philanthropy does not necessarily endorse our conclusions, nor do the organizations represented by those who were interviewed.

Our report focuses on exploring hypertension in low-and middle-income countries as a potential new cause area for Open Philanthropy. We assessed the health and economic burden of hypertension, provided an overview of current interventions and the main gaps and barriers to address the burden, and discussed some plausible options for philanthropic spending. We reviewed the scientific and gray literature and spoke with six experts.

We revised the report for publication, but it represents our state of knowledge as of 2022. In particular, our case study of efforts in India is likely to be out of date and readers should also investigate newer guidelines and initiatives.

We don't intend this report to be Rethink Priorities' final word on hypertension. We have tried to flag major sources of uncertainty in the report and are open to revising our views based on new information or further research.

Key takeaways

- Hypertension—or high blood pressure—is a medical condition and one of the most important risk factors for cardiovascular diseases, chronic kidney disease, and dementia. Our best, highly uncertain guess is that 75% of the hypertension burden is preventable through lifestyle changes (e.g., reducing salt intake, being more physically active, avoiding tobacco use). It is diagnosed by taking blood pressure readings and highly treatable through a combination of medication and lifestyle changes. Yet the widespread use of hypertension reduction strategies is still limited ([link to section](#)).
- We summarized the hypertension prevalence, treatment, and control, and found ([link to section](#)):
 - The number of people with hypertension almost doubled since 1990 and reached 1.27 billion adults worldwide in 2019. This increase was driven by a steep rise in low- and middle-income countries (LMICs), which now carry most of the hypertension burden, and was mainly due to population growth and aging. The growing number of hypertensives has outpaced steady improvements in the numbers of diagnosed, treated, and controlled individuals.
 - The global age-standardized prevalence of hypertension remained stable over the last three decades at about one-third of adults. Treatment and control (i.e., blood pressure consistently below certain threshold values for treated individuals) rates have improved in most countries (though mainly in high- and middle-income countries), but have only reached ~43% of hypertensive adults for treatment and ~20% of hypertensive adults for control globally, with lower rates for low- and middle-income countries.
- We investigated the death and DALY burden of high blood pressure and found that ([link to section](#)):
 - Globally, there were 10.8 million deaths and 235 million DALYs annually due to high blood pressure in 2019, more than 80% of which which occurred in low- and middle-income countries. About 50% of the global DALYs lost occurred in only 4 countries (China, India, Indonesia, and Russia).
 - The global numbers of deaths and DALYs due to high blood pressure have steadily increased since 1990, and are predicted to increase further over the next two decades. This rise is mainly driven by middle-income countries, and due to both population growth and aging, as well as an increase in hypertension risk factors.
 - About 92% of both deaths and DALYs related to high blood pressure were due to cardiovascular disease, with the remaining deaths and DALYs being lost due to chronic kidney disease. Almost all of the death and DALY burden is concentrated among individuals aged 45 years or older.
- Our low confidence, tentative best guess is that the global economic burden from hypertension and hypertension-attributable cardiovascular disease is in region on \$1.6 trillion-\$3.2 trillion per year ([link to section](#)).
- Common barriers to mitigating hypertension in LMICs are costs for patients and limited availability of measuring devices, medicines, and medical staff ([link to section](#)).

- We researched what is currently being done to reduce hypertension and found that:
 - Our best guess is that philanthropic spending on hypertension is roughly \$50 million-\$150 million per year (80% confidence interval), \$45 million of which goes towards Resolve to Save Lives ([link to section](#)).
 - Several international hypertension initiatives exist, such as the WHO Global Hearts Initiative, Resolve To Save Lives, and the World Heart Federation Hypertension Roadmap, which all share a multi-pronged approach focused on improving both prevention and treatment ([link to section](#)).
 - Hypertension research is growing, but still neglected relative to its DALY burden and mostly focused on high-income populations. More context-specific studies (especially implementation trials and clinical trials to find optimal treatment combinations) are needed in LMICs ([link to section](#)).
- To understand the situation in LMICs, we present a case study of hypertension in India. India has been active in combating hypertension, but barriers to progress remain, including the availability of blood pressure devices, medicines supply, and access to health care ([link to section](#)).
- We investigated plausible interventions for a philanthropic organization and found:
 - Organizations are working to prevent modifiable risk factors of hypertension, and experts suggest salt as the most promising factor to address ([link to section](#)).
 - There are plausible interventions to improve the diagnosis of hypertension, but these are likely to be limited by reduced capacity for treatment in LMICs ([link to section](#)).
 - Single pill combinations of antihypertensive medicines appear to be promising for philanthropic involvement. A rough BOTEC suggests direct provision does not pass the bar (~450x), but there may be an opportunity for impactful market-shaping, given evidence of large margins on antihypertensives and significant (> 100x) price variation across LMICs ([link to section](#)).
- **Overall, we recommend a further investigation of hypertension as a cause area, primarily due to a very large and growing health burden. We also deem the area sufficiently neglected and tractable for a philanthropic funder to intervene.**

Hypertension 101

Hypertension—or high blood pressure—is a chronic medical condition in which the force of blood against the artery walls is consistently too high. It is **one of the top risk factors for cardiovascular diseases (CVDs), such as heart attacks and strokes, chronic kidney disease, and dementia** ([Zhou et al., 2021](#), p. 758). It can also lead to vision loss and sexual dysfunction ([American Heart Federation website](#)). Hypertension affects 1.25 billion people globally, two-thirds of which live in low-and middle-income countries (LMICs) ([NCD-RisC, 2021](#), p. 957). It is also the **world’s leading risk factor for death** ([GBD, 2019](#)).

In line with most sources we found, we use hypertension and high (or elevated) blood pressure as synonyms, and, as a default, we define hypertension as systolic blood pressure (SBP) ≥ 140

mm Hg and/or diastolic blood pressure (DBP) ≥ 90 mm Hg ([WHO, 2021](#), [CDC website](#)).¹² We indicate throughout this report when we deviate from this definition.

Various risk factors are known to adversely affect blood pressure, though the exact risk factors are somewhat inconsistent across different sources. Thus, we focus on the risk factors that we saw mentioned in most sources. Commonly mentioned **lifestyle-related (i.e. modifiable) risk factors are being overweight, eating too much salt, too much trans- or saturated fats, and not enough fruits and vegetables, low physical activity, high alcohol intake, smoking, and stress** (e.g. [WHO website](#); [International Society of Hypertension, 2020](#); [Carretero and Oparil, 2000](#)). Moreover, there are also “environmental factors such as fine particulate matter and extreme weather conditions”,³ and non-modifiable risk factors, such as family history and age ([Jeemon et al., 2021](#), p. 4). In about 5% of cases, high blood pressure is due to an underlying health condition (e.g. diabetes, sleep apnea, kidney infections) ([NHS website](#)).⁴

We have not been able to find a clear ranking or relative contributions of different risk factors to the global or LMIC hypertension burden, but **several studies pointed to age** (e.g. [Aparicio et al., 2015](#), p. 1), **obesity** (e.g. [Tang et al., 2022](#), p. 2), and **excessive salt intake** (e.g. [Xu et al., 2021](#), p. 6) as the most important risk factors.

A commonly used framework to investigate population-level progress towards controlled blood pressure and the extent of delivery gaps at different stages of care is the hypertension care cascade ([Peters et al., 2022](#), pp. 2-3). It involves measuring progress in four stages:

- **Prevalence:** The percent of the population with elevated blood pressure.
- **Awareness:** The percent of hypertensives who have been diagnosed.
- **Treatment:** The percent of hypertensives who report recently taking antihypertensive medicines.
- **Control:** The percent of hypertensives who report taking antihypertensive medicines and have non-elevated blood pressure.

In this report, we rely on the care cascade framework to assess the burden of hypertension and progress towards hypertension control.

Hypertension is diagnosed by taking blood pressure readings. Blood pressure is variable, so most guidelines suggest taking two or more readings on separate days and comparing the average to the aforementioned (or slightly different, depending on the respective guidelines) threshold values ([US NHLBI website](#)).

According to the World Hypertension League, “**much of hypertension is preventable**” ([Campbell et al., 2016](#), p. 320). Moreover, **hypertension is highly treatable, for example through lifestyle interventions reducing the modifiable risk factors, or through medication.** [Resolve to Save Lives](#) provides a “[Lives Saved Calculator](#)” which “models how many lives could

¹ According to WHO ([2021](#)), “the first (systolic) number represents the pressure in blood vessels when the heart contracts or beats. The second (diastolic) number represents the pressure in the vessels when the heart rests between beats.”

² This definition is based on commonly used medical diagnosis guidelines, but there are indications that lower blood pressure levels are also associated with elevated risks. For example, according to the GBD study, SBP of ≥ 110 mm Hg has been associated with increased health risks ([Forouzanfar et al., 2017](#), p. 166).

³ We also read in some (though not many) sources that lead exposure increases hypertension risk (e.g. [Vaziri, 2008](#), [Tsoi et al., 2021](#)), but we have not investigated whether this is a well-established or controversial finding.

⁴ In some cases, high blood pressure can also be due to taking a certain medicine, such as a contraceptive pill or steroids, but in these cases the blood pressure “may return to normal once you stop taking the medicine or drug” ([NHS website](#)).

be saved in countries around the world by scaling up hypertension control and reducing salt consumption by the year 2040.” For example, by “**achieving a 50% blood pressure control rate and a 4g reduction in daily salt intake**”, an estimated 10 million lives in China and 5 million lives in India could be saved by 2040, i.e., roughly 550,000 per year in China and 275,000 per year in India.⁵

Our highly uncertain **best guess is that 75% of hypertension is preventable**. We estimated this figure by comparing age-related increases in SBP in societies exposed to Western lifestyles to age-related SBP increases in isolated societies unexposed to lifestyle risk factors of hypertension. Moreover, if **40-44 year olds in countries with the highest prevalence of lifestyle risk factors reduced their risk factor exposure to the same level as countries with the lowest exposure, their hypertension prevalence would roughly drop by 35-43 percentage points** (see [Appendix K](#) for more detail).

Traditionally, medication for hypertension has been prescribed using a ‘multi-visit individualized-titration approach’, whereby a physician initially treats the patient with a low dose of one or more medications, and adjusts the medication (by increasing dosages or changing combinations) if blood pressure is not controlled ([Patel et al., 2022](#), p. 1).⁶ In 2021, the WHO hypertension guidelines ([2021](#), p. 13) were updated to **recommend that the initial treatment should comprise a combination of drugs** rather than a single drug, “preferably with a single-pill combination”.

However, hypertension is typically asymptomatic and **almost half of adults with hypertension are unaware of their condition**. Only 1 in 5 hypertensive adults have their condition under control ([WHO, 2021](#)). Levels of awareness, treatment, and control are **especially low in LMICs**, as the widespread use of hypertension reduction strategies is still limited ([Geldsetzer et al., 2019](#)).

We would like to point out that while medication can be used to effectively control blood pressure, recent evidence suggests that **antihypertensive medication cannot undo all the damage done by raised blood pressure**. For example, Liu et al. ([2015](#)) found that individuals with medically controlled blood pressure still had roughly twice the cardiovascular disease risk of those who have always had ideal blood pressure levels.⁷

Given that age is an important risk factor and the proportions of older people in populations are predicted to increase ([WHO website](#)), it is likely that the number of hypertensive people will increase further in the future. For example, Kearney et al. ([2005](#), p. 217) **predicted that the number of adults with hypertension would increase to 1.56 billion until 2025** as a result of population ageing.⁸

⁵ Default intervention settings: “50% antihypertensive therapy effective coverage scaled up from 2021 to 2030 and 4g mean salt reduction achieved by policy scale up from 2021 to 2025.”

⁶ For example, see the multi-step approaches outlined by the sample evidence-based protocols in the WHO HEARTS technical package ([2018](#), pp. 13 - 31).

⁷ “Among MESA participants aged ≥ 50 years at baseline, those with BP $<120/<80$ mm Hg on treatment had [...] twice the incident cardiovascular disease rate over 9.5 years of follow-up than those with BP $<120/<80$ mm Hg without treatment” ([Liu et al., 2015](#), p. 1). We have not vetted this study and have not found figures for CVD risk in absolute terms.

⁸ We have not found more recent forecasts for the number of adults with hypertension.

How big is the health and economic burden of hypertension in LMICs?

Hypertension affects 1.27 billion people worldwide, almost half of whom are still undiagnosed and, consequentially, untreated

[Confidence: High. We are confident that we found the best available study, as of 2022, that estimated worldwide trends in hypertension prevalence, treatment, and control. We trust the prevalence figures, especially for high-income countries. We are somewhat less certain about the treatment and control figures (due to self-reported nature), and all figures for sub-Saharan Africa due to low data availability.]

Several recent studies estimate the global burden of high blood pressure based on pooling multiple data sources. The most comprehensive and recent estimates we found were made by the NCD Risk Factor Collaboration ([NCD-RisC, 2021](#)), which we summarize in this section.⁹ We outline the methodology and limitations of this study in [Appendix A](#).

NCD-RisC ([2021](#)) estimated global trends in hypertension prevalence, treatment, and control from 1990 to 2019 for adults aged 30-79 years in 200 countries or territories.¹⁰ Their estimates are based on a pooled analysis of 1,201 population-representative studies with 104 million participants, covering 99% of the global population. They only used data from studies that included blood pressure measurements.

Findings of NCD-RisC ([2021](#)) are reported in absolute and age-standardized figures.¹¹ Crude (i.e. not age-standardized) prevalence is more useful for assessing the total health burden in populations. For convenience reasons, we focus on the age-standardized figures as reported in NCD-RisC ([2021](#)).¹² To get a rough sense of how much results differ across age-standardized and crude rates, we compare crude and age-standardized prevalence for men in Figure F2 in [Appendix F](#). The differences are small to moderate (0-6 percentage points).

Some of NCD-RisC's ([2021](#)) key findings are:

- **The number of people with hypertension almost doubled, increasing from 648 million in 1990 to 1.27 billion worldwide in 2019.** This increase is **mainly driven by a steep rise in LMICs**, whereas the rate of increase seems to have tapered off in high-income countries (HICs). The vast majority (> 1 billion) of currently hypertensive people live in LMICs (see [Figure 1](#) below). According to NCD-RisC ([2021](#), p. 976), the growth in the number of hypertensive people is **primarily “due to population growth and ageing.”**

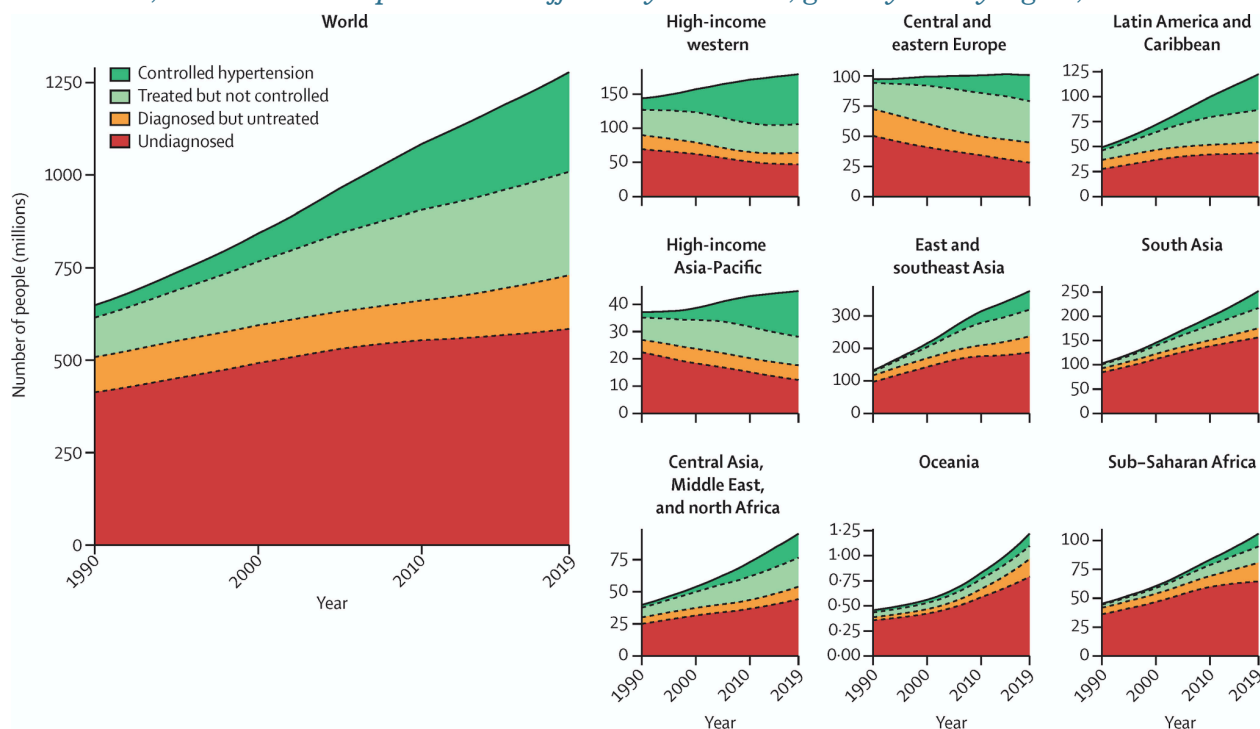
⁹ Other recent studies that investigated trends in blood pressure and hypertension across countries are summarized in Zhou et al. ([2021](#), pp. 786-789). The most noteworthy study is Forouzanfar et al. ([2017](#)), which is based on the 2015 Global Burden of Disease (GBD) Study. At a quick glance, the main findings of Forouzanfar et al. ([2017](#)) are broadly comparable with NCD-RisC ([2021](#)) (the predecessor study of NCD-RisC [[2021](#)]). We decided not to summarize Forouzanfar et al. ([2017](#)) in this report as, compared to NCD-RisC ([2021](#)), it is less recent, based on a smaller data set, and did not provide estimates on diagnosis, treatment, and control of hypertension.

¹⁰ NCD-RisC ([2021](#)) did not estimate hypertension figures for people below 30 years of age due to a relatively low hypertension prevalence among young people.

¹¹ Our understanding is that NCD-RisC ([2021](#)) use a [direct standardization](#) approach. This means that they first estimate age-group-specific prevalence, and the rates for detection, treatment and control, and they then compute a weighted average of the age-specific rates using weights from the WHO standard for age standardization of rates ([WHO, 2001](#)).

¹² Crude rates can be downloaded from the [NCD RisC website](#).

