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Hypertension in the South African Public Healthcare System: Health and Economic Burden of Disease

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Abstract

Objectives

Hypertension is a leading cause of morbidity and mortality in South Africa. It exerts a significant burden on the public healthcare system and reduces workforce productivity. This study aimed to quantify the health and economic burden of hypertension in the South African public healthcare system.

Design

A worksheet-based model synthesized data from multiple sources to estimate the burden of disease, direct healthcare costs, and societal costs associated with hypertension in South African adults (aged ≥20 years) from the perspective of the public healthcare system. Population demographic and health data were derived from the National Income Dynamics Study 2017. Costs were derived from public healthcare fee schedules. The incidence, prevalence, and disability-adjusted life years associated with hypertension-related complications were taken from the Global Burden of Disease Study 2019. Population-attributable fractions were estimated for these complications. Societal costs were calculated using a human capital approach with disability-adjusted life year indexing.

Results

Approximately 8.4 million (30.8%, 95% confidence interval [CI]: 29.3-32.5%) South African adults with no private health insurance have hypertension. Hypertension was estimated to cause 14,100 (95% CI: 10,900-17,300) ischemic heart disease events, 13,600 (95% CI: 10,900-16,300) strokes, and 6,140 (95% CI: 5,020-7,450) cases of chronic kidney disease annually. The direct costs associated with hypertension were estimated to be ZAR 10,834 million (USD 764 million) and societal costs were estimated to be ZAR 23,175 million (USD 1,634 million).

Conclusion

Hypertension exerts a heavy health and economic burden on South Africa. Establishing cost-effective best practice guidelines for treating hypertension requires further research.

Strengths and limitations of this study

- No previous studies have estimated the economic burden of hypertension in South Africa.
- A bottom-up costing approach was used to estimate direct medical costs.
- A human capital approach with disability-adjusted life year indexing was used to estimate societal costs.
- Despite data limitations, model inputs regarding the prevalence of hypertension, healthcare utilization, and the price of healthcare resources were all derived from South African data.
- Our estimate of societal costs may underestimate activity in the informal labour market and informal work (e.g., housekeeping, caretaking).

Hypertension in South Africa: Health and Economic Burden of Disease

Background

High blood pressure (BP) is a highly prevalent condition in South Africa.[1–3] While the proportion of the population with uncontrolled hypertension has fallen in recent years,[3] rates of diagnosis, treatment, and control remain poor.[2] These rates are worse for low-income individuals, those with fewer years of education, and those who receive care in the public healthcare system.[1,4] Funding preventive interventions, public screening, and treatment campaigns may improve population health and reduce health disparities.

Around 85% of the South African population has no private health insurance,[5] yet private healthcare accounts for more than half of the country's health-related expenditure.[6] The government is in the process of creating a National Health Insurance (NHI) programme to address inequalities in access to comprehensive healthcare.[7] The NHI programme will produce a centralized financing source for public healthcare which aims to improve the quality of public healthcare and increase its allotted budget.

There are considerable knowledge gaps related to the health and economic cost of hypertension and cardiovascular disease (CVD) in low- and middle-income countries.[8] No previous studies have considered the economic burden of hypertension in South Africa. Calculating the cost of hypertension and the prevalence of its complications will help decision-makers target public healthcare resources more efficiently, improving the sustainability of the NHI programme.

The first objective of this study was to estimate the incidence and prevalence of hypertension and hypertension-related complications amongst individuals who receive care in the South African public healthcare system. The second objective was to calculate the annual healthcare and societal costs associated with hypertension in these individuals.

Methods

Study Parameters

We adopted a public healthcare sector perspective. The population of interest was individuals aged ≥20 years receiving healthcare in the public healthcare system. We estimated prevalence of hypertension, number of hypertension-related complications, and costs associated with hypertension in this population. Costs were disaggregated into two categories: direct healthcare and societal costs. A time horizon of one year was adopted. No discount rate was applied.

Approach

A worksheet-based costing model was developed in Microsoft Excel to synthesize data from multiple sources. After communication with the National Department of Health, non-governmental research institutions, and examination of the open data portal for health services research,[9] it was established that there is no national data which details public healthcare expenditure disaggregated by disease type. It was determined that a bottom-up costing approach with secondary data sources was necessary. Analysis was disaggregated into three age-groups: young adults (aged 20-39 years), middle adults (aged 40-69 years), and older adults (aged ≥70 years).

Population Size and Public Healthcare Utilization

Population size was informed by Statistics South Africa (SSA) mid-year estimates.[10] Care-seeking behaviour was informed by recent national surveys. The proportion of screening and other outpatient care that occurs in the public healthcare system (70.7%) was derived from the Demographic and Health Survey 2016.[11] The proportion of acute care that occurs in the public healthcare system (71.5%) and the proportion of the population who have no private health insurance (83.6%) were derived from the General Household Survey 2018.[5] In both cases, the 'public healthcare system' referred to healthcare provided in government hospitals, government clinics, community health centres, and other public sector facilities.

Hypertension Rates

Hypertension prevalence, diagnosis, treatment, and control were estimated in the National Income Dynamics Survey (NIDS) 2017, a largescale national survey of population health. Analysis was conducted in the subset of respondents without private health insurance. All NIDS 2017 analysis was completed in the *R* programming language (Version 4.0.4, R Core Team). Participants were asked about hypertension diagnosis, medications, and CVD risk factors.[12,13] In addition, respondents had systolic blood pressure (SBP) and diastolic blood pressure (DBP) measured twice. We used the average of these values in our analysis. Individuals without SBP readings were omitted from the analysis. Cross-sectional sample weights were used to ensure that results were representative of the contemporary South African population.[14] Further information on NIDS 2017 and the way participants' blood pressure was recorded is contained in the **supplementary material**.