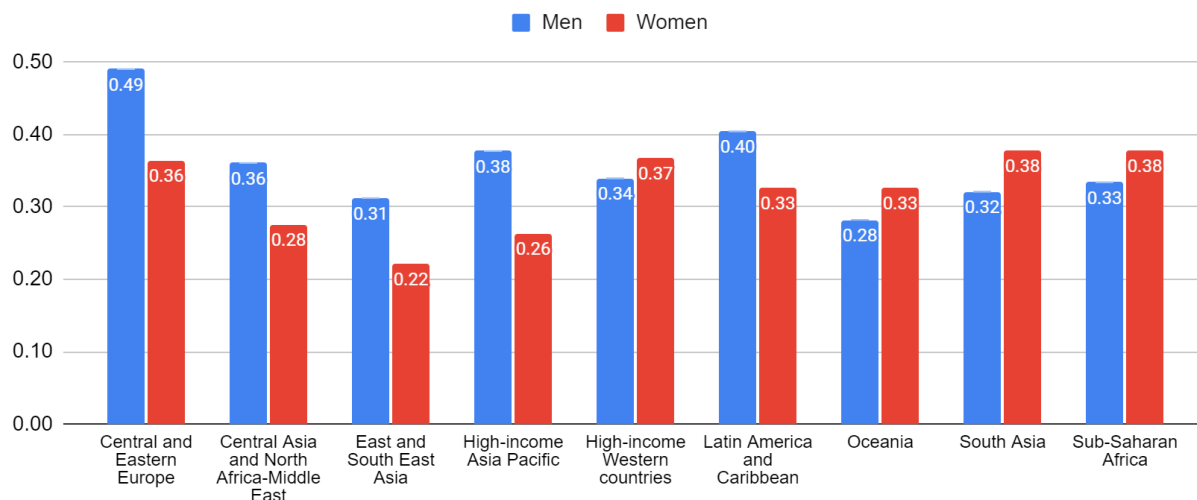
Figure 1. Trends in the number of people with hypertension who reported a diagnosis, who used treatment, and whose blood pressure was effectively controlled, globally and by region, 1990–2019



Note. From NCD-RisC (2021, p. 968, Figure 6).

- Although the absolute number of hypertensive people has increased, **global age-standardized prevalence of hypertension remained stable over the last three decades (32% in women and 34% in men in 2019)**, with significant heterogeneity across regions. Age-standardized prevalence decreased in high-income countries and increased or remained stable in most LMICs (one exception is Peru, in which prevalence decreased slightly among women) (NCD-RisC, 2021, p. 964). Figure 2 below shows the age-standardized hypertension prevalence across regions in 2019.

Figure 2. Prevalence of hypertension as a percentage of age-standardized population aged 30-79 years across regions (NCD-RisC, 2021; link to sheet)



- The last three decades have shown **steady improvements in diagnosis, treatment, and control in every region of the world, but these improvements have been outpaced by a steep increase in the number of hypertensive people, particularly in LMICs.** There is a large heterogeneity across different world regions and some MICs (such as Costa Rica) now outperform most HICs in terms of treatment and control. In HICs, the number of hypertensive people without diagnosis, treatment, and control declined. In LMICs, improvements have been made across the whole treatment cascade, but the number of undiagnosed hypertensive people has nonetheless steadily increased, which has led to a shift of the burden away from HICs to LMICs (see [Figure 1](#) above).
- Globally, only 59% of women and 49% of men (age-standardized) with hypertension reported having received a previous diagnosis in 2019. Among the hypertensive population, 47% of women and 38% of men were treated, and 23% of women and 18% of men had achieved hypertension control. **Generally, diagnosis, treatment, and control rates are lower for LMICs than for HICs** (see [Figure 3](#) below).

Figure 3. Hypertension treatment cascade in 2019, for women and men globally and by region (95% confidence intervals in parentheses)



Note. From NCD-RisC (2021, p. 961).

- Figure F1 in [Appendix F](#) shows the proportion of hypertensive people with a diagnosis, treatment, and control, by region for three different age groups in 2019. A general pattern is that **the older individuals are, the more likely they are to have their hypertension diagnosed, treated, and controlled**. Diagnosis, treatment, and control rates are especially low among men aged 30-44 years across all regions, with up to ~80% of hypertensive 30-44 year-old men being undiagnosed in Oceania, sub-Saharan Africa, and South Asia.
- Age-specific numbers of people with hypertension diagnosis, treatment, and control were not readily available from NCD-RisC (2021). However, we were able to combine prevalence figures from NCD-RisC (2021) and census data from India to obtain age-specific numbers for India (see [Appendix G](#)). This could be done for other countries as well, but as it is quite time-consuming, we only focused on India.

Every year, high blood pressure is responsible for 10.8 million deaths and 235 million DALYs worldwide, with more than 80% of the burden being in low- and middle-income countries

[Confidence: Medium. We are confident that the GBD study is currently the best available source for the global DALY and death burden of high blood pressure, but we are somewhat less certain about the accuracy of the GBD estimates. We briefly reviewed the methodology of the GBD study, but a more extensive review might yield a more concrete picture on the likely error margins of the estimates.]

The best available data on blood pressure-related DALYs and deaths we found is from the 2019 Global Burden of Disease (GBD) study ([GBD, 2020](#)). They define high blood pressure as “blood pressure higher than 110-115 mm Hg” ([IHME health data terms defined](#)), which we understand to be systolic blood pressure.¹³ Thus, in this section, we deviate from our definition of high blood pressure (as explained in [Hypertension 101](#)), which is SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg, and use GBD threshold values instead. Please see [Appendix B](#) for a brief summary of the methodology and limitations of the GBD study estimations.

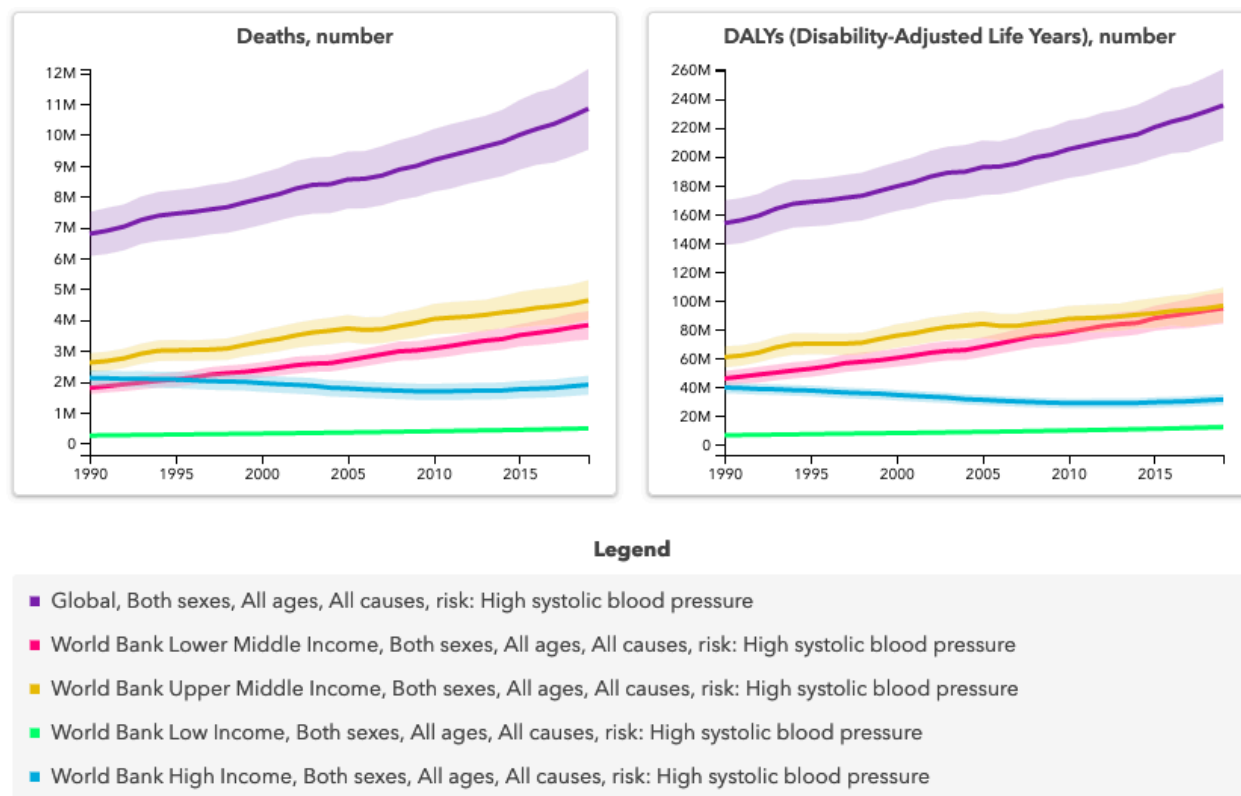
Some key findings on the DALY and death burden of high blood pressure are:

- **Globally, 10.8 million deaths were due to high SBP (> 110-115 mm Hg) in 2019**, 8.9 million of which occurred in LMICs, and 8.5 million of these in MICs alone. Moreover, **worldwide, 235 million DALYs¹⁴ were lost in 2019** due to high SBP. Out of these, 204 million DALYs were lost in LMICs, and 191 million in MICs alone (see [Figure 4](#) below).
- **Both the numbers of DALYs and deaths due to high blood pressure have increased steadily since 1990 at the global level.** This increase is predominantly **driven by a rise in MICs**. In HICs, deaths and DALYS have slightly decreased whereas there was a slight increase in LICs (see [Figure 4](#) below).

¹³ This range comes from the GBD methodology to calculate the burden attributable to high blood pressure. According to [Supplementary Appendix 1](#) (p. 272) from GBD (2020): “We estimated that the TMREL [Theoretical minimum-risk exposure level] of SBP ranges from 110 to 115 mm Hg based on pooled prospective cohort studies that show risk of mortality increases for SBP above that level. [...] To include the uncertainty in the TMREL, we took a random draw from the uniform distribution of the interval between 110 mm Hg and 115 mm Hg each time the population attributable burden was calculated”.

¹⁴ We would like to note that GBD DALYs are somewhat different from Open Philanthropy DALYs as explained [here](#). We have not looked into the details of how they differ.

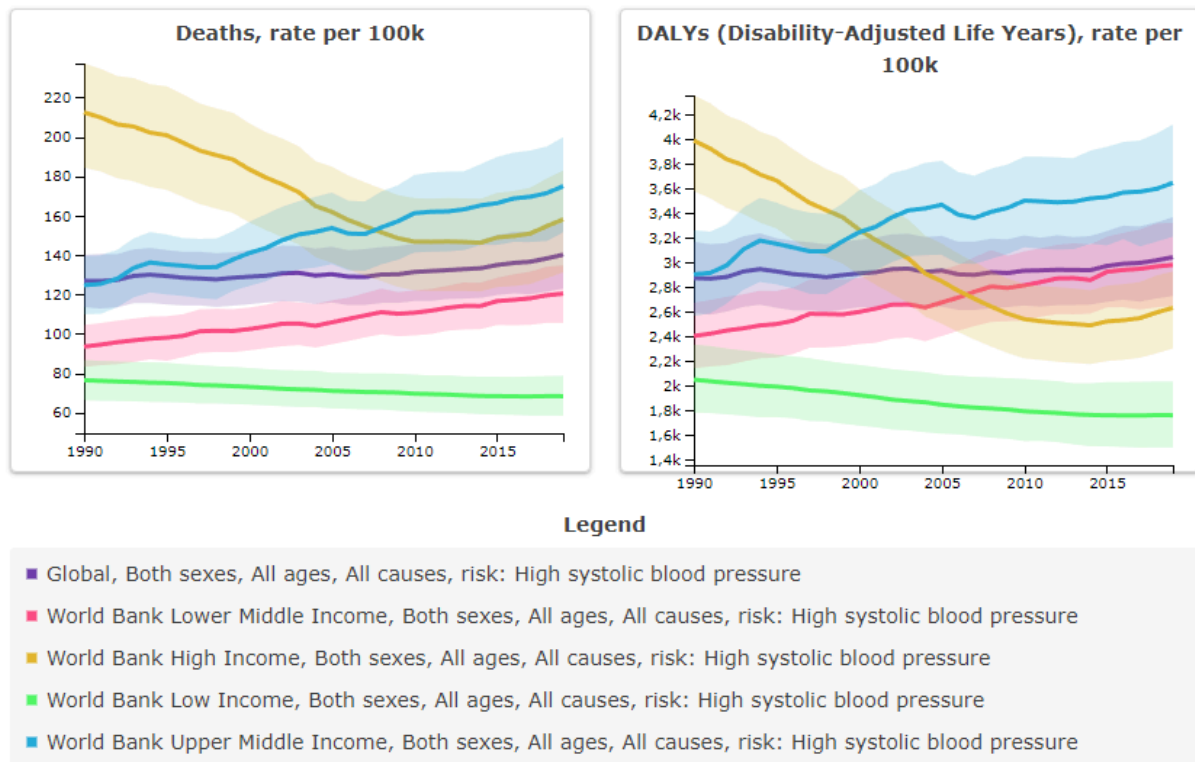
Figure 4. Deaths and DALYs attributed to high systolic blood pressure in countries classified according to the World Bank income levels (95% CI in parentheses)



Note. From [GBD Results Tool \(2019\)](#).

- **DALY and death rates per 100,000 people have increased only slightly from 1990 to 2019, and reached 140 for deaths and 3,000 for DALYs in 2019.** This increase was driven by a rise in MICs. The rates have declined for both HICs and LICs, though HICs rates have been rising again since 2015 (see [Figure 5](#) below).

Figure 5. Deaths and DALYs attributed to high systolic blood pressure per 100,000 people in countries classified according to the World Bank income levels (95% CI in parentheses)



Note. From [GBD Results Tool \(2019\)](#).

- **Elevated blood pressure below the 140 mm Hg threshold can still increase health burdens.** In 2015, 29% of global DALYs lost due to high SBP occurred in individuals with a SBP in the range of 115-140 mm Hg, 26% occurred in those with a SBP of 140-150 mm Hg, and 45% in those with SBP \geq 150 mm Hg ([Forouzanfar et al., 2017](#), pp. 169-170). The 2019 GBD estimates did not provide this breakdown.
- In 2019, the vast majority of deaths and DALYs lost related to high SBP were due to **cardiovascular disease**¹⁵ (~92% for both metrics) with the remaining deaths and DALYs being lost due to chronic kidney disease ([GBD Results Tool, 2019](#)).
- Of the global burden of 235 million DALYs lost related to SBP in 2019, **about 50% occurred in 4 countries (China, India, Indonesia, Russia)**. China was home to 23% of DALYs lost and India was home to 16% of DALYs lost ([GBD Results Tool, 2019](#) and [own calculations](#)).
- Both the numbers of deaths and DALYs due to high blood pressure are more **concentrated among older individuals**, with relatively few deaths/DALYs among individuals below 45 years of age. In LMICs, both the death and DALY burden are relatively evenly spread across older age groups (> 45 years). Overall, the lower the income level of a region, the more the death and DALY burden are concentrated among relatively younger individuals (see [Appendix C](#) for more detail).

¹⁵ In the GBD study, cardiovascular disease includes ischemic heart disease, ischemic stroke, hemorrhagic stroke, rheumatic heart disease, hypertensive heart disease, cardiomyopathy and myocarditis, atrial fibrillation and flutter, aortic aneurysm, peripheral vascular disease, endocarditis, and other cardiovascular and circulatory diseases ([Forouzanfar et al., 2017](#), p. 170).

- Numbers of **deaths and DALYs due to high blood pressure are fairly evenly distributed across men and women**, with DALYs being slightly more concentrated among men in all World Bank regions (see [Appendix C](#) for more detail).
- The **percentage of all deaths and DALYs lost in a country due to high SBP is highest in upper-middle income countries (24% of deaths; 13% of DALYs) and lowest in LICs (10% of deaths; 4% of DALYs)**. We have not investigated in detail what drives these results, but we suspect that these differences across regions are driven by a number of factors, such as differences in demographic competing hazards and differences in detection, treatment, and control rates. It is also possible that these differences are partly driven by racial differences in hypertension-related outcomes (as discussed by [Gopal et al., 2021](#)), but we have not reviewed this literature (see [Table 1](#) below).

Table 1. Percentage of deaths and DALYs attributed to high systolic blood pressure in 2019 by World Bank income regions (95% confidence intervals in parentheses)

	Percentage of all deaths	Percentage of all DALYs
Global	19 (17-21)	9 (8-10)
High-income countries	17 (14-20)	9 (8-10)
Upper-middle income countries	24 (21-27)	13 (11-15)
Lower-middle income countries	18 (16-20)	9 (8-10)
Low-income countries	10 (9-11)	4 (3-4)

Note. From [GBD Results Tool \(2019\)](#).

- According to GBD forecasts, the **number of deaths related to high SBP are predicted to increase over the next two decades**, albeit with wide confidence intervals (14.2 million predicted deaths in 2040, 95% CI: 10.1 million - 19.5 million) ([GBD Foresight Visualization](#)). The death rate per 100,000 is also predicted to slightly rise until 2040, though also with very wide confidence bands ([GBD Foresight Visualization](#)).

A brief literature review did not reveal reliable estimates of the economic burden from hypertension in LMICs

[Confidence: Moderate confidence that there are no other existing evaluations of economic costs in LMICs that are more reliable or generalizable than those we've found.]

We spent roughly 3 hours reviewing the literature on the economic burden of hypertension. The best studies we found in HICs were Tsao et al. (2022) and Hird et al. (2019),¹⁶ and in LMICs Wierzejska et al. (2020), and Gheorghe et al. (2018). We also found estimates referred to by advocacy organizations that “the global direct medical costs of hypertension are estimated at \$370 billion per year” ([Frieden and Jaffe, 2018](#)), but put little weight on them as the methodologies used were not fully transparent.

We attempted to calculate estimates of the economic burden for both hypertension itself and the proportion of cardiovascular diseases attributable to hypertension (detailed in [Appendix](#)

¹⁶ Note that one of the authors of this report was among the co-authors of Hird et al. (2019).

J).¹⁷ For example, based on Tsao et al., (2022), the total hypertension and hypertension-attributable CVD costs in the US were 161.9 billion USD in 2017, consisting of 51.1 billion from hypertension itself and 140.8 billion from hypertension-attributable CVD.

Extrapolating from the average cost of hypertension per person from Wierzejska et al. (2020) and assuming a similar ratio of hypertension to hypertension-attributable CVD costs as those found in the US (Tsao et al., 2022), our very tentative best guess is that the the global economic burden from hypertension and hypertension-attributable CVD is plausibly in region on \$1.6 trillion-\$3.2 trillion per year. However, we are not confident that the estimates from Wierzejska et al. (2020) are reliable and have low confidence that the assumption that a ratio of costs in the US is generalizable globally. However, we do find it plausible that hypertension exerts considerable economic burden in LMICs and that our estimates might be suggestive of the order of magnitude of this burden.

What are the barriers to progress on reducing hypertension and what is currently being done in LMICs?

Common barriers complicating hypertension control efforts in LMICs are out-of-pocket costs for patients, and limited availability of measuring devices, medicines, and medical staff

[Confidence: High that these are significant barriers in LMICs, but we haven't researched which of these are most important. We don't expect that spending more time on this will give us a stronger sense of the relative importance of each barrier, however we do go into more detail for the case of India below.]

The barriers to mitigating hypertension can be categorized into three stages: pre-diagnosis (or prevention), diagnosis, and treatment and adherence. These stages correspond to the stages in the care cascade introduced in [Hypertension 101](#). At each stage the barriers can be further categorized into the patient level on the one hand, and the healthcare system or population level on the other hand (though some barriers could be attributed to both levels).

We give an overview of the main barriers at each stage in [Table 2](#) below, based on Jeemon et al. (2021, Table 3) and Schutte et al. (2021).

Table 2. Main barriers to reducing hypertension in LMICs

Stage	Barrier	Level
Pre-diagnosis, prevention	Lacking awareness of the risks of hypertension	Patient
	Difficulty to encourage people to change unhealthy behavior at a large scale, especially given external factors encouraging unhealthy	System

¹⁷ The international society of hypertension calculated that about 54% of stroke and 49% of heart disease are attributable to hypertension (Lawes et al., 2008), other estimates vary slightly but it appears to be generally accepted that about half of heart disease and stroke are attributable to hypertension (Fuchs & Whelton, 2019). We therefore assume 50% of the costs of heart disease and stroke can be attributed to hypertension.

	habits ^{18*}	
Diagnosis	Hypertension is asymptomatic , so people are not aware that they might have it	Patient
	Lack of time or money to get blood pressure checked	Patient
	Low accuracy of single measurement due to the variable nature of blood pressure (and barriers for more intensive measurements such as 24 hour ambulatory measurement of blood pressure)*	Patient
	Limited access to testing centers (i.e., few testing locations, long travel distances, lack of means to travel there)	Patient/ System
	Too few healthcare professionals	System
	Limited availability of blood pressure measurement devices* and use of inaccurate measurement devices*	System
Treatment and adherence	Unwillingness to take medication (i.e., doubt that it helps, unwillingness to take medicine for asymptomatic hypertension, fear of negative side effects of medication)	Patient
	Treatment being too costly for households with low-income, due to direct costs (such as consultation and medicines) as well as indirect costs (like travel).*	Patient
	Lack of patient understanding and awareness for the need of medication	Patient
	Trouble adhering to medicine schedule , potentially due to lack of time/ structure to take medicines, forgetfulness, or complexity of schedule	Patient
	Lack of awareness or understanding of guidelines by health care professionals, or lack of willingness to follow them	System
	Too few healthcare professionals	System
	Lack of available medicines (in general, or specific types for combination therapy, i.e., combining different types of drugs)	System
Poor relations between patients and health workers	System	

Note. Adapted from Schutte et al. (2021; marked with an asterisk) and Jeemon et al. (2021).

¹⁸ According to Schutte et al. (2021), “[t]he dominant contributors include the availability and uptake of cheap ultra-processed food and beverages and activity-saving technologies resulting in major reductions in physical activity at work and in leisure times. Several environmental factors may also discourage people from becoming more active, such as low air quality and pollution, high-density traffic, fear of crime and violence in outdoor areas, and limited green space, parks, sidewalks, and recreation facilities for activities.”

Many of these barriers will exist in countries of all income levels, but we **expect that some barriers will be particularly relevant in LMICs, including:**

- **Treatment being too expensive (direct and indirect costs)**
- **Lack of available medicines** due to both supply chain inefficiencies and lack of resources. [The Prospective Urban Rural Epidemiology \(PURE\) study](#), conducted in randomly selected urban and rural communities in LMICs, strongly suggests that even those patients that have access to some medication are generally being treated with a single drug, rather than the WHO-recommended combination of drugs. Chow et al. (2013) reports the results, which indicate that across all LMICs, 69.2% of those on treatment for hypertension were only taking one medication. Brian Hutchinson pointed out that this proportion varies across income groups, reaching 95% in low-income countries.¹⁹
- Our 80% confidence interval for the proportion of patients still receiving monotherapy in low- and middle-income countries is 55% - 75%.
- **Too few healthcare professionals:** The availability of healthcare professionals is also a problem in some HICs, but overall the ratio of population to healthcare professionals within a population is much lower in LMICs.²⁰ This is particularly constraining in the context of the ‘multi-visit individualized-titration approach’ that is common in HICs.
- **Lack of reliable measuring equipment:** Tom Frieden and Andrew Moran confirmed that this is an ongoing issue in LMICs, but that costs are quite affordable, with quality-assured equipment in the US \$50 - \$100 range able to last for years with tens or hundreds of thousands of readings.
- **Lack of local regulations requiring procurement of blood pressure measurement devices that are validated according to international standards:** According to Tom Frieden and Andrew Moran, the WHO and PAHO are supporting countries to require manufacturers to document validation evidence in order to be eligible for government blood pressure monitoring device procurement contracts.

What is currently being done?

Philanthropic spending on hypertension is roughly \$50 million-\$150 million per year (80% confidence interval)

[Confidence: Medium. Although we spent only 3 hours reviewing the literature and the websites and reports of four large philanthropic organizations, we think it's unlikely that an additional 10 hours of research would yield substantially different figures.]

We spent roughly 3 hours searching the scientific and gray literature and the websites and annual reports of four large philanthropic organizations (Gates Foundation, Bloomberg Philanthropies, Wellcome Trust, Chan Zuckerberg Initiative) to gauge the philanthropic

¹⁹ As shown in eTable 5 of the [supplementary online content](#) (p. 6), which shows the breakdown of results by World Bank income group: 94.9% in low-income countries, 61.7% in lower-middle-income countries, and 69.9% in upper-middle-income countries.

²⁰ Schutte et al. (2021): “For the year 2018, India, Nigeria, and Mozambique, all LMICs, reported 0.9, 0.4, and 0.1 physicians per 1000 people, respectively. This is in contrast to Japan, an HIC, which reported 2.4 physicians per 1000 people in 2016. Similarly, India, Nigeria, and Mozambique reported 1.7, 1.2, and 0.7 nurses and midwives per 1000 people in 2018, respectively, far lower than 12.2 for Japan in the same year.”

spending towards hypertension. We focused on those four as they are among the largest philanthropic organizations in global health and we expect that they drive the majority of philanthropic funding in the area.²¹ We have not been able to find precise figures, as hypertension-related spending is usually not directly labeled as such.²²

The best figures we have been able to find in the literature were provided by Jailobaeva et al. (2021) who mapped the spending and policies of key global actors related to non-communicable diseases (NCDs) in LMICs. Some key findings are:

- **In 2019, \$733 million** (out of \$41 billion on global health in total) **was spent on NCDs through mechanisms of Development Assistance for Health—41% of this came from private philanthropies.**
- According to the IHME [Financing Global Health Database](#), about 10% of NCD funding in 2019 (\$73 million) came from the Gates Foundation, which was the highest among all philanthropic actors reviewed by Jailobaeva et al. (2021). About half of this went to tobacco control and the other half went towards other (largely unspecified) NCDs.

A quick search of the websites and annual reports of the four philanthropic organizations did not yield spending figures related to hypertension or, more broadly, cardiovascular diseases or NCDs. NCDs did not appear to be a focus area of the Gates Foundation²³ (e.g. [2021 Annual Report](#)), the Wellcome Trust²⁴ (e.g. [Annual report and Financial Statements 2021](#)), or the Chan Zuckerberg Initiative (e.g. [Chan Zuckerberg website](#)). The promotion of cardiovascular health features prominently on the [Bloomberg Philanthropies website](#) and in their [2021 Annual report](#) (p. 32), but we have not found concrete spending figures.

Our impression from skimming these reports and websites is that the vast majority of these organizations' hypertension-related spending goes towards Resolve to Save Lives. The **Gates Foundation, Bloomberg Philanthropies, and the Chan Zuckerberg Initiative jointly committed \$225 million over five years, i.e. \$45 million per year, to support Resolve to Save Lives in 2017** ([NCD Alliance website](#)).

Overall, taking these different pieces of information together, **our best guess is that annual philanthropic spending on hypertension is about \$50 million-\$150 million (80% confidence interval)**. Our reasoning is as follows: Annual philanthropic spending for hypertension is at least \$45 million, and we expect that the true figure is likely somewhat higher than that (we expect that we missed some smaller funding streams). We also know that total spending on NCDs from philanthropies is \$300 million/year, which likely goes only partly towards hypertension, and partly to other NCDs (e.g. cancers, mental health conditions). As hypertension represents a large part of NCDs and also shares some risk factors with other NCDs, we think that plausibly half of the NCD funding could go towards hypertension.

²¹ Other philanthropic donors, including the American Heart Association and the British Heart Foundation, are also active and non-negligible funders in this space. However, we judged that much of their most relevant funding was in R&D around CVD and not specific to LMICs. Further investigation of their role could further illustrate the philanthropic landscape.

²² Philanthropic spending that could be categorized under hypertension is often labeled by risk factor (e.g. smoking), or by disease type (e.g. non-communicable diseases).

²³ The vast majority of the Gates Foundation's global health spending goes towards infectious diseases, according to its [2021 Annual report](#) (p. 4).

²⁴ The Wellcome Trust has three focus areas: Climate and health, infectious diseases, and mental health ([Wellcome Trust website](#)).

Some figures point to spending ‘downstream’ of hypertension, that is for CVDs, being higher than spending for hypertension directly. For example, in 2021, [NIH](#) (National Institutes of Health) spending was \$292 million for hypertension research vs. \$2.54 billion for research on CVDs ([NIH RePORT website](#)). We are unsure whether this also holds for non-research spending and for philanthropies specifically.

Advocacy landscape: Several international and national organizations are concerned with the burden of high blood pressure

[Confidence: Medium. We are confident that many international hypertension initiatives exist, but we only outline some examples and do not have a full overview of the advocacy landscape. It is possible that 10 hours more research would reveal many more international (or national) initiatives.]

We spent roughly 2 hours reviewing international organizations that are concerned with the burden of high blood pressure. [Table 3](#) below provides a non-exhaustive overview of several international hypertension initiatives and programs, their target regions, and their key areas of action. This list is only meant to be exemplary. Many initiatives exist that we did not have time to review, e.g. the [International Society of Hypertension](#), the [NCD Alliance](#), the [World Hypertension League](#), and the [Global Alliance for Chronic Diseases](#). Moreover, there are also various national initiatives, such as the India Hypertension Control Initiative, which we discuss [here](#). The initiatives we outline in [Table 3](#) below target different regions, but they all share a multi-pronged approach, focusing on both prevention and treatment. We have not evaluated the impacts of these initiatives.

Table 3. Features of global initiatives and programs for hypertension treatment

Initiative or programme	Target regions	Key areas of action
WHO Global Hearts Initiative	24 countries had expressed interest in participating in 2017 (CDC website)	HEARTS (six technical packages for the prevention and control of cardiovascular disease): healthy lifestyle counseling; evidence-based treatment protocols; access to essential medicines and technology; risk-based CVD management; implementing team-based care and task shifting; and improved monitoring system with standardized indicators (e.g. hypertension control rate) and data collection tools
World Heart Federation Hypertension Roadmap	N/A	The roadmap is a global framework that can be adapted and used at national or regional level and has several components: Opportunistic screening; promoting use of inexpensive, good-quality generic medications for hypertension; education on adherence to lifestyle modification and medication use
PASCAR (Pan-African Society of Cardiology Roadmap)	Sub-Saharan Africa	A 10-point action plan for African ministries of health, including: creating or adopting clinical evidence-based hypertension management guidelines; monitoring of detection, treatment and control rates of hypertension, with a clear target for improvement by 2025;

		integrating hypertension management within existing health services such as disease-specific vertical programmes (e.g. HIV and tuberculosis); task-sharing with community health workers; and ensuring availability of essential equipment and medicines
Resolve To Save Lives	31 countries, some of which are LMICs	Practical treatment protocols with specific medications, dosages and steps to take if blood pressure is not controlled; adopting community-based care and task sharing; ensuring supply of medications; adopting easy-to-take medicine regimens, using free or low-cost medications and follow-up visits, and making blood pressure monitoring readily available; and leveraging technology to develop information systems that allow for continuous, real-time improvement
Global Standardized Hypertension Treatment Project	Barbados, Malawi	Framework for standardizing the treatment of hypertension globally, consisting of: using a core set of medications for hypertension treatment; ensuring availability and affordability of these medications; strengthening healthcare delivery systems (e.g., by using standardized treatment protocols and team-based care, and by developing hypertension registries and monitoring targets)
HOPE Asia Network (Hypertension Cardiovascular Outcome Prevention and Evidence in Asia)	13 Asian countries	Focus on improving the management of hypertension and organ protection in Asian countries. HOPE Asia organizes webinars and conferences, as well as providing some information online and publishing some papers (e.g. on home blood pressure monitoring)

Note. Adapted from Zhou et al. (2021, p. 797, Table 1).

Research landscape: Hypertension research is growing, but more context-specific studies are needed to improve prevention, treatment, and control in LMICs

[Confidence: Medium. We are fairly confident that our big picture view on hypertension research is accurate and that we identified the most important research gaps in LMICs. However, we are less sure about the order of importance of the different research gaps.]

We spent ~2 hours reviewing the literature on the current research and research gaps on hypertension in LMICs. Our key findings are:

- **Global hypertension research has grown exponentially in recent decades in terms of publication numbers.** According to a recent bibliometric analysis, almost 450,000 scientific articles have been published on hypertension in about the last 30 years (and almost 600,000 in the last 100 years). In recent years, about 15,000 articles have been published annually (Abba et al., 2022, pp. 2-3).

- **Nonetheless, hypertension research appears neglected relative to its large health burden.** Annually, there are 64 hypertension-related publications per 1 million DALYs lost due to the condition. As a rough comparison, the figure is 417 HIV/AIDS-related publications per 1 million DALYs lost due to HIV/AIDS.²⁵
- Generally, **most knowledge on hypertension seems to be coming from studies in high-income populations**, which is often not directly applicable to LMICs due to differences in disease patterns, risk factors, and health systems ([Aifah et al., 2019](#), p. 104).
- Based on Schutte et al. ([2021](#)), Jeemon et al. ([2021](#)), WHO ([2011](#)), and conversations with several experts, the **most important research gaps related to hypertension in LMICs appear to be context-specific studies**, such as:
 - **Implementation trials** to improve screening and blood pressure control in local contexts
 - **Clinical trials** to identify optimal treatment combinations in LMIC populations
 - **Local cost-effectiveness analyses of interventions**
 - Research to understand **emerging risk factors (e.g. air pollution)** and their importance for hypertension in LMICs
 - **Improving blood pressure monitoring devices** suited for LMICs
 - **Evaluation of novel treatment approaches** (e.g., [renal denervation](#), a novel treatment for resistant hypertension) and their appropriateness for LMICs
- We provide a more detailed discussion of these research gaps and specific examples in [Appendix I](#).

Country case study: India has been active in combating hypertension in recent years but barriers to improvements remain, including the availability of blood pressure devices, medicines supply, and access to health care

[Confidence: High confidence in India's National Multisectoral Action Plan for Prevention and Control of Common Non-Communicable Diseases and the India Hypertension Control Initiative being two key programs in combating hypertension prevalence. A further 2 hours of research did not produce any other initiatives active at the national level. However, we have lower confidence that these activities can be directly linked to the improved rates. We are confident that important barriers remain to combating hypertension, but lower confidence on which barriers are the most impactful in India.]

India is home to 16% of the global hypertension-related DALY burden ([GBD Results Tool, 2019](#) and [own calculations](#)). The estimated prevalence of hypertension amongst the Indian population older than 30 years is 30%. Among people with hypertension, 36% have been diagnosed, 29% have been treated, and 15% have their hypertension controlled ([NCD-RisC, 2021](#) and [own calculations](#)).²⁶ We show the figures for men and women with corresponding confidence intervals, in [Table 4](#) below. These numbers do vary between sources, so we do not

²⁵ We calculated this using recent HIV/AIDS-related publication figures from Elsevier Analytical Services ([2019](#), p. 10), and DALYS lost due to HIV/AIDS in 2019 according to the 2019 GBD study ([Wu et al., 2021](#)).

²⁶ We have taken the average of the crude prevalence for men and women as reported by NCD-RisC, weighted by population above 30 years in India in 2011.

have high confidence in them. They should be viewed as a rough idea of the care cascade in India.²⁷ In [Appendix G](#) we have included a figure of the care cascade by age group in India.

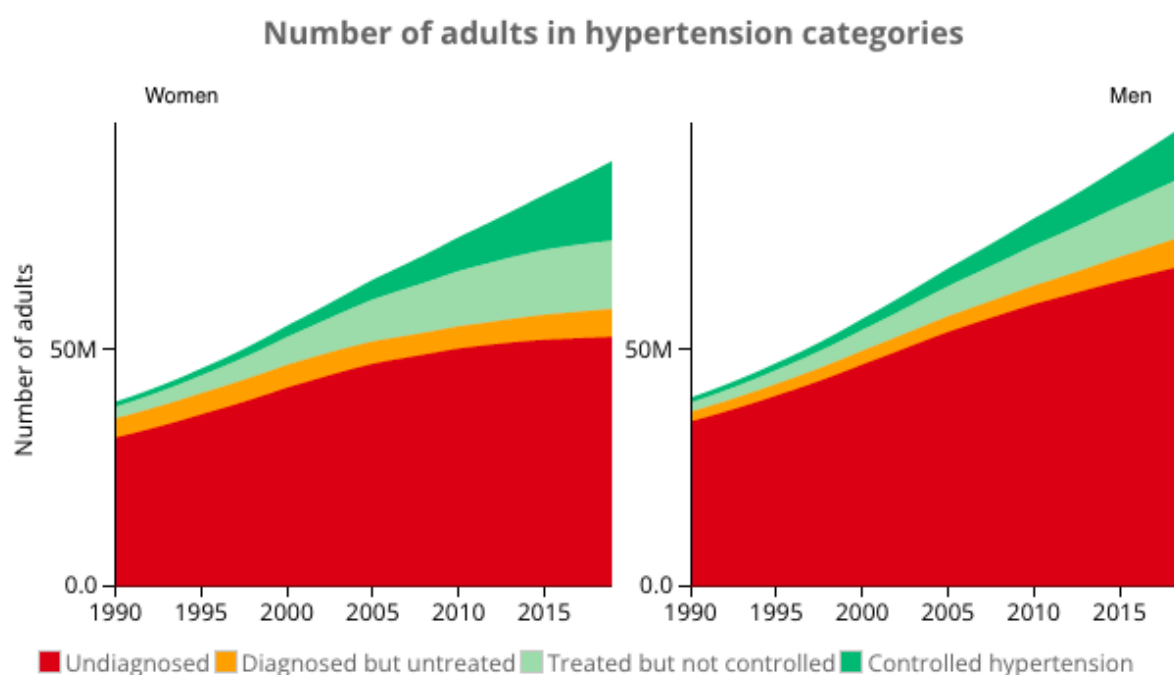
Table 4. Hypertension treatment cascade for men and women in India in 2019.

	Prevalence (% of population)	Diagnosis (% of hypertensive)	Treatment (% of hypertensive)	Control (% of hypertensive)
Men	31% (24% - 38%)	30% (22% - 39%)	24% (16% - 32%)	11% (6% - 18%)
Women	30% (23% - 37%)	41% (30% - 53%)	35% (25% - 46%)	18% (10% - 29%)

Note. From [NCD-RisC \(2021\)](#). See data in [this sheet](#) (95% confidence intervals in parentheses).

The rates of diagnosis, treatment, and control have improved significantly between 1990 and 2019 in India. From our [own calculations](#) using the NCD-RisC data we find that the rate of diagnosis increased by about 21 percentage points in this time period, treatment increased by 22 percentage points, and control by 13 percentage points.²⁸ In the meantime, the prevalence of hypertension has also increased by four percentage points, and the absolute number of people with hypertension has grown a lot more due to population growth. [Figure 6](#) below shows these trends.

Figure 6. Trend in hypertension care cascade in India between 1990 and 2019.



²⁷ For example, [Lee et al., 2022](#) report that an estimated 46% of the Indian population above 45 years old has hypertension (95% CI 45.4%–46.5%). Of that group, they estimate that about 56% (54.9%–56.5%) are diagnosed, 39% (38.1%–39.6%) are treated, and 32% (31.0%–32.4%) have it controlled. The difference in prevalence is likely to lie in differences in age groups. However, we don't think this explains the difference in diagnosis, treatment, and control. That could lie in study design or different measurement times. Both studies give these figures for the year 2019; however, NCD-RisC is based on other studies and could therefore be an extrapolation of older data. Also, in our calculations to translate between age-standardized and true prevalence, we used census data from 2011. For more on the method and limitations of NCD-RisC, see [Appendix A](#). Overall this finding makes us more skeptical about the accuracy of the numbers reported on hypertension.

²⁸ Lee et al. ([2022](#)) report a similar trend between 2010 and 2017-2019. They found that diagnosis had increased by 20 percentage points, treatment by 14 percentage points, and control by 13 percentage points respectively. These numbers are uncertain since they are based on a small sample size.

Note. From [NCD-RisC. country profile India](#).

India has been active in preventing and combating hypertension in recent years, setting a goal to reduce the prevalence of hypertension by 25% between 2017 and 2025 ([MoHFW, 2017](#), p. 47). Below we describe the main initiatives in terms of prevention, diagnosis, and treatment of hypertension in India. We don't imply that these initiatives have caused the improvement described above, since they only started around 2017.

Prevention

- The goal to reduce hypertension by 25% is part of India's National Multisectoral Action Plan for Prevention and Control of Common Non Communicable Diseases (NMAP) by the Ministry of Health & Family Welfare ([MoHFW, 2017](#)). The plan consists of four strategies to prevent and control NCDs: coordination, health promotion, health system strengthening, and evaluation (summarized in [Appendix E](#)). Actions focused on prevention include raising taxes on tobacco and unhealthy foods and the goal to reduce the mean salt intake of the population by 30% between 2017 and 2025 (p. 47), with actions for several ministries linked to this goal. We are not certain of the progress on these goals so far.
- Based on a conversation with an expert, we understand that other programs focused on prevention are typically at the state or district level and of smaller scale. An example of this is a research project on salt reduction in Andhra Pradesh and Delhi/Haryana, run by the Global Alliance for Chronic Diseases (GACD) ([Vedanathan, 2018](#))

Diagnosis, treatment, and adherence

- The largest intervention in India is the **India Hypertension Control Initiative (IHCI)**, which was launched in 2017. It is a cooperation between several partners in India, both governmental and non-governmental.²⁹ The initiative focuses mainly on low-barrier and locally available screening for hypertension, standardized treatment protocols, monitoring systems, and increasing drug accessibility, including access to free drugs ([IHCI, 2021](#), pp. 12-14). The full list of intervention strategies can be found in [Appendix D](#).
- The outreach of the project is large. As of December 2021, it operated in more than 15,000 health facilities and more than 2 million patients with hypertension were enrolled ([IHCI, 2021](#), p. 7). In the 26 districts where the program was first initiated, IHCI estimates that 22% of all patients with hypertension are enrolled in the program.
- According to an expert, the program makes use of health and wellness centers that the government has set up and is still expanding as part of the general health program in India. The aim is to bring primary care closer to the population, with the aim that each center serves 5,000 people. These centers offer low-barrier treatment by nurses trained for specific care.
- Our impression is that IHCI is a promising program, with capacity to decrease hypertension in India at a large scale. However, a lack of baseline and methodological clarity in progress reports lowers our confidence in this (more detail in [Appendix D](#)).

²⁹ "IHCI is a multi-partner initiative with the Ministry of Health and Family Welfare Government of India, Indian Council of Medical Research (ICMR), and WHO Country Office for India. Resolve to Save Lives (RTSL) is an international technical partner" ([IHCI progress report, 2021](#), p. 12).

Tom Frieden shared that more than 10 million patients have been started on treatment as part of this Government of India program.

- The most recent **government guideline** on hypertension in India is from March 2016 ([MoHFW, 2016](#)). According to an expert, a new set of guidelines is due to come out soon, in which many practices developed in the IHCI will be incorporated. The interview with this expert raised questions about how closely the current guidelines are followed, indicating that clearer and simpler guidelines would help.
- National availability of medicines and cost of medicines do not appear to be barriers in India. Because of the in-country production of generics, **prices of antihypertensive drugs in India are much lower than in other countries**, and in the public sector they are provided for free ([Sahoo et al., 2022](#)).

Below, we describe the main barriers in India in prevention, diagnosis, and treatment from our 3-hour search and expert interviews. **Treatment and adherence are in our view the main category of barriers in India**, based on what we have read and heard in interviews.

- **Prevention.** We have not researched specific barriers to prevention in India, but we expect both **lacking awareness of the risks of hypertension and difficulty in changing unhealthy habits of the population at a large scale to be problems in India as in all countries**. The latter point was confirmed specifically for rural areas in an interview with an expert.
- **Limited availability of accurate blood pressure measurement devices.** The IHCI progress report highlights a “Lack of validated high-quality digital blood pressure monitors in several health facilities affected accuracy of hypertension diagnosis.” ([IHCI, 2021](#), p. 41). According to an expert, many manufacturers do not get their devices validated. The devices that have been validated are expensive.³⁰ One study found that 83% of health care providers had a functioning blood pressure monitor ([Peters et al., 2022](#), Table 3). This percentage seems high to us in comparison to the image IHCI presents. However, Peters et al. do not report how they assess whether a device is functioning—we expect that they also count unvalidated devices. Weighing the evidence, we think limited availability of accurate blood pressure measurement devices is a relevant barrier in India, though we do not have high confidence in this.
- **Lack of available medicines due to capacity for procurement.** Procurement and keeping stocks of necessary medicines is an issue for state governments in India. One study in Bihar³¹ found that only 43% of health care providers had at least one hypertensive drug available ([Peters et al., 2022](#), Table 3).³² An expert interview highlighted that state governments often do not have capacity to calculate the number of pills needed, to keep track of stocks, or to request the relevant federal funding. The procurement process also appears to be slow: in a recent program to improve hypertension care, it took a year to go from planning to availability of drugs at health care facilities ([IHCI 2021](#), p. 41).
- **High indirect costs for treatment due to long travel distances.** Hypertension drugs are provided for free in the public health care system. However, according to an expert,

³⁰ According to an expert, the validated devices are more expensive than the national ceiling for them if states want to receive federal grants.

³¹ The third-largest state by population in India ([Wikipedia](#)).

³² The study assessed 390 providers.

until recently hypertension care was mainly available in hospitals often requiring long travel distances for many patients, causing a barrier for people to get treatment. This is likely to improve as the number of health and wellness centers increases, as mentioned above.

- **Too few health care professionals to treat the large number of people with hypertension.** Moran et al. (2022) (p. 5), cite estimates from an ongoing study indicating that, given the current workforce and task division, only around 8% of the adults with hypertension in India can be treated by physician-led services, assuming they visit monthly for drug prescriptions. According to the study, 70% of hypertensive patients in India *could* be treated with the current task force if they allow a 3-month period and apply task-sharing (i.e., delegation of basic tasks to non-physician health workers) among health workers. India had 0.9 physicians and 0.7 nurses and midwives per 1000 people in 2018, compared to 2.4 and 12.2 respectively in Japan, a high-income country for comparison (Schutte et al., 2021).

What are the most plausible areas that a private philanthropic funder could make a difference?

In this section, we follow the overall structure of the three stages that we have so far outlined in this report: prevention, diagnosis, and treatment.

It is worth noting that this distinction is somewhat academic; many of the interventions that we list below may be implemented as elements of larger packages. For example, the WHO's flagship programme—the Global Hearts Initiative (described above [here](#))—contains multiple interventions that span all three categories. We did not investigate these kinds of packages in our research, as we judged that they would be less easy for a philanthropic organization to fund.

For similar reasons, we have not included any mention of awareness campaigns or health system strengthening, though these would be relevant across all stages. Nor have we investigated solutions that are not unique to hypertension as they could not be successfully investigated within the scope of this report (e.g., improving procurement and supply chains could be cost-effective, but the benefits would span across many diseases).

We have placed more emphasis on researching plausible interventions to improve treatment than diagnosis or prevention. We discussed this approach in each of our interviews, and the experts we spoke to were supportive of this method.³³ The general logic was twofold:

- 1) While prevention is important, many of the associated risk factors are non-modifiable (e.g. age) or limitedly tractable (e.g. physical exercise). This could limit the overall impact of prevention efforts.
- 2) At present, the shortcomings of treatment in LMICs are so large (as illustrated by the significant dropoff in the care cascade between treatment and control) that improving screening without improving treatment is less likely to be cost-effective.

³³ We only conducted four interviews during this research, and this may not represent the majority view on this topic.

As a result, while we highlight possible interventions across prevention, diagnosis, and treatment in the following sections, we only provide a deeper dive for one plausibly cost-effective way to improve treatment.

An initial review of the literature did not reveal useful existing comparisons of cost-effectiveness

[Confidence: Moderately high that there are no other existing evaluations that could inform our research.]

We spent approximately 4 hours finding and skimming papers on the cost-effectiveness and effectiveness of hypertension interventions, with a focus on reviews and meta-analyses. Similarly, we spent 1.5 hours reviewing cardiovascular cost-effectiveness research for analysis specific to blood pressure. While we found some relevant reviews, they did not allow us to make meaningful comparisons.³⁴

Overall, cost-effectiveness calculations on this topic appear neglected, particularly for LMICs. For example, in a recent review of 31 RCTs focusing on hypertension in LMIC settings, only two studies (6% of total) published a cost-effectiveness analysis ([Gyamfi et al., 2022](#), p. 12).³⁵ None of the reviews we read included policy-level interventions aimed at prevention, making it difficult to compare the cost-effectiveness of solutions targeting the different stages we have outlined in this report.

Our major takeaway from this exercise was that the evidence reviewed in [Kostova et al. \(2019\)](#) **suggests that hypertension treatment is likely more cost-effective when targeted at populations with higher risk.**

Prevention: our review captures all risk factors, but experts we spoke to are most confident about prospects of addressing salt consumption

[Confidence: Moderately high that salt is viewed by experts as the most promising approach, and that we have captured the most mainstream policy proposals.]

Earlier in the report, we identified a number of risk factors of hypertension ([here](#)). When considering the plausible interventions to prevent hypertension in this section, we excluded the non-modifiable elements (i.e. age and family history) and air pollution, and spent approximately 3 hours reviewing policies to address the six remaining factors.³⁶ The results of this are summarized in [Table 5](#), along with our initial impressions of tractability.

Our overwhelming impression from the experts we spoke to was that they were more optimistic about population-level policies than attempting to change individuals' behavior.³⁷ **The collective view seemed to be that addressing salt consumption was the most promising intervention, primarily due to a stronger evidence base than for other prevention areas, and**

³⁴ The most useful reviews we identified were Kostova et al. ([2019](#)), Mills et al. ([2018](#)), and Aminde et al. ([2018](#)).

³⁵ The authors are focused on “scale-up”, and exclude RCTs that do not explicitly mention the concept. The frequency of cost-effectiveness analysis may be higher in the excluded research, but we would not expect the true value to be above 20% of total (85% confidence).

³⁶ The brief indicated that air pollution was out of scope. Note also that we did not research obesity independently, but rather reviewed policies for poor diet and physical activity.

³⁷ An expert particularly highlighted the difficulty of conducting any interventions to affect individual behavior in rural areas, due to lack of bandwidth.

evidence of scalability.³⁸ In two interviews the experts acknowledged that the relationship between salt consumption and high blood pressure had been challenged in the past, but were generally positive about the current state of the evidence. Tom Frieden stated that new research disproved the previous concerns, and Rachel Nugent described this as “starting to become a more settled area”.

GiveWell ([2021](#)) published a review of salt substitution in February 2021, but this focused on evaluating the cost-effectiveness of direct substitution in communities rather than public health regulation.³⁹ The Centre for Exploratory Altruism Research has also written a shallow report on hypertension, and estimates the cost-effectiveness of a sodium tax as \$2 per DALY ([Tan, 2022](#)). This report was published at a late stage in our research process, and as such, we have not had the opportunity to evaluate these calculations.

³⁸ Stated in all interviews except our short interview with JD Schwalm. In our discussions, we did not explicitly differentiate between salt reduction and salt substitution. In a recent Cochrane review, Brand et al. ([2022](#)) suggest salt substitution has minimal impact on hypertension; we did not discuss this result with any of the experts we interviewed.

³⁹ Their tentative conclusion was that community-level substitution is not cost-effective, though they suggested that they might re-evaluate the intervention once an ongoing large-scale randomized trial in China was completed. These results were published earlier this year in Li et al. ([2022](#)). We have not investigated how this updates GiveWell’s recommendation.

Table 5. Risk factors and policy proposals for prevention

Risk factor	Potential policy proposals	Who is working on this	Initial thoughts on tractability in LMICs
Excessive salt consumption	<ul style="list-style-type: none"> Adopt high-salt warnings on packaging Set and enforce limits for salt in processed foods, e.g. bread Replace household use with low-sodium salts 	WHO (SHAKE program) The George Institute Resolve to Save Lives	Consumption habits limit interventions targeting processed/ packaged foods, though there are some signs of progress in South Africa (Charlton et al., 2021). Experts we spoke to suggest there is evidence of scalability for salt reduction/ replacement. There are likely to be both demand- and supply-side barriers (e.g. low-profit product) for industry-wide implementation.
Poor diet (related to obesity)	<ul style="list-style-type: none"> Enforce marketing bans for advertisement of unhealthy food and beverages Tax unhealthy foods, e.g. sugary beverages Require healthy food in the public sector, including schools Adopt food labels on packaging 	Bloomberg Food Policy Program	Consumption habits limit success of food labels, and meals are unlikely to be provided in the public sector. Minimizing the spread of such foods and beverages to these countries would be impactful. Full prevention is likely intractable, but taxes on sugar and sugar-sweetened beverages have shown some success at scale (World Bank, 2020).
Low physical activity (related to obesity)	<ul style="list-style-type: none"> Set targets for elements of urban design/ development that facilitates physical activity, e.g. cycle lanes, green spaces Promote physical activity through schools 	WHO (ACTIVE program)	Difficult to change behavior at the individual level. Long timelines for impact through schools or via urban design.
Trans-fat	<ul style="list-style-type: none"> Set limits on industrially produced trans fatty acids (e.g. 2g per 100g of fat) Ban production or use of partially hydrogenated oils 	WHO (REPLACE program) Resolve to Save Lives	Uptake in LMICs so far is low but there appears to be traction, e.g. Nigeria . Some LMICs have high use but have not yet adopted policies, e.g., Pakistan, Nepal, and Egypt.

Tobacco use	<ul style="list-style-type: none"> • Make public spaces smoke-free • Regulate tobacco packaging (e.g. graphic warnings or plain packaging) • Ban direct and indirect advertising • Raise taxes on tobacco products 	WHO (MPOWER program) Bloomberg Initiative to Reduce Tobacco Use WHO FCTC 2030 program	<p>Demonstrated progress on tobacco labeling, restrictions on sales to minors, and efforts addressing tobacco pricing and taxation. Tobacco industry power in some LMICs is strong and significant lobbying may limit tractability.</p>
Alcohol	<ul style="list-style-type: none"> • Set and enforce drink driving measures • Ban or restrict advertising, sponsorship and promotion • Restrict alcohol availability • Raise taxes on alcohol products 	WHO (SAFER program) RESET Alcohol by Vital Strategies ⁴⁰ Global Alcohol Policy Alliance	<p>The extent to which alcohol is sold informally in LMICs may limit tractability. Lobbying activities of the alcohol industry are also a factor.</p>

Note. Compiled by Rethink Priorities based on materials in the “Who is working on this” column.

⁴⁰ This is funded by GiveWell: \$15m grant over three years to operate in ~15 countries.

Diagnosis: interventions could increase the number of people screened accurately, but effectiveness depends on linkages to/ capacity for treatment

[Confidence: Medium confidence that potential interventions would increase the proportion of hypertensives diagnosed, with low confidence in tractability due to minimal research on this topic.]

As demonstrated earlier ([here](#)), much of the hypertensive population in LMICs remains undiagnosed. It seems **plausible that increased screening and diagnosis could reduce the burden of hypertension by leading to more (and earlier) treatment**. Our research and interviews have suggested a number of ways to address this issue, and we outline our thoughts on the most plausible below.

Note that the effectiveness of any of these interventions will be limited by:

1. what proportion of those screened and diagnosed actually follow the referral to go to a clinic to receive treatment, aka. ‘linkage’ to treatment,
2. the capacity of the health system to provide effective treatment.

Our overall impression is that the limitations of both in LMICs will greatly reduce the cost-effectiveness of any screening intervention.

Increase the number of people who are screened

Broadly, there are three potential approaches to screening: opportunistic (of those who present to clinics), targeted (of those individuals who are likely to be at risk), or mass (of the entire population). A recent Cochrane review attempted to evaluate which screening strategy was best, and found no evidence to conduct a review and discriminate between them ([Schmidt et al., 2020](#)).

Potential interventions would be more tractable if there was an existing organization to support and scale. The most obvious candidate is the [May Measure Month](#), a program launched by the **International Society of Hypertension to offer free screening each year**. While we did not look at this effort in detail, one study suggests that the 2019 program reached 1.5m people, one-third of whom had never had a blood pressure measurement, and had a central coordination cost of USD 0.65 per person identified to be hypertensive but untreated or inadequately treated ([Beaney et al., 2020](#)).⁴¹ The 2022 campaign is running across 85 countries. We have not investigated the program’s funding situation.

Lower the price of validated blood pressure monitors

An expert spoke to us about their desire to increase opportunistic screening in India, and highlighted a shortage of accurate blood pressure monitors as a barrier to doing so. They described a market that is predominantly made up of cheap, unvalidated monitors, with **only a small number of manufacturers making validated monitors at a higher price point**.⁴² The latter are difficult for health systems to procure: for example, they explained that federal grants in India will not allow for the purchase of the more expensive brands.

This may be an opportunity for market-shaping. Increasing the number of validated monitors could lead to greater competition, and make accurate monitors more affordable overall. It

⁴¹ This does not account for support from ‘local benefactors’ or the equivalent cost of the large number of volunteers involved in the effort.

⁴² Omron and A&D were specifically mentioned as making validated monitors.

seems as though the WHO prequalification program will start to assess blood pressure monitors in the near future, which could provide a foundation for this work—or suggest that another organization is already tackling this ([WHO, 2022](#)).

Advocate to simplify the algorithms for diagnosis

Speaking with JD Schwalm, he suggested that simplifying the diagnosis of hypertension could be impactful. At present, most guidelines require multiple blood pressure measurements—which is particularly challenging in (rural areas of) LMICs. In a recent study in Malaysia and Colombia, his team simplified the algorithms such that a person was diagnosed as hypertensive if their **blood pressure was over 160 mm Hg on a single visit**.⁴³ Such an approach could reduce the resources needed for screening, and potentially lead to a system that targets those most at risk. However, it could also lead to inefficiencies in treatment if the screening is not accurate. We have not comprehensively evaluated this option but rather highlight it for consideration.

Treatment: Antihypertensive single pill combinations may be a promising intervention

As explained [above](#), our approach to investigating plausible interventions for combating hypertension has primarily focused on treatment.

We identified three interventions that we judged might be a good fit for philanthropic efforts:⁴⁴

- **Task-sharing:** in almost all expert interviews, the benefits of task-sharing were discussed. This approach addresses the shortage of physicians by upskilling other healthcare staff, like nurses and community health workers, to manage hypertension. A systematic review of task-sharing in LMICs does confirm that this approach is effective, leading to reductions in blood pressure ([Anand et al. 2019](#)). It would also be an efficient way to use limited resources. We did not find any indication that existing philanthropic organizations are working on scaling/ implementing this approach for hypertension.⁴⁵
- **Protocol trials:** Tom Frieden and Andrew Moran, highlighted that hypertension treatment is not standardized, in contrast to diseases like tuberculosis, and they do not anticipate that research to determine the best protocols is likely to be forthcoming. Brian Hutchinson noted that the cost of treatment can vary significantly depending on which drugs are prescribed and purchasing power. Opportunities exist to forge consensus on cost-effective treatment protocols that are suited to countries' unique economic circumstances. Philanthropic organizations may play a role by funding studies (e.g., economic evaluations of cost-effectiveness) that assist national health authorities to examine tradeoffs in medication choices and to develop tailored clinical

⁴³ More detail is available in Schwalm et al. ([2019](#)). This was not the only criteria for being diagnosed with hypertension; others included the more standard 140 mm Hg threshold.

⁴⁴ After reading an advance copy of our report, Andrew Moran suggested two additional possibilities that philanthropists could consider. We mention these here for completeness, but did not have time to consider them during our research. The gaps that he identified were 1) need for supervisory and mentoring staff to support program implementation and quality improvement activities in HEARTS countries, and 2) need for general activities around medicines access (broader than single pill combo area), including improved capacity for facility-level inventory, forecasting, a procurement, and regional and global efforts to shape the market, ensure quality, and lower prices.

⁴⁵ For example, we asked JD Schwalm, who is a proponent of this approach, and he was not aware of any. It's possible that task-sharing is being pursued as part of broader "health-system strengthening" efforts supported by governments and international donors.

practice guidelines. Frieden and Moran noted that with experience from hundreds of thousands of patients, it now appears that one drug—the long-acting calcium channel blocker amlodipine—should be the first-line medication for nearly all patients. This is likely owing to low amlodipine cost (available as a generic formulation and need not cost more than 1 cent per pill) and safety profile (no metabolic side effects hence no laboratory monitoring required).

- **Single pill combinations (SPCs):** this is a type of medication whereby fixed doses of multiple drug components are combined into a single pill. SPCs have been implemented to treat other diseases such as HIV/AIDS: these were approved by the WHO in the early 2000s ([Fleck, 2003](#)), and South Africa adopted a single-pill regimen for HIV in 2013 ([Bor et al., 2022](#)).

We elected to conduct a deeper dive into single pill combinations because of the evidence of effectiveness and the potential to tackle multiple barriers in LMIC contexts, as detailed below.

Single-pill combinations are more effective than monotherapy, without adverse effects

[Confidence: High, particularly given evidence from WHO hypertension treatment guidelines and evidence supporting WHO EML application.]

SPCs make sense for hypertension medication, because there is **strong evidence that a combination of antihypertensive drugs is more effective than monotherapy**, i.e. treatment with a single drug. The World Heart Federation Roadmap ([Jeemon et al., 2021](#), p. 6) states that: “Low-dose combinations of antihypertensive agents in general are more effective in BP lowering **with fewer side effects than high-dose monotherapies**”. In a meta-analysis of 42 trials, the impact of **combinations of drugs lowered blood pressure by five times as much as monotherapy** ([Salam et al., 2020, p. 1773](#)).

There is also evidence of significant impact on cardiovascular disease and mortality. Salam et al. ([2020](#), p. 1772) conducts a meta-analysis of RCTs measuring the impact of combination therapy versus placebos or non-treatment, and find “a 26% reduction in CHD, a 32% reduction in stroke, a 48% reduction in heart failure, and a 16% reduction in all-cause mortality”. We did not find any similar analysis comparing monotherapy and combination therapy, and so instead followed the WHO hypertension guidelines ([2021](#), p. 14) in highlighting the results of a nonrandomized study from Italy involving 125,000 patients. This study employed propensity matching to compare patients that initially received monotherapy and combination therapy, and found “significant reductions in the risk of death (–20%, 11% to 28%) and hospitalization for cardiovascular events (–16%, 10% to 21%)” ([Rea et al., 2018, p. 846](#)).

In July 2019, the WHO added four combinations of antihypertensive medications in a single pill to its Essential Medicines List (EML). The WHO hypertension guidelines ([2021](#), p. 15) acknowledge that there are some challenges to using SPCs, including “limited flexibility in modifying the doses of individual components, and difficulty in attributing side-effects to one of its components”. However, ultimately the guidelines conclude that the benefits outweigh the challenges and the resulting **recommendation is to use SPCs for initial treatment of hypertension.**

Note that **the SPC discussed in this report contains antihypertensive medicines only.** We have deprioritized consideration of the cardiovascular polypill (containing antihypertensive medicines, a statin, and sometimes aspirin) given that it is a) further from use, as it has not been

included on the EML or in WHO guidelines, and b) more expensive. Patel et al. (2022) provides a good overview of the polypill’s development and potential routes to adoption.

Single-pill combinations could address multiple barriers to treatment in LMICs, but are not yet widely used

[Confidence: Moderately high, though we did not find any sources that would allow us to quantitatively estimate the current levels of treatment with SPCs in LMICs.]

[Earlier](#) in the report, we outlined a number of barriers to treating hypertension. SPCs have the potential to provide solutions to a number of these simultaneously:

- *Trouble adhering to medicine schedule:* the WHO hypertension guidelines (2021, p. 14) cite results that indicate SPCs increase adherence by 8-14%.
- *Lack of available medicines:* simplifying logistics could potentially lead to fewer stock-outs and improved access. Additionally, given our [expectation](#) that most patients in LMICs are currently treated with monotherapy, using SPCs could provide access to combinations of drugs that are otherwise unavailable.
- *Too few health care professionals:* increasing the proportion of patients that have achieved controlled blood pressure would reduce the number of consultations with doctors to adjust medication.

Our impression is that SPCs are not yet widely used to treat hypertension in LMICs. We found two sources that assess the current availability, but the weakness of both is that they answer the binary question of whether or not such medication is available, rather than evaluating the level of use, e.g. the number of patients treated. Bruyn et al. (2022) found that **in 30 LMICs reviewed, branded and generic SPCs are available (29/30 and 26/30, respectively)**.⁴⁶ A report on hypertensive single-pill combinations authored by RTSL and the Medicin Sans Frontiers Access Campaign conducts a deep dive on five LMICs and illustrates that **general availability does not necessarily mean public sector availability**.⁴⁷

Table 6. Availability of SPCs for hypertension in selected countries

Country	Availability	% of SPC formulations available	
		Private sector	Public sector
Brazil	Y	64%	0%
Lebanon	-	50%	50%
Nigeria	Y	57%	64%
South Africa	Y	68%	0%

Note. Availability from Bruyn et al. (2022). Percentage of SPC formulations available from RTSL & MSF Access Campaign (2022, p. 26).

⁴⁶ The review covers five LICs, 13 LMICs, and 12 UMICs, amounting to 71% of the global population. Countries were evaluated by searching the records of pharmacies online, in English and local languages, and asking local contacts when needed. They do not find evidence of generics being available in Ethiopia, Morocco, Afghanistan, or Turkey.

⁴⁷ The LMICs are the four countries shown in [Table 6](#), and the Philippines (for which the ‘% of SPC formulations’ data was not available).

Tom Frieden and Andrew Moran at RTSL described **overall low levels of use: particularly low in Africa, with more widespread use of SPCs in Latin America** where incomes are higher. They also noted that SPCs are **widespread in the Indian private sector, but largely absent in the public sector**. This is further supported by Sahoo et al. (2022, p. 4) and Negi et al. (2020), with the latter reporting that 20 billion SPCs were sold in the private sector in India in 2018. An expert shared that two states in the India Hypertension Control Initiative will be trialing SPCs as part of their program delivery.

A back-of-the-envelope calculation suggests that direct provision of single pill combinations would not be cost-effective, even at the lowest available cost

[Confidence: Moderately high, given the current estimate]

A philanthropic organization could consider directly providing single pill combinations to hypertensive populations in LMICs. We created a BOTEC for this, assuming that pills would only be provided to people with blood pressure > 140 mm Hg.

The 2019 GBD study estimates that the annual burden of high systolic blood pressure in low- and lower-middle income countries is roughly 5,000 DALYs per 100,000 persons (aged 25 and over).⁴⁸ This estimate includes the burden for those with elevated blood pressure but not hypertension (i.e. 115-140 mm Hg), and as established earlier ([here](#)) we estimate that this accounts for ~30% of the total burden. Focusing on those with blood pressure > 140 mm Hg only, the burden is therefore 3,500 DALYs per 100,000 persons. To adjust to Open Philanthropy (OP) DALYs, we multiply by a ratio of 0.75, to get 2,625 DALYs per 100,000 persons. Assuming roughly 30% of the population has hypertension (see [here](#)), this works out to 2,625 DALYS per 30,000 people, or 0.0875 DALYs lost per hypertensive person. A conservative estimate of the impact of patients starting combination therapy is a 15% reduction in mortality and cardiovascular disease, such as strokes or heart failure (based on the results summarized [here](#)). This results in $0.0875 * 15\% = 0.013$ DALYs averted per person using SPCs.⁴⁹

Using the OP value of \$100,000/ DALY, this is a **benefit of \$1,300 per person**. The price of SPCs varies significantly between countries, as discussed in the next section, but using the **lowest price we have seen quoted for an annual supply of SPCs (see Table 7), we estimate cost-effectiveness as \$1,300 / \$2.91 = 447x**. Note that our current cost estimate of \$2.91 does not include the costs of delivery. It also assumes that any patient can successfully control their blood pressure using only the lowest-dosage, which is unlikely to be the case.⁵⁰ Incorporating these elements would further reduce cost-effectiveness. To reach the OP bar of 1000x, a year's treatment using SPCs would need to cost \$1.30.

Based on these calculations, it seems **unlikely that direct provision of SPCs would be cost-effective using OP's metrics**. We have very low confidence about the 15% reduction in DALYs, particularly as this is a conservative blanket assumption across all sources of burden. It does not capture, for example, that the impact on the DALYs lost due to strokes could be closer

⁴⁸ The point estimates from GBD are 4,678.11 per 100,000 persons in low-income countries, and 5,822.38 per 100,000 persons in lower-middle income countries. We use 5,000 as a convenient rounded figure, though it is likely conservative given that a larger population lives in lower-middle income countries. We assume that upper-middle income countries are out of scope.

⁴⁹ Note that this calculation assumes that all of this burden is attributable to cardiovascular disease, and as such can be reduced by 15%. In fact, only 92% of this burden is attributable to cardiovascular disease ([here](#)).

⁵⁰ Rough calculations based on Sahoo et al. (2022) suggest that the average price of treatment could be up to 36% higher than the cost of simply buying the lowest-dosage SPC, such that: $\$1,300 / (\$2.91 * 1.36) = 328x$.

30%. A more detailed calculation could capture this variance to better estimate the DALYs reduction, and incorporate the other costs of direct provision. However, as these two elements work in opposition, it is possible that they would wash out and produce a similar magnitude estimate of ~500x that does not pass the bar.

We also spent ~30 minutes considering the cost-effectiveness of direct provision of pills for monotherapy only. We found a source that compared the effects of monotherapy and combination therapy: Paz et al. (2016). Assuming that the reduction in blood pressure is directly related to DALYs averted, then this source suggests that the benefits of monotherapy would be 55% of the benefits of combination therapy, or \$715 (12.5 mm Hg/ 22.5 mm Hg * \$1,300). To estimate costs, we can take the Indian public procurement price in Sahoo et al. (2022, Table 4) for the cheapest, lowest-dose SAP (amlodipine 5mg), which is \$0.69 per year. However, Table 5 in the same article suggests that only 30-60% of the population would control hypertension with this dosage. Conservatively, we assume 50% of the population would require a double dose, and this would be only 40% more expensive (loosely based on the comparison of the prices from amlodipine 5mg and 10mg pills in RTSL & MSF Access Campaign [2022, p. 38]). The resulting price would be $50\% * \$0.69 + 50\% * (\$0.69 * 140\%) = \$0.83$. Our estimate becomes $\$715 / \$0.83 = 863x$, which remains below the OP bar, and strongly suggests that monotherapy would not be cost-effective outside of India where prices are higher. This also does not account for DALYs lost due to higher side effects from high-dose monotherapy.

A philanthropic organization could work to reduce the price of single pill combinations, particularly outside India

[Confidence: Moderately high that there is room for improvement, low confidence in what the future trend would be without intervention. Additional research is needed to investigate specific actions and their cost-effectiveness.]

We also investigated a number of factors that could be limiting the widespread use of SPCs. Overall, our impression is that the **price of the medication is likely the most important factor**. In this section, we outline the potential for a philanthropic organization to reduce the price of single pill combinations. Our assessment of five other factors can be found in [Appendix H](#).⁵¹

Two aspects of the price of SPCs are important. The *absolute price* determines whether they are affordable for patients in LMICs. Their *relative price* versus the cost of buying two equivalent single agent pills (SAPs) determines whether LMICs switch from current treatment (predominantly monotherapy, with some combination therapy) to SPCs.⁵² **Reducing the price of SPCs could facilitate this shift to SPCs, with associated increases in the effectiveness of treatment, and rates of control** (see [here](#)).

Information on the prices of antihypertensive medication is limited, but available data suggests:

- The price of antihypertensive SPCs varies **significantly between countries and between the public and private sector**, as illustrated for one formulation in [Table 7](#). The comparison shows that a year's supply of the same pill costs the Indian government \$2.59 to supply in the public sector, but costs \$295 in the private sector in the Philippines. In some countries, SPCs are not affordable.

⁵¹ In order of our assessment of decreasing importance, these are: national registration, treatment guidelines, national EMLs, physician attitudes, and manufacturing capacity.

⁵² Keeping in mind that adherence is improved with SPCs, it may be cost effective to switch at a point where two SAPs are still slightly cheaper.

- **SPCs can be more or less expensive than their constituent SAPs:** there is no established trend. In some countries (Brazil, South Africa and the Philippines), buying an SPC is cheaper; in contrast, in Nigeria and Lebanon it is cheaper to buy two separate pills ([RTSL & MSF Access Campaign, 2022](#), p. 29). In their analysis of Indian private sector prices Negi et al. ([2020](#)) find that the lower bound for purchasing pills separately or buying an SPC is similar.
- Tom Frieden and Andrew Moran shared that in their experience, overall **the price of SPCs is not yet low enough to induce LMICs to switch away from SAPs** given government budget constraints.

From our research, our impression is that there is **significant scope to reduce the prices of SPCs** because:

- **There is a significant mark-up on hypertension medication (high confidence):** The RTSL and MSF Access Campaign report ([2022](#), p. 29) compares estimated cost-based generic prices (including a 10% profit margin) with actual prices, and concludes there is a significant mark-up on both SAPs and SPCs.⁵³ Prices in the private sector can be 40x the cost-based estimate, and public sector prices are also significantly higher than estimated costs (e.g. 12x for Nigeria in [Table 7](#) below). Some of this difference will be explained by the other costs not captured by the estimate (e.g. shipping), but it seems unlikely that these would explain the entirety of the gap. In addition, Sahoo et al. ([2022](#), p. 3) report a price for public sector procurement of SPCs in India that is lower than the cost-based estimate. As such, it may be possible to reduce prices further than the table suggests.⁵⁴
- **There is evidence that there is an additional mark-up on SPCs over SAPs (medium confidence):** Analysis of the prices in India suggests that SPCs produced by a manufacturer tend to be more expensive than their equivalent SAPs ([Negi et al., 2020](#)). Tom Frieden and Andrew Moran also confirmed that manufacturers most often price SPCs higher than their separate SAPs.
- **SPCs may be cheaper to manufacture than two SAPs (low confidence):** In reviewing the generic cost-based prices in the RTSL & MSF Access report ([2022](#), p. 38), their estimates for eight formulations suggest that they expect SPCs to retail for 61% - 71% of the cost of the two constituent SAPs together (our own calculations [here](#)). We have not investigated this estimate in detail, but it does seem plausible to us that SPCs are cheaper to manufacture: the cost of active ingredients should remain the same, while variable costs like labor and packaging should be reduced.

Table 7. Price of Telmisartan 40mg + Amlodipine 5mg SPC

	Price per pill (USD)	Price per year (USD)	Comparison to cost-based generic price
Estimated cost-based generic price*	0.0192	7.01	-
India (public)†	0.008	2.91	0.4x

⁵³ The estimates included the additional costs of “formulation, packaging, taxation and a 10% profit margin” ([RTSL & MSF Access Campaign, 2022](#), p. 27).

⁵⁴ This is true only if the manufacturer was not selling at a loss.

	Price per pill (USD)	Price per year (USD)	Comparison to cost-based generic price
PAHO Pooled procurement [‡]	0.09	32.85	4.7x
Nigeria (private)*	0.095	34.68	4.9x
India (private) [†]	0.14	52.78	7.5x
Nigeria (public)*	0.244	89.06	12.7x
South Africa (Private)*	0.651	237.62	33.9x
Brazil (private)*	0.7005	255.68	36.5x
Philippines (private)*	0.81	295.65	42.2x

Note. *Data from RTSL & MSF Access Campaign (2022, p. 38). [†]Data from Sahoo et al. (2022, p. 3), median price in INR converted using an exchange rate of 74 INR: 1 USD. [‡]Data from RTSL & MSF Access Campaign (2022, p. 33).

There are a number of market shaping approaches that a philanthropic organization could work to lower prices (see [Kudymowa et al. \(2023\)](#) for an overview of market shaping approaches in global health), for example:

- **Pooled procurement:**
 - Facilitating pooled procurement could be an option to aggregate demand and thereby increase buyers' bargaining power. It is well-established that pooled procurement can, under the right circumstances, substantially reduce prices and increase and speed-up access to drugs ([Kudymowa et al., 2023](#), pp. 30-31).
 - There are several pooled procurement models with different degrees of coordination ([Nemzoff et al., 2019](#), p. 3), for example:
 - On the low end of coordination, Rachel Nugent suggested that an initial step towards market shaping could be for a philanthropic organization to support more systematic sharing of price information. Greater transparency on medicines prices can increase the negotiating power of purchasers from LMICs.
 - On the higher end of coordination, there are group purchasing organizations such as the Pan-American Health Organization (PAHO) Strategic Fund. The Fund was established in 2000, and purchases health supplies for 35 Latin American and Caribbean countries. Each country establishes its requirements and the Fund issues tenders based on the consolidated demand, financed by a 4.25% fee per order.⁵⁵ The RTSL and MSF Access Campaign report (2022, p. 33) shows that pooled procurement by the PAHO Strategic Fund has been successful for SAPs,

⁵⁵ This fee covers both the administrative costs of the Fund (1.75%) and contributions to a capital account (2.5%) set up to extend a line of credit to participating countries. See PAHO (2021) for a brief overview.

with prices the same as cost-based estimates. However, the same analysis still shows a substantial pricing gap for SPCs.⁵⁶

- Tom Frieden suggested the idea of a global or regional hypertension drug facility, an initiative that he has been trying to set up.⁵⁷ This could provide for at-cost, efficiently procured, and quality-assured hypertension medications for middle-income countries and subsidized costs for lower-income countries. The same facility could open access to other NCD medicines (e.g., medicines for diabetes or high cholesterol).
- **Volume guarantees:**
 - Volume guarantees constitute an agreement by buyers to purchase a minimum quantity of a product from a seller. It is “typically matched with a long-term supply contract that sets the price for multiple years” and often results in lower prices ([USAID, 2014](#), p. 34). We think this could potentially be a useful tool for reducing SPC prices as markets for antihypertensives are “fragmented” ([RSTL, 2022](#), p. 13). Volume guarantees have, for example, successfully been used to reduce prices and increase uptake for contraceptive implants in low-income countries ([USAID, 2014](#), p. 35).

The cost-effectiveness of any market shaping would depend on expectations about the trend in SPC prices in the future, without intervention. This is not a question that we have considered in detail. On the one hand, the 2019 recommendation of SPCs in the WHO guidelines and use of SPCs in the Americas may suggest growing demand that could reduce prices. On the other hand, funding for NCDs is relatively limited and may not be directed towards such a narrow intervention. Tom Frieden and Andrew Moran shared the opinion that demand for SPCs may not be large enough to lower prices in the short-term, meaning that an SPC manufacturer would need to be incentivized by longer-term market growth potential. Our tentative, low confidence conclusion is that without intervention we could expect SPC prices to fall a small amount, but would not expect decreases to approach the cost-based estimate without outside intervention.

Conclusion

In this shallow review, we investigated the importance, neglectedness, and tractability of hypertension globally, with a special focus on LMICs. We conclude that:

- **The importance of hypertension is high due** to its very large and growing health and economic burden, costing 235 million DALYs and \$400 billion-\$800 billion in economic costs globally per year. Most of the burden is borne by LMICs. While steady improvements have been made in terms of diagnosis, treatment, and control, these have been outpaced by a steep rise in hypertension prevalence.

⁵⁶ Tom Frieden and Andrew Moran suggest this gap remains because volumes are not yet sufficient to significantly drive down prices. Countries in the region have not yet agreed on a small number of specific formulations, and so demand is split across many formulations. Although the PAHO Strategic Fund is able to procure specific SPCs, these formulations may not yet have regulatory approval within countries. In some cases, another contributing factor is the desire to continue to purchase from in-country producers, rather than the lowest-cost producer.

⁵⁷ This was not mentioned by Frieden, but a successful example of an existing drug facility is the [Stop TB Partnership's Global Drug Facility](#) for tuberculosis (TB) drugs. It is a variant of a pooled procurement mechanism that is currently the largest TB procurer and reported \$31M of savings in 2018 due to price reductions, which represents 14% of TB drug costs delivered by the Facility in 2017 ([Stop TB, 2018](#)).

- **Hypertension appears to have a medium level of neglectedness.** Governments and several international organizations work on reducing the hypertension burden, but philanthropic spending (\$50 million-\$150 million/year) and research seem to be low relative to the health burden and large existing barriers to reducing hypertension.
- **We think the tractability of hypertension (for a philanthropic funder) is medium.** Reducing salt consumption seems to be the most promising prevention approach. Improvements in diagnosis seem tractable, but may not be cost-effective unless simultaneous improvements in treatment are made. Improvements in treatment in terms of improving access to single pill combinations of antihypertensive medicines are, in our view, the most promising for philanthropic involvement. Significant variation in the price of SPCs across LMICs, as well as the evidence of large margins on antihypertensives, points to an opportunity to reduce prices.

Overall, we recommend further investigating hypertension as a potential cause area. A medium should prioritize investigation of the likely costs of specific interventions for market-shaping, as well as the expected benefits of lowering prices and the counterfactual trend without OP involvement. This exercise could also potentially be expanded to evaluate other approaches that we did not consider in detail, such as funding protocol trials to standardize treatment (more [here](#)), or filling research gaps highlighted in [Appendix I](#).

What we would do with more time

- Compute the number of people affected by hypertension per country and age group by combining NCD-RisC ([2021](#)) age- and country-specific prevalence estimates and population estimates broken down by age (e.g. from census data).
- Get a better sense of the credibility and likely error margins of GBD estimates of DALYs and deaths by spending more time to understand the GBD methodology and limitations.
- Look through individual studies on direct and indirect hypertension costs, score based on quality, and form our own selection from which to derive an estimate of per person cost for hypertension in LMICs (and in turn estimate a total economic burden figure) which we expect to be more reliable than current systematic review efforts.
- Given a lack of comparable cost-effectiveness estimates, attempt to back-calculate or convert from existing papers using one unit (e.g. \$/mm Hg reduction).
- Read further on salt reduction and substitution policies in LMICs, including:
 - Santos et al. ([2021](#)) on salt reduction initiatives globally
 - Rosewarne et al. ([2022](#)) on national strategies for packaged foods
 - Brand et al. ([2022](#)) on low-sodium salt replacement
 - Charlton et al. ([2021](#)) on the effects of South Africa's 2016 policy to reduce salt in processed foods
- Determine a counterfactual trend for future SPC prices.

- Look into statins—both JD Schwalm and Tom Frieden highlighted that these are underutilized.⁵⁸

⁵⁸ According to Frieden, they can substantially increase the health impact of treatment of hypertension and diabetes for patients for whom they are indicated.



Contributions and acknowledgments

Jenny Kudymowa, Aisling Leow, and Carmen van Schoubroeck jointly researched and wrote this report. Jenny Kudymowa also served as the project lead. Tom Hird supervised the report. Special thanks to Tom Hird, Melanie Basnak, and Chris Smith (Open Philanthropy) for helpful comments on drafts. Thanks also to James Hu for report formatting, Shaan Shaikh for copy editing, and Rachel Norman for assistance with publishing the report online.

Further thanks to JD Schwalm (McMaster University), Rachel Nugent (Research Triangle Institute), Brian Hutchinson (Research Triangle Institute), Tom Frieden (Resolve to Save Lives), Andrew Moran (Resolve to Save Lives), and an India-based professor and public health expert (who preferred not to be named) for taking the time to speak with us.

Open Philanthropy provided funding for this report, but it does not necessarily endorse our conclusions.

Appendices

Appendix A. Methodology and limitations of NCD-RisC (2021)

Methodology:

In the following, we outline the data and methodology used in NCD-RisC (2021) as summarized in the [Supplementary appendix](#) (pp. 2-3) of the study:

- Data: NCD-RisC (2021) used data from 1990 to 2019 from publicly available population-representative studies at the national, subnational, or community surveys that included measurements of participants' blood pressure and data on hypertension treatment, and were selected according to various other inclusion and exclusion criteria. In total, 1,201 data sources from all over the world with 104 million participants aged 30-79 years were used. Data was available for 184 countries, covering 99% of the global population. They defined hypertension as “having systolic blood pressure 140 mm Hg or greater, diastolic blood pressure 90 mm Hg or greater, or taking medication for hypertension” (p. 957).
- Statistical analysis: The primary outcomes were estimated using a [Bayesian hierarchical model](#).⁵⁹ According to the [Supplementary appendix](#) (p. 4), “the model had a hierarchical structure in which estimates for each country and year were informed by their own data, if available, and by data from other years in the same country and from other countries, especially those in the same region and super- region, with data for similar time periods”. More weight was given to national data than to subnational or community data sources. The model allowed for non-linear and age-specific time trends.

Limitations and threats to validity:

NCD-RisC (2021) is the first study to estimate hypertension prevalence, treatment, and control trends for all countries worldwide. To avoid bias, only data from studies that included blood pressure measurements were included in the analysis. In several ways, its findings are consistent with the results of other recent studies, such as hypertension patterns across geographic regions. Remarkably, the study covered “eight times as many studies as were in the previous largest analysis” done by Mills et al. (2016) (p. 969).

Nonetheless, the study is subject to a number of limitations. Examples are (adapted from NCD-RisC [2021], p. 969):

- Low data availability in sub-Saharan Africa: The data availability for some countries is relatively low. For example, 5 or fewer data sources were available for many countries in sub-Saharan Africa, whereas more than 40 data sources were available for many HICs (see NCD-RisC [2021], Figure 1).
- Self-reported diagnosis and treatment of hypertension: Diagnosis and treatment are self-reported in most health surveys and might be subject to measurement error.
- Inconsistent methods of measuring blood pressure: Different underlying studies of NCD-RisC (2021) measured blood pressure in different ways and are therefore not fully comparable. For example, studies varied in whether they measured blood pressure once

⁵⁹ According to [Wikipedia](#), “Bayesian hierarchical modeling is a statistical model written in multiple levels (hierarchical form) that estimates the parameters of the posterior distribution using the Bayesian method. The sub-models combine to form the hierarchical model, and Bayes' theorem is used to integrate them with the observed data and account for all the uncertainty that is present.”

or several times, the types of measuring devices they used, and the cuff sizes of the devices.

Overall, we are impressed with the rigorous methodology and the sheer scale of the data, which is the largest available study on global trends in hypertension to date and based on eight times as many studies as were used in the previous largest analysis. Our current impression is that the estimates for hypertension prevalence are fairly reliable and unlikely to be highly over- or underestimated, especially for HICs and MICs where data availability is good. We have more doubts on the accuracy of the estimates for sub-Saharan Africa and to a lesser extent Southeast Asia due to low data availability, and the estimates for diagnosis and treatment, as these are based on self-reported figures from health surveys. We are highly confident that no other study currently exists with a better cross-country comparability and long-term trends of hypertension patterns covering all countries worldwide, but we expect that studies with a higher accuracy are available for individual countries.

Appendix B. Methodology and limitations of Global Burden of Disease study

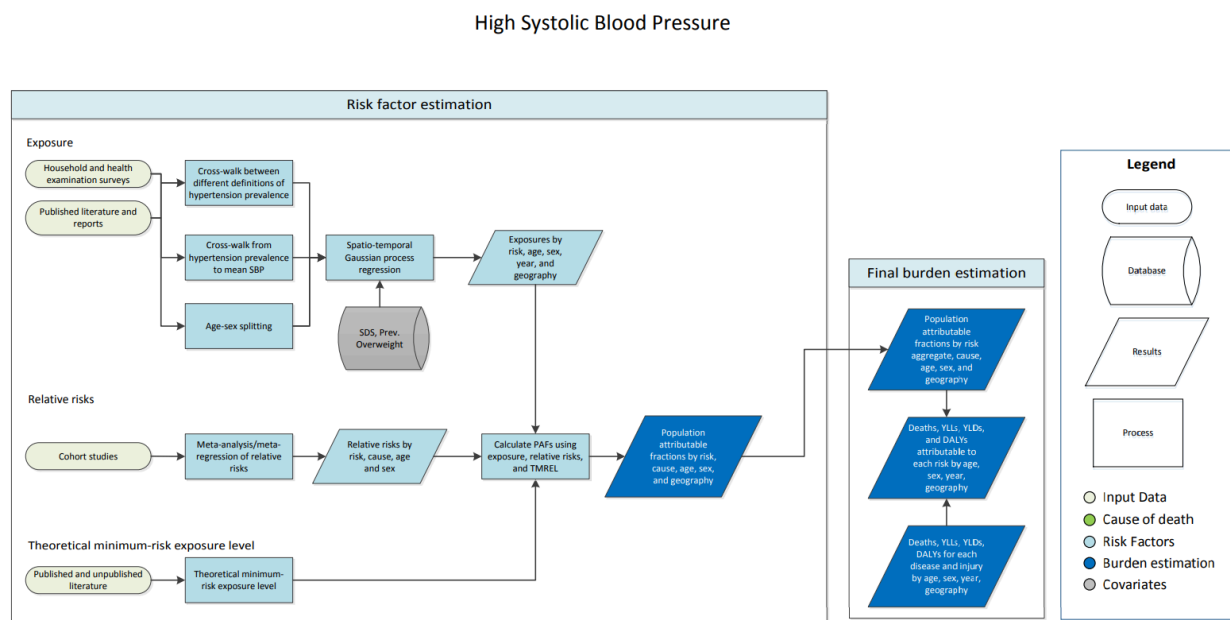
The Global Burden of Disease (GBD) Study estimates the attributable disease burden for risk factors using its **framework for comparative risk assessment (CRA)**, which was developed in 2002 and adjusted in each iteration of the study ([GBD, 2020](#), p. 1225). [Figure B1](#) below shows a flowchart of the estimation process related to SBP.

For each risk factor estimation, the CRA consists of six steps, which we outline for SBP (adapted from [Supplementary appendix 1](#) of GBD [2020], pp. 265-273):

1. **Estimation of exposure levels and distributions:**
 - a. Collection of more than 1,100 data sources on mean SBP from various household and health examination surveys and published reports
 - b. Various adjustments of exposure data, e.g.:
 - i. Corrections for representativeness of data sources
 - ii. Cross-walk between different definitions of hypertension and from hypertension prevalence to mean SBP
 - c. Estimation of exposure levels by age-sex-location-year using spatiotemporal Gaussian process regression, based on socio-demographic status and prevalence of overweight
2. **Determination of the theoretical minimum risk exposure level (TMREL) (= counterfactual level of exposure):**
 - a. The TMREL is the risk exposure level that minimizes risk at population level
 - b. Estimation of TMREL of SBP ranging from 110 to 115 mm Hg based on pooled prospective cohort studies that show mortality risk increases for SBP above that range
3. **Estimation of relative risk (RR) as a function of exposure:**
 - a. Estimation of RR based on cohort studies, meta-analyses and meta-regressions of RRs
 - b. Pooling of effect sizes from studies and generating dose-response curves for each outcome associated with high SBP
4. **Estimation of population attributable fractions (PAFs):**
 - a. Calculation of aggregated PAFs (= proportion of risk that would be reduced in a given year if the exposure to a risk factor in the past were reduced to an ideal exposure scenario) based on exposure, relative risks, and TMREL by age-sex-location-year
5. **Estimation of attributable burden (e.g. deaths and DALYs):**

- a. Estimation by multiplication of PAFs by the relevant outcome quantity for each age-sex-location-year
6. Estimation of burden attributable to various combinations of risk factors:
 - a. Estimation of mediation of different risk factors through other risk factors, such as body-mass index mediated through high SBP

Figure B1. Flow chart for modeling of high systolic blood pressure



Note. From GBD (2017, Supplementary Appendix 1, p. 139).

Limitations and threats to validity:

We spent roughly 1 hour looking for critical evaluations of the GBD methodology and results. We found several critique points outlined by Schiffman and Shawar (2020), Cooper et al. (2017), and Joseph et al. (2017), some of which we outline here:

Some of the critiques we found refer to the GBD estimation methodology in general and are not specific to high blood pressure, e.g:

- The GBD methodology relies on **imputation methods, which are not fully transparent**. The estimates are “generated by opaque techniques and are potentially flawed and misleading” (Schiffman and Shawar, 2020, p. 1452).
- There is a substantial **divergence between country statistics and GBD figures** for many estimates. Moreover, “little effort is made to adjudicate between different sets of estimates” (Schiffman and Shawar, 2020, p. 1453).
- Cooper et al. (2017) questioned the validity of the GBD approach to estimating blood pressure values for countries in sub-Saharan Africa and countries with non-existing data (e.g. Myanmar), which were imputed from regional estimates.

Other critiques we found were more specific to either cardiovascular disease or elevated blood pressure:

- According to Joseph et al. (2017, p. 682), “estimates of CVD burden attributed to elevated BP which use a lower counterfactual to define the threshold of BP at which the general population is at lowest risk for developing CVD (eg, 115 mm Hg systolic as in the GBD)

may overestimate the modifiable disease burden from elevated BP.”

- According to Cooper et al. (2017), the GBD study estimated a high DALY burden from coronary heart disease in sub-Saharan Africa and many parts of Asia, which is at odds with the “well-established” finding that coronary heart disease is rare in those regions. They claimed that the GBD estimation method “will provide **biased estimates of cardiovascular outcomes.**” Two lead authors of the GBD study replied to this critique stating their disagreement. According to Roth and Murray (2017) “the empirical evidence behind their [Cooper et al.’s (2017)] claim is unclear as they only cite a few older studies. In contrast, the GBD study relied on a larger and more recent set of primary sources regarding the mortality due to ischemic heart disease (IHD) in these regions.”⁶⁰

To assess the validity of these claims, we briefly reviewed the literature on IHD rates and mortality in sub-Saharan Africa and also asked Andrew Moran, who led the global burden of ischemic heart disease analysis for the GBD 2010 study.

We have not seen any individual study that reported a high IHD rate or mortality in sub-Saharan Africa that was not derived from GBD estimates. Instead, we found a few studies relatively recent studies that found IHD rates and mortality to be rather low (e.g. [Dokainish et al., 2016](#); [Agbor et al., 2018](#); [Damasceno et al., 2012](#)), but increasing in recent decades (e.g. [Jablonski-Cohen et al., 2003](#)). However, some evidence suggests that “low IHD rates in SSA might not be real, but rather related to poor ascertainment, and that IHD may be underdiagnosed due to paucity of biomarker, electrocardiography, invasive angiography, and diagnostic imaging capabilities” ([Yuyun et al., 2020](#), p. 4). While there seems to be a consensus that IHD used to be historically low in sub-Saharan Africa (ibid, p. 4), it seems less well-established that this still holds today.

According to Andrew Moran,

It is good to separate GBD mortality estimates from chronic disability estimates when assessing the data quality. Despite some flaws, cause-specific mortality data are more solid and reliable than non-fatal condition prevalence and disability data. This makes **high case-fatality conditions like ischemic heart disease intrinsically more reliable estimates within GBD than predominantly non-fatal conditions like major depression.** Yes, there are chronic forms of IHD and stroke, but these contribute very little to overall DALYs.

I would also counsel against lumping Asia and sub-Saharan Africa together in terms of data quality (which feed into GBD). **East Asia, China in particular, has a very strong epidemiology tradition. South Asia data have improved in recent years,** with studies like PURE. And mortality data have improved and are quite good for most countries in the region. **Sub-Saharan Africa data have improved, but there remain vanishingly few studies of CVD incidence or prevalence.**

Overall, the methodology used for GBD estimates for DALYs and deaths is quite complex with many layers of assumptions and relies on several steps and a combination of different types of data sources and estimation techniques. We do not have a

⁶⁰ In our understanding, coronary heart disease and ischemic heart disease are generally used as synonyms.

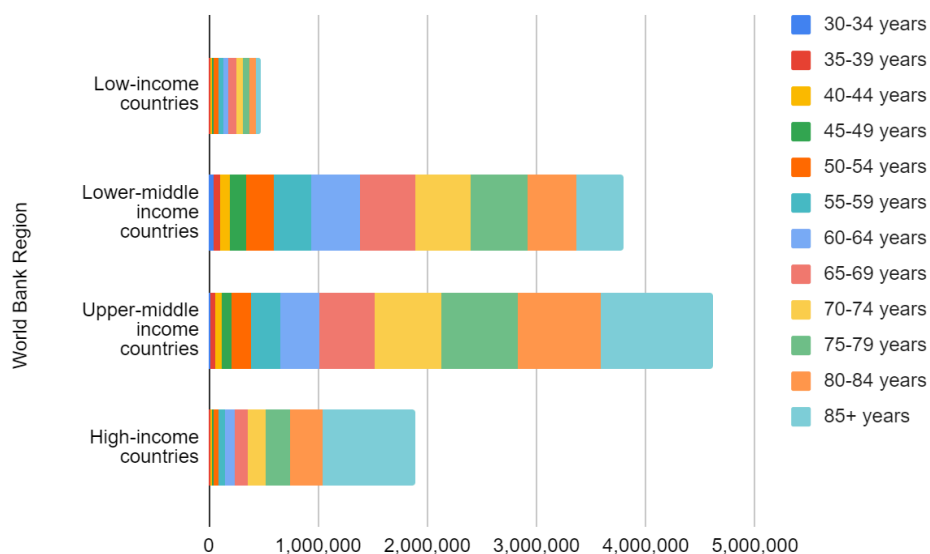
sufficiently deep understanding of the methodology to fully evaluate the accuracy of GBD study estimates, but we found the aforementioned critique points pointed out in the literature plausible.

Appendix C. Deaths and DALYs due to high systolic blood pressure by age group and sex

Figure C1 and Figure C2 below show the numbers of deaths and DALYs due to high SBP disaggregated by World Bank regions and age groups. As one would expect, **both the death and DALY burden are relatively low for individuals below 45 years. The majority of both the death and DALY burden is carried by older individuals.**

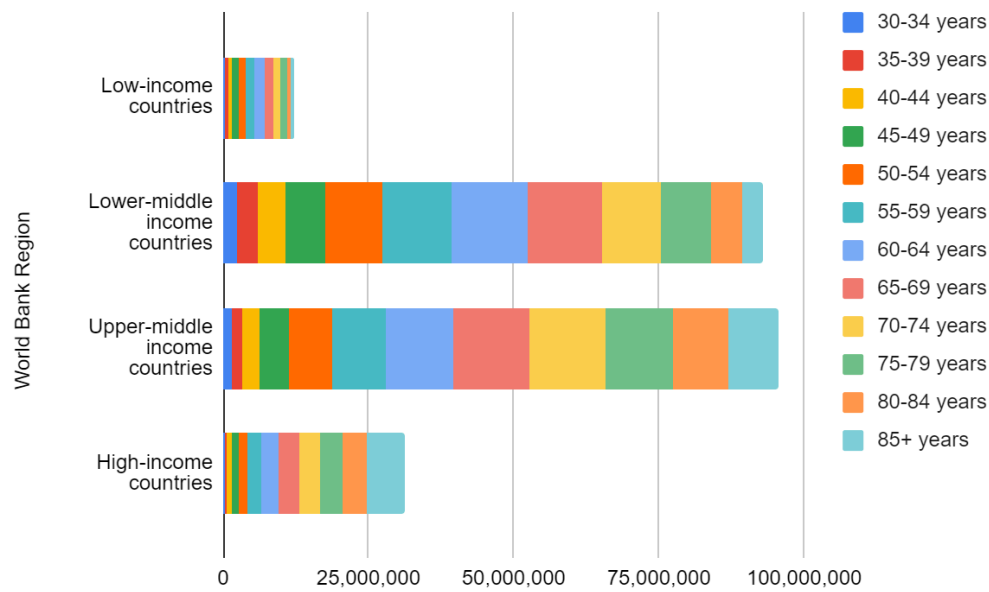
Almost half of the death burden in HICs is carried by individuals aged 85+ whereas in LMICs, the death burden is somewhat more evenly spread across older age groups, i.e. 45 years or older. Similarly, the DALY burden is also distributed relatively evenly across individuals aged 45+, with the difference that very old individuals (aged 85+) carry a relatively small share of the burden, at least in LMICs. Overall, **the lower the income level of a region, the more the death and DALY burden are concentrated among relatively younger individuals.**

Figure C1. Numbers of deaths due to high systolic blood pressure across World Bank regions and age groups



Note. Data from [GBD Results Tool \(2019\)](#).

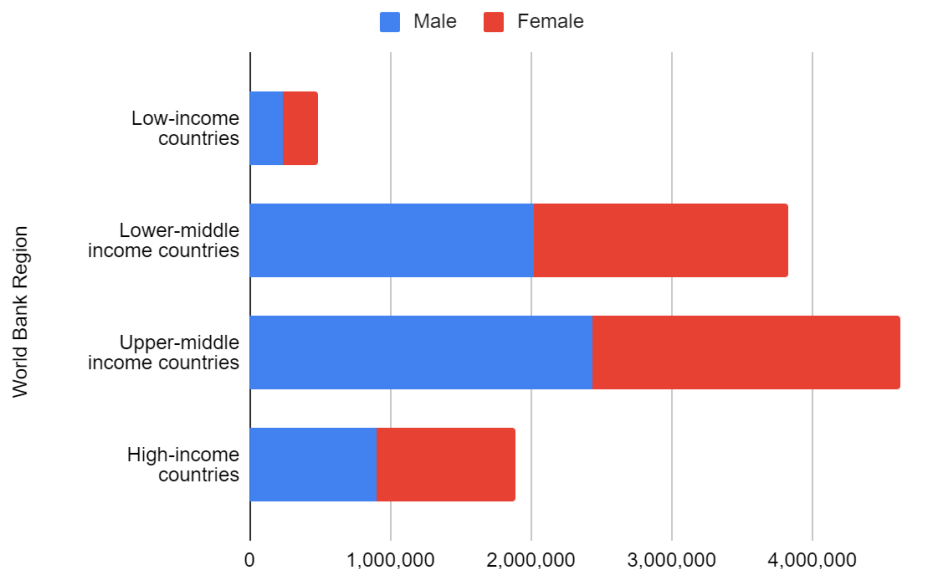
Figure C2. Numbers of DALYs lost due to high systolic blood pressure across World Bank regions and age groups



Note. Data from [GBD Results Tool \(2019\)](#).

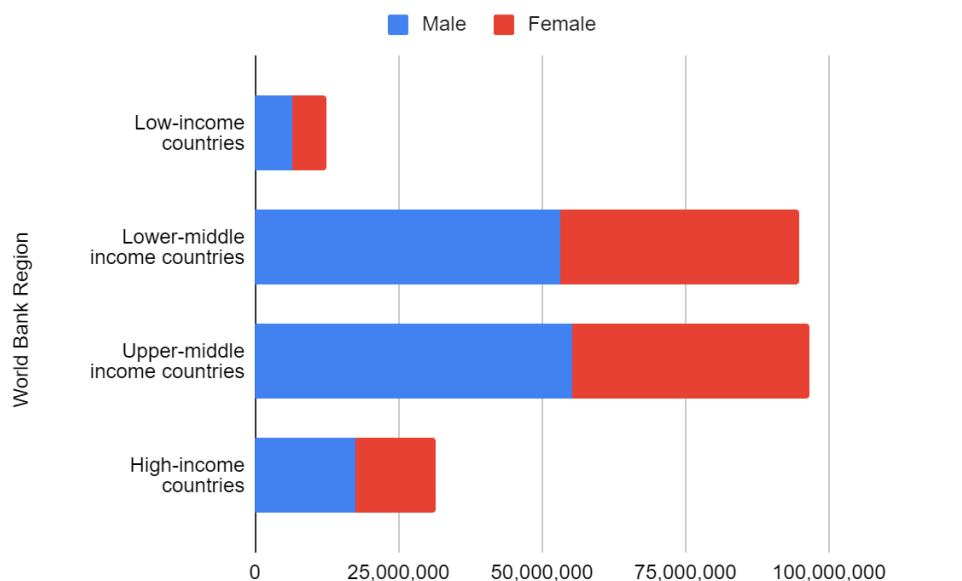
In Figure C3 below we show the number of deaths due to high SBP, disaggregated by World Bank region and sex. As can be seen, **deaths are relatively evenly spread across men and women in all four regions**. Similarly, Figure C4 below shows the same figure using DALYs instead of deaths. **DALYs are also fairly evenly distributed across men and women, with a somewhat higher concentration of DALYs lost among men in all four World Bank regions.**

Figure C3. Numbers of deaths due to high systolic blood pressure across World Bank regions and sex



Note. Data from [GBD Results Tool \(2019\)](#).

Figure C4. Numbers of DALYs lost due to high systolic blood pressure across World Bank regions and sex



Note. Data from [GBD Results Tool \(2019\)](#).

Appendix D. India Hypertension Control Initiative (IHCI) key intervention strategies

The IHCI names 9 key intervention strategies ([IHCI, 2021](#), p. 14):

1. “Use of state-specific simple, standard drug and dose-specific algorithms for hypertension management.
2. Uninterrupted supply and availability of drugs as per protocol in all health facilities
3. Training of staff at all levels in the management of hypertension as appropriate to enhance the health system’s capacity.
4. Provision of high-quality services using patient- centric approaches such as blood pressure monitoring using validated digital BP monitors, minimum 30-day drug prescriptions, patient counseling, access to free drugs, and documentation of visits (Simple App and treatment card).
5. Opportunistic screening: Setting up NCD corners at health facilities to promote opportunistic screening and streamline patient flow.
6. Team-based care for hypertension management by strategic redistribution of tasks among various healthcare staff within the public health clinics to enhance patient care efficiencies.
7. Decentralization of patient care by using Health and Wellness Centres and Sub-centres for follow-up visits, patient education and prescription refills.
8. Monitoring systems (Simple App and paper-based) with standard indicators and documentation mechanisms that facilitate data collection and records maintenance.
9. Dedicated workforce (CVHOs & STSs) for supportive supervision and monitoring to accelerate IHCI implementation, strengthen program quality and enable rapid feedback to the stakeholders”

Below we share our analysis of the achievements of the program, based on the progress reports.

The annual progress report over 2021 states that overall 6.1% of the expected number of hypertensive patients in these districts had their blood pressure under control in Jan-March 2021, compared to 4.9% in 2020 and 1.4% in 2019 ([IHCI, 2021](#), p. 38).⁶¹ This is an increase of almost 219,000 patients who had their blood pressure controlled over two years.

We are cautious about putting too much weight on these numbers. It is unclear to us how they are calculated and they differ from the numbers that other sources report, like those in the [section above](#). Also, these are not causal estimates, and we don't know how much of this figure can be attributed to the IHCI program.

The report also mentions that drug availability has increased in all five states in which the program was initially rolled out, with most states having a stock of at least 60 days of three different types of drugs.⁶² The base rates of availability are not shown, so the improvement here is not quantified. The procurement of the three drugs increased between 2017 and 2019. The report also mentions that procurement of drugs was a challenge in most states in the second scale-up of the program ([IHCI progress report, 2021](#), p. 20 & p. 41).

The progress brief ([IHCI, 2022](#)) also mentions some other challenges. One is the treatment outcomes, with 23% of patients in care not having their blood pressure under control and 27% of them not returning for follow-up in the first quarter of 2021.⁶³

Secondly, lack of digital high quality validated blood pressure monitors in some healthcare facilities is a challenge (not quantified). Lack of dedicated nurses for NCD work in most healthcare facilities is also mentioned. Finally, the COVID pandemic formed an obstacle in the program, slowing the enrollment in 2020.

Based on the results in April 2021, the World Heart Federation judged that the IHCI should not be scaled up before overcoming existing obstacles: “the lack of detailed data on programme coverage especially in vulnerable groups, the need to improve treatment follow-up and hypertension control rates, and the need to improve medication supply chain and inventory management are crucial obstacles to overcome before recommending scale up of similar strategies in other LMICs” ([WHF, 2021](#), p. 22).

Appendix E. National Multisectoral Action Plan for Prevention and Control of Common Noncommunicable Diseases

Below we give a short description of the goals of each strategy in the National Multisectoral Action Plan for Prevention and Control of Common Noncommunicable Diseases ([MoHFW, 2017](#)). We also provide some examples of actions linked to it.

- **Integrated and Multisectoral Coordination Mechanisms.** Goals: “increase advocacy, create mechanisms for promoting multisectoral partnerships and strengthen capacity for effective leadership” (p. 6).

⁶¹ Having blood pressure under control is defined as having a measurement of systolic blood pressure below 140 mm Hg and diastolic below 90 mm Hg during the most recent visit in the period of time.

⁶² These drugs are: Amlodipine, Telmisartan, and Chlorthalidone/H-Thiazide.

⁶³ The monitoring results from the first quarter of 2021 show that about 74% of the registered patients were under care for the year preceding it (meaning they had at least one visit in the last twelve months). Of the patients under care, nearly 47% had their blood pressure under control during the most recent visit, this is about 35% of registered patients ([IHCI progress brief, 2022](#)).

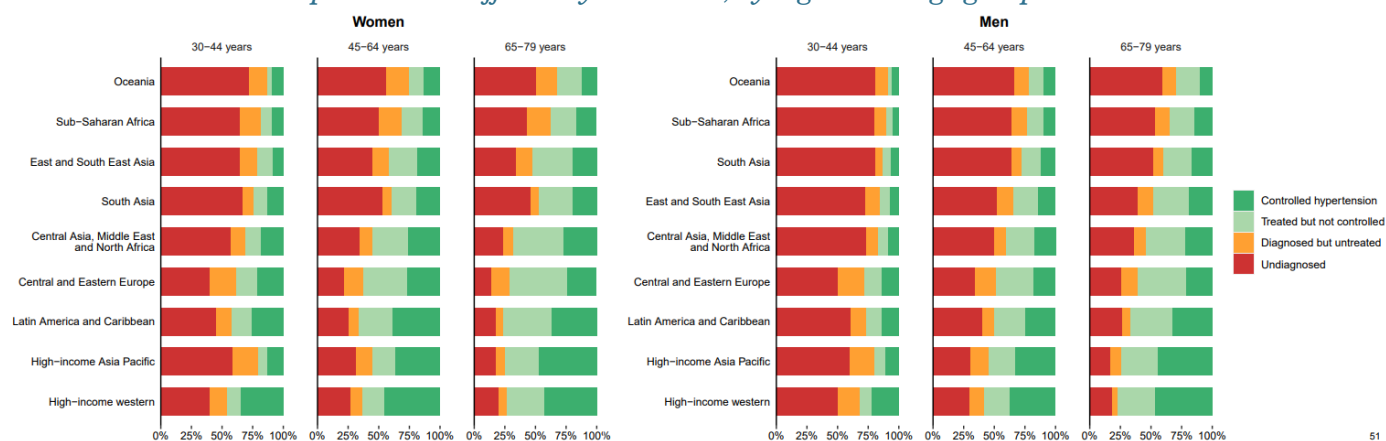
- **Health promotion.** Goals: “reduction of risk factor levels in children, adolescents and adults. The risk factors include behavioral risk factors such as tobacco use, alcohol use, unhealthy diet, physical inactivity, environmental pollution including household air pollution and other social determinants.” (p. 6)
- **Health Systems Strengthening.** Goals: “strengthen the health system, particularly the primary health care system, including the health workforce for moving towards universal health coverage.” (p. 7)
- **Surveillance, Monitoring, Evaluation and Research.** Goals: “[...] information on time trends of key indicators identified as a part of the National Monitoring Framework for prevention and control of NCDs are regularly made available.” (p. 8)

Below we give some examples of the most concrete actions. For a complete overview of the actions, we refer to pages 29 to 31 in the action plan ([MoHFW, 2017](#)).

- “Under GST, raise taxes on all types of tobacco products, Sugar Sweetened Beverages, HFSS [High in Fats, Salt and Sugar] food and alcoholic beverages to reduce Consumptions”
- “Include essential NCD medicine in National List of Essential Medicine for each level for health care”
- “Develop/ Revise Standard Management Guidelines (SMGs) for major NCDs for different levels of health care”
- “Setting up of training mechanism including creating a pool of institutions/trainers in public and private sector and conduct training of existing workforce”
- “Set-up a National Steering Committee for Monitoring, Surveillance and Evaluation for activities outlined in NMAP”

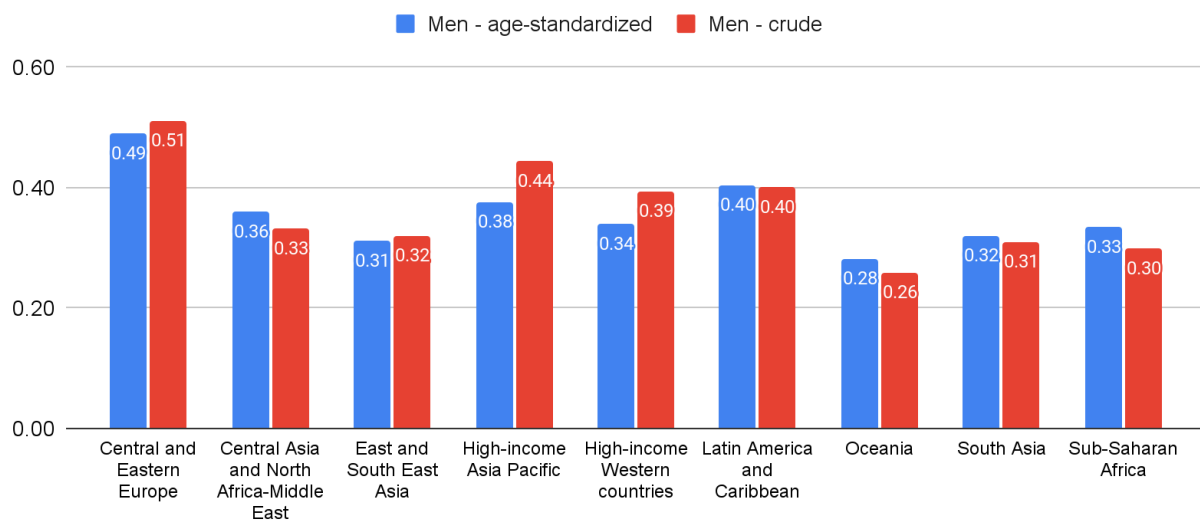
Appendix F. Additional figures on hypertension prevalence, diagnosis, treatment, and control

Figure F1. Proportion of people with hypertension who reported a diagnosis, who used treatment, and whose blood pressure was effectively controlled, by region and age group in 2019



Note. From NCD-RisC ([2021, supplementary appendix, p. 51](#)).

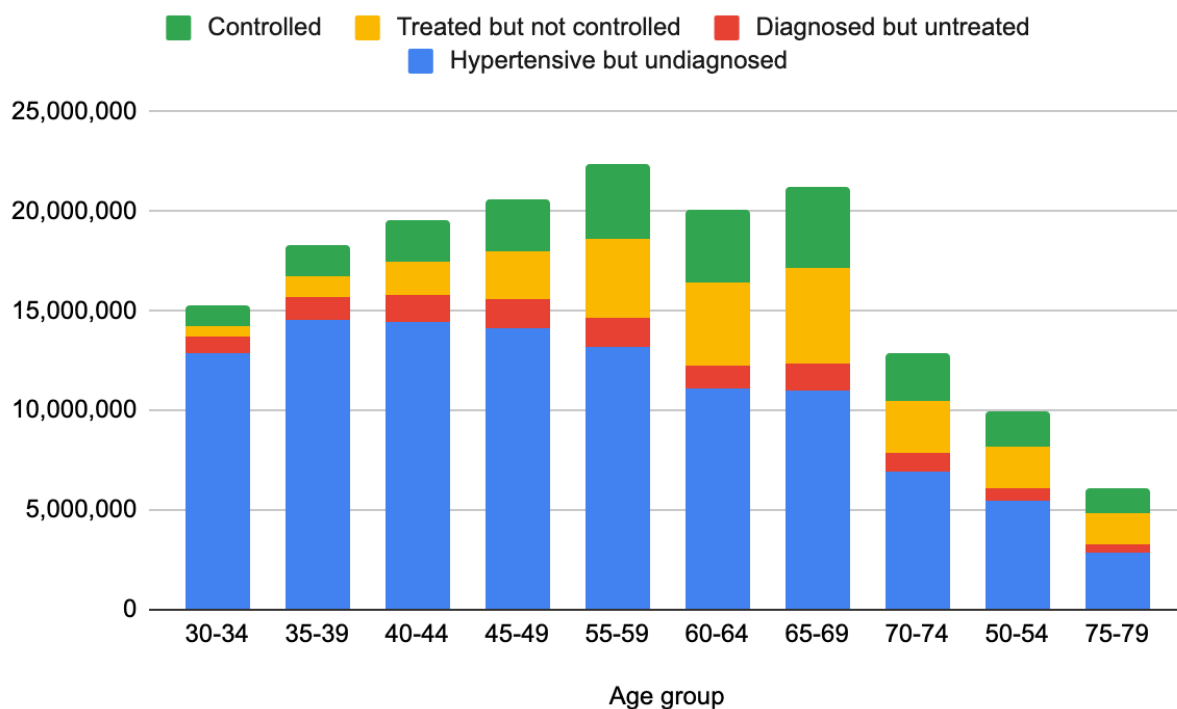
Figure F2. Prevalence of hypertension as a percentage of male age-standardized and crude population aged 30-79 years across regions



Note. Data from NCD-RisC (2021); [link to sheet](#).

Appendix G. Hypertension care cascade by age group in India

Figure G1. Hypertension care cascade by age group in India



Note. Data from [NCD-RisC \(2021\)](#) and [UNSD \(2011, p. 234\)](#) combined in [own calculations](#). This is based on population figures of 2011, multiplied by 1.13 to extrapolate to 2019 population size, combined with the rate of treated, diagnosed and controlled in 2019.

Appendix H. Assessment of non-price factors that could limit use of single-pill combinations

In the main body of the report we investigate the extent to which price is a limiting factor for the use of SPCs, and to what extent this can be addressed. In addition, in our research we also assessed the possible role of five additional factors, as shown below in order of relative impact.

1. Price (see [here](#))

2. National registration

In many countries, medicines may not be bought and sold unless they have been registered by the relevant national authority. The RTSL & MSF Access Campaign ([2022](#), p. 22) highlights that **manufacturers do not register as many of their formulations in LMICs as they do in HICs**. The report attributes this to a lack of perceived demand in LMICs, particularly due to a 'lack of dedicated programs to promote antihypertensive treatments' ([RTSL & MSF Access Campaign, 2022](#), p. 15). We interpret this as a comparison to the role that the Global Fund plays for malaria, TB and HIV/AIDs.

3. Treatment guidelines

Bruyn et al. ([2022](#), p. 11) review national treatment guidelines in 23 LMICs, and find that only five recommend SPCs for initial treatment (as in the 2021 WHO guidelines). In a further 13 countries, guidelines recommend SPCs only for the treatment of higher risk patients or uncontrolled cases of hypertension. This **limits the proportion of diagnosed patients that receive SPCs**.

4. National EMLs

Inclusion of SPCs on national EMLs could be a necessary precursor to widespread use. Bruyn et al. ([2022](#), p. 10) find that **only 12 of 29 EMLs reviewed include any form of SPC**. Sahoo et al. ([2022](#), p. 4) highlights that lack of inclusion on the EML is limiting public sector use in India. Lack of inclusion on the EML may also be reducing SPC use in Nigeria ([RTSL & MSF Access Campaign, 2022](#), p. 19).

However, our impression is that this problem is **less pressing than those listed above** as many of the EMLs are from before SPCs were added to the WHO EML (in 2019). As many national EMLs are modeled on the WHO EML, it may be that SPCs are naturally included in the next update.

5. Physician attitudes

Our experts presented two points of view on this topic:

- JD Schwalm suggested this would be one of the main barriers to introducing SPCs: if physicians are uncomfortable with the new formulations or want to retain the ability to titrate medication for the patient, then they will continue to prescribe SAPs.
- Tom Frieden and Andrew Moran suggested that this would be most true of cardiologists who have developed strong opinions about treatment protocols. Given the shortage of specialists in LMICs, and the high prevalence of

hypertension, it is more likely that physician and non-physician health workers who staff primary care facilities will be treating hypertensive patients following national guidelines.

Given the countries where OP is most likely to implement, we find the latter view more convincing, and **tentatively conclude that if national guidelines change to recommend SPCs, most physicians will follow.**

6. Manufacturing capacity

Tom Frieden and Andrew Moran confirmed that they have no concerns about manufacturing capacity for SPCs. This could **easily be scaled up**. With technical assistance and/or technology transfer, LMIC manufacturers have the capacity to manufacture SPCs.

Appendix I. More detailed list of hypertension-related research gaps in LMICs

- **Implementation trials to improve screening and blood pressure control in LMICs:** Major research gaps exist in understanding how to implement evidence-based prevention, screening and treatment strategies in LMICs in practice, especially in poor, rural, and remote areas. Implementation trials could help determine how to effectively roll out interventions in LMIC settings (see the Kathmandu Declaration for more detail on gaps in implementation research [[Aifah et al., 2019](#)]). Recent studies showed promising, but still under-researched approaches. For example:
 - Task sharing with non-physician health workers have been shown to improve hypertension detection and control and could be useful in resource-poor health systems. However, further research is needed to understand the implications for health systems (e.g. [Anand et al., 2019](#), p. e769).
 - Risk factors tend to cluster at the household level. Thus, more research could focus on exploring family- or community-based interventions to implement blood pressure reduction strategies ([Schutte et al., 2021](#), p. 821).
 - Little is known about the effectiveness of different screening strategies (e.g. mass, targeted, and opportunistic screening) ([Schutte et al., 2021](#), p. 821).
 - While lifestyle-related interventions (e.g. promoting healthy diets, increasing physical activity) are effective at reducing blood pressure (e.g. [Dickinson et al., 2006](#)), it is unclear how to effectively scale them (Tom Frieden from Resolve to Save Lives) (see Campbell et al., [[2022](#)] for a list of proposed public health dietary sodium research priorities).
- **Clinical trials to identify optimal treatment combinations in LMIC populations:** Most patients with hypertension require at least two hypertensive agents for blood pressure control ([Ojji et al., 2019](#), p. 2430), but optimal treatment combinations have not been identified for some populations in LMICs (e.g., black, South Asian, or East Asian patients). Clinical trials could focus on the effectiveness, cost-effectiveness, and safety of treatment combinations in under-researched populations to provide clear recommendations for each major ethnic group ([Jeemon et al., 2021](#), p. 6). Another example of emerging and still underexplored clinical trial research are novel treatment regimens for [resistant hypertension](#) (i.e., blood pressure that remains uncontrolled with three medications) ([Jeemon et al., 2021](#), p. 8).
- **Determining the cost-effectiveness of interventions to reduce blood pressure:**

As we explain in more detail [here](#), little is known about the cost-effectiveness of hypertension interventions in LMICs. More cost-effectiveness analyses (e.g., of policy-level interventions aimed at prevention) could help compare different interventions to reduce blood pressure in LMICs ([Schutte et al., 2021](#), p. 821).

- **Emerging risk factors and their importance for hypertension in LMICs:** Recent research has shown that various environmental factors affect blood pressure, such as air and noise pollution, fine particulate matter, a low temperature, and a low greenness ([Jeemon et al., 2021](#), p. 8). More research could help determine the importance of these emerging risk factors, particularly in LMICs where air pollution is high and increasing ([Bartington and Avis, 2020](#)).
- **Improve blood pressure monitoring devices suited for LMICs:** Accurate blood pressure monitoring devices are a key element of hypertension control. However, according to an expert, there is a lack of trustworthy devices in LMICs. Most current measuring devices have not been validated for their accuracy and many devices currently on the market are inaccurate ([Jeemon et al., 2021](#), p. 20). According to this expert, validated devices tend to be expensive and may thus not be affordable in low-resource settings. Thus, more research could be used to develop accurate, yet affordable devices, specifically for use in low-resource settings (see also Brady et al. [2020] for a discussion of selecting blood pressure measurement devices in low-resource settings).
- **Evaluation of novel treatment approaches:** Recent research has identified new treatment approaches for hypertension, such as “renal denervation, baroreflex activation therapy, and carotid body ablation” ([Schutte et al., 2022](#), p. 822). More research could investigate the effectiveness of these emerging treatment options and their appropriateness for LMICs.

Appendix J. More detail on estimates of the costs of hypertension in LMICs

We attempted to breakdown economic burden into three cost categories (based on [Krol et al. 2013](#)):

- **Direct medical costs** are costs in the health system (e.g. for diagnosis, drugs, medical staff salaries, and equipment).
- **Direct non-medical costs** are costs outside the health system accruing with patients and their families while receiving health care (e.g. for travel and time-costs of providing informal care).
- **Indirect costs** are costs outside the health care system, including productivity loss.⁶⁴

We then attempted to find estimates of each cost category for both hypertension itself and the proportion of cardiovascular diseases attributable to hypertension.⁶⁵

National estimates appear to be more transparently calculated than global estimates.

⁶⁴ Productivity loss includes loss to the labor force (the shortfall in employment among people with hypertension compared to those without hypertension either because of morbidity and disease-related premature mortality), work days lost to ill health (absenteeism) and reduced efficiency at work (presenteeism) ([Krol et al., 2013](#)).

⁶⁵ The international society of hypertension calculated that about 54% of stroke and 49% of heart disease are attributable to hypertension ([Lawes et al., 2008](#)), other estimates vary slightly but it appears to be generally accepted that about half of heart disease and stroke are attributable to hypertension ([Fuchs & Whelton, 2019](#)). We therefore assume 50% of the costs of heart disease and stroke can be attributed to hypertension.

According to the American Heart Association (see Table J1 below), in the US in 2017 hypertension costs were estimated at 51.1 billion USD, with 45.5 billion USD in direct costs and 5.6 billion in indirect costs (Tsao et al., 2022).⁶⁶ We calculated that the proportion of heart disease and stroke costs attributable to hypertension⁶⁷ were an additional 140.8 billion USD, 71.1 billion in direct costs and 69.7 billion in indirect costs, and therefore that the total hypertension and hypertension-attributable CVD costs in the US were 161.9 billion USD in 2017 (Tsao et al., 2022). This also shows that diseases attributable to hypertension are nearly 3x more costly than hypertension itself.

Table J1. Estimated direct and indirect costs (in billions of USD) of cardiovascular disease, United States, average annual, 2017 to 2018

	HD*	Stroke	Hypertensive disease†	Other circulatory conditions‡	Total CVD
Direct costs§					
Hospital inpatient stays	54.2	19.7	6.4	19.3	99.6
Hospital ED visits	4.6	1.4	1.4	1.9	9.3
Hospital outpatient or office-based health care professional visits	25.6	3.7	14.1	11.9	55.3
Home health care	10.5	7.4	6.2	2.6	26.7
Prescribed medicines	13.9	1.2	17.4	2.8	35.3
Total expenditures	108.8	33.4	45.5	38.5	226.2
Indirect costs¶					
Lost productivity/mortality	119.9	19.4	5.6	6.9	151.8
Grand totals	228.7	52.8	51.1	45.4	378.0
Numbers do not add to total because of rounding.					
CVD indicates cardiovascular disease; ED, emergency department; and HD, heart disease.					
*This category includes coronary HD, heart failure, part of hypertensive disease, cardiac dysrhythmias, rheumatic HD, cardiomyopathy, pulmonary HD, and other or ill-defined HDs.					
†Costs attributable to hypertensive disease are limited to hypertension without HD.					
‡Other circulatory conditions include arteries, veins, and lymphatics.					

Note. From Tsao et al. (2022).

Hird et al. (2019) took a different approach, estimating that based on productivity losses alone (not taking direct costs into account) \$90.7 billion (converted at today's exchange rate from AUD

⁶⁶ Indirect costs were calculated based on lost future productivity attributed to premature CVD mortality and did not incorporate morbidity-related productivity costs (absenteeism, presenteeism, loss to labor force). The authors cited a lack of contemporary data and acknowledged that this is likely to lead to an underestimate of the total costs (Tsao et al., 2022).

⁶⁷ Calculated with the addition of 50% of the HD and Stroke columns in Table J1. This doesn't take into account other major hypertension sequelae, for example chronic kidney disease, so is likely to be an underestimate.

to USD) would be lost to gross domestic product over the working lifetime of the current Australian population. They further modeled that a 25% reduction in hypertension prevalence, in line with the World Health Organisation Global Action Plan [targets](#) and the adequate treatment and control of all of those with hypertension would lead to \$22.7 billion and \$50.6 billion in gross domestic product retained over the working lifetime of the cohort, respectively. The latter is based on reduced mortality and morbidity-based loss to workforce, and reduced productivity losses due to those with controlled hypertension being more productive than those with uncontrolled hypertension.

Estimates of economic burden from high-income countries are unlikely to be generalizable to LMICs with both direct and indirect costs likely to vary by population depending on a range of factors including demography, risk factor epidemiology, health service provision and labor force characteristics.

We reviewed two recent systematic reviews on the economic burden of hypertension from different countries, including LMICs:

- Wierzejska et al. (2020) reviewed the costs of hypertension incorporating data from 15 countries. They estimated an average total annual hypertension cost of \$81.1 billion per country equating to an average of \$630 per hypertensive person per year. However, the majority of the studies included in the review came from HIC or upper-middle income countries so we find it plausible that this average is higher than a true average. Direct costs per hypertensive person per year were lowest in Indonesia at \$30 and highest in the USA at \$6,250 whilst indirect costs per hypertensive person per year were lowest in Indonesia at \$50 and highest in Jamaica at \$515. However, the methods of the studies included in this review were highly variable, were not always comparing like for like hypertension care and the categorisation of costs was not consistent.
- Gheorghe et al. (2018) focused on the economic burden of CVD in LMICs, incorporating data from 28 LMICs. They included a sub-analysis calculating the ratio of the total annual cost of hypertension care to total health expenditure per capita and found that the annual direct cost per patient of hypertension could be as high as 5.9 times the total health expenditure per capita, with a median ratio of 0.7. However, the study acknowledges that the quality of the studies included was generally low and rarely incorporated indirect costs.

A simple multiplication of the \$630 average cost per hypertensive person, from Wierzejska et al. (2020), by the global estimate of 1.27 billion people with hypertension in 2019 (discussed [here](#)) gives an estimate of \$800 billion annual global economic burden from hypertension. This is higher than estimates referred to by advocacy organizations that “the global direct medical costs of hypertension are estimated at \$370 billion per year” (Frieden and Jaffe, 2018). However, this lower estimate did not incorporate indirect costs and was based on an older model for the 2001 global population, when the number of people with hypertension would have been considerably lower (Gaziano et al., 2007, Gaziano et al. 2009). **Our tentative best guess is that the global economic burden from hypertension is between \$400 billion-\$800 billion per year.**

However, none of the above estimates for LMICs take into account the economic burden of costs from CVD attributable to hypertension. In the US estimates, [above](#), these were 3x as costly as hypertension itself. If we assume that this also applies in LMICs (we have very low

confidence in this assumption⁶⁸) then the global economic burden from hypertension and hypertension-attributable CVD could plausibly be in the region of \$1.6 trillion-\$3.2 trillion per year.

Overall, we are not confident that the estimates from either systematic review ([Wierzejska et al., 2020](#); [Gheorghe et al., 2018](#)) nor the figures provided by advocacy organizations can be relied on for LMICs. However, we do think it is likely that hypertension exerts considerable economic burden in LMICs and that our estimates might be suggestive of the order of magnitude of this burden.

Appendix K. More detailed discussion of how much of hypertension is preventable

Although we have seen many sources stating that “a large percentage of hypertension is preventable” (e.g. [Premanandh et al., 2014](#), p. 27), we have not been able to find any concrete quantification of this. To our knowledge, such estimates only exist only for conditions ‘downstream’ of hypertension, e.g. “80% of premature heart attacks and strokes are preventable” according to the WHO ([2015](#)).

Aging is known to be a major predictor of high blood pressure. According to [Gurven et al. \(2012, p. 25\)](#), “among Westerners over age 40 years, systolic BP (SBP) increases by ~7 mmHg per decade.” However, it is less clear how much of this steep increase of blood pressure with age is due to age itself vs. due to preventable lifestyle risk factors or comorbidities increasing along with age—it is likely a combination of both. However, these effects are difficult to disentangle, as Western lifestyles are very prevalent.

One way of disentangling the effects of modifiable vs. non-modifiable risk factors on hypertension is to study adults from isolated societies who are not exposed to Western lifestyles. For example, [Gurven et al. \(2012, p. 25\)](#) investigated age-related increases in blood pressure among Tsimane forager-farmers and [Mueller et al. \(2018\)](#) did the same for Yanomami hunter-gatherers. We assume that the age-related rise in blood pressure for those societies is purely due to age itself. [Gurven et al. \(2012\)](#) found that SBP among Tsimane increases by only 1.8 mm Hg per decade⁶⁹ and [Mueller et al. \(2018\)](#) found virtually no increase in blood pressure with age. This suggests that in Western societies exposed to lifestyle risk factors, blood pressure increases at least ~3.9 times more with age than for those unexposed to Western lifestyles.

Thus, if SBP increases by ~7 mm Hg per decade of life for Westerners over 40, and only 1.8 mm Hg of this increase (i.e. ~25%) is due to aging, the remaining ~75% of increase in SBP are due to modifiable lifestyle risk factors. We use these results as a very rough approximation of how much hypertension is preventable. However, we are aware that this comparison is far from perfect as it is only based on differences in the rate of increase in blood pressure. Thus, it inevitably excludes time-constant risk factors (e.g., family history of hypertension or lifestyle risk factors which remain constant over time).

Another way to get a rough sense of the extent to which modifiable risk factors matter for hypertension prevalence is by comparing hypertension prevalence across different countries

⁶⁸ We have low confidence in this assumption because differences in direct costs, indirect costs, and competing hazards in LMICs compared to the US are likely to affect this.

⁶⁹ More precisely, 2.86 for women and 0.91 for men ([Gurven et al., 2012](#), p. 25). We took the simple average.

within the same age group, e.g. 40-44 year olds. This allows us to factor out any variation in age and only consider differences in hypertension prevalence due to modifiable risk factors.⁷⁰ Hypertension prevalence among 40-44 year old men ranges from 12%-55% across countries and from 7%-42% among women. Thus, **if countries with the highest lifestyle risk factors reduced their risk factor exposure to the same level as countries with the lowest lifestyle risk factors, their hypertension prevalence would drop by 35-43 percentage points, at least for 40-44 year olds.** Unfortunately, this comparison doesn't allow for a quantification of how much lifestyle risk factors matter relative to age and other non-modifiable factors, and we have only considered one age group.

⁷⁰ This is not quite correct, as there might also be differences in some non-modifiable risk factors across countries, such as differences in family history or ethnicity. For the sake of this quick analysis, we ignore those factors.