Hypertension was split into five categories, in accordance with the National Department of Health's Adult Primary Care (APC) Guidelines 2019-20.[15] These were: normotension (SBP <140 mm Hg and DBP <90 mm Hg), Grade 1a (SBP 140-159 mm Hg or DBP 90-99, with no other cardiovascular risk factors), Grade 1b (SBP 140-159 mm Hg or DBP 90-99, with another cardiovascular risk factor), Grade 2 (SBP 160-179 mm Hg or DBP 100-109 mm Hg), and Grade 3 – or 'severe' hypertension (SBP ≥180 or DBP ≥110 mm Hg). Individuals who met two criteria (e.g., SBP 150 mm Hg and DBP 105 mm Hg) were included in the more severe hypertension category. 'Other cardiovascular risk factors' considered in the APC guidelines were smoking,

diabetes, age ≥55 years for men, age ≥65 years for women, waist circumference ≥94 cm for men, and waist circumference ≥80 cm for women.

Prevalence of SBP categories was estimated in two subsets of the population: all individuals and individuals not currently receiving antihypertensive medication. Overall prevalence was calculated as the sum of hypertensive individuals not currently receiving antihypertensive medication plus the number receiving antihypertensive medication. Confidence intervals were derived for hypertension prevalence, diagnosis, treatment, and control rates using incomplete beta functions with sample size based on the estimated variance of the proportion.[16]

Screening Costs

Costing for facility use and healthcare worker time came from the Uniform Patient Fee Schedule (UPFS) 2020.[17] The UPFS is a set of tariffs for public health services, including both health practitioner and facility fees. The tariffs are updated annually and apply to all patients using public services.[18] There are three types of facility in the public healthcare system, which generally increase in price: district, regional, and tertiary.

There is limited guidance regarding screening in the APC 2019-20 or the South African Hypertension Society (SAHS) practice guidelines.[19] It was assumed that all screening would be undertaken by a nurse practitioner in a district-level health facility. The cost of a screening visit was estimated to be ZAR 144 (USD 10) (**Table 1, Supplementary Table 1**).

Management Costs

To estimate the cost of hypertension management, recommended resource use in the APC 2019-20 guideline was itemized. Resource use included medication, testing, and check-up visit costs (**Table 1, Supplementary Table 1**). The proportion of the population that reported antihypertensive medication use in NIDS 2017 received ongoing treatment. We assumed a proportion of the population with untreated hypertension would commence treatment over the course of a year. Specifically, we assumed that new treatment would commence according to the overall treatment rate of individuals with hypertension in the wider population.

The treatment steps contained in the APC guidelines are described in the **Supplementary Material**. Initial treatment intensity depended on untreated BP and treatment intensified with failure to control BP on lower treatment steps. A decision tree was constructed to predict the number of patients receiving each treatment step (**Supplementary Figure 1**). The tree predicted the number of steps required to control hypertension in different subgroups of patients. Probability of successful BP control during treatment was estimated in NIDS 2017.

Unit costs for antihypertensive medications were derived from National Treasury contracts.[20] Outpatient visit costs came from the UPFS 2020. It was assumed that all check-ups would be

administered by physicians in district-level facilities. The overall cost for a check-up visit was ZAR 229 (USD 16).

Hypertensive Crises

Most patients with severe hypertension are asymptomatic.[19,21] Some will experience hypertensive crises and require acute medical care. Hypertensive crises can be classified as urgencies or emergencies. The latter are more severe and involve ongoing organ damage. Published studies were used to estimate the proportion of patients with severe hypertension that experience a hypertensive crisis (5.5%) and the proportion of crises that are emergencies (32%).[22–24] Optimal treatment for hypertensive crises are outlined in the SAHS 2014 guidelines.[19] These guidelines were itemized and costed (**Table 1, Supplementary Table 2**), producing costs of around ZAR 2,500 (USD 176) for urgencies and ZAR 17,600 (USD 1,239) for emergencies.

Hypertension-Related Complications – Event Rates

We estimated the proportion of complications attributable to hypertension along with their acute and chronic costs. Five types of complication were considered: ischemic heart disease (IHD), stroke, chronic kidney disease (CKD), heart failure (HF), and hypertensive heart disease (HHD). While this is not an exhaustive list of conditions affected by hypertension, they were the complications most commonly included in previous costing studies[8,25] and there is strong evidence that hypertension is causative in their incidence.[26] We estimated the population-attributable fraction for each of these conditions associated with hypertension.

Overall rates of conditions which may be caused by hypertension were derived from the Global Burden of Disease Survey (GBDS) 2019, which combined multiple national surveys of demographics and health to produce estimates of incidence, prevalence, and disability-adjusted life years (DALYs) for different illnesses in South Africa.[27] We took age-specific data from the GBDS and adjusted them with SSA population data (**Supplementary Table 3**). Due to perceived issues with HF coding, GBDS researchers decided to distribute its morbidity and mortality among multiple conditions. The majority of HF events are redistributed to IHD, stroke, and HHD.[28]

The GBDS provides direct estimates for the proportion of CKD events caused by hypertension. The population-attributable fraction (PAF) of IHD, stroke, and HHD associated with hypertension were estimated separately.[29] The PAF quantifies the proportion of events attributable to a given risk factor. It is estimated by predicting how many events would have occurred in subgroups of a population if a risk factor had been eliminated and comparing that number to actuality. We estimated the number of complications that would be prevented if mean SBP values in hypertensive subgroups were lowered to the mean value for normotensives. Hazard ratios of 1.24 and 1.16 per 10 mm Hg increase in SBP were employed

for IHD and stroke, respectively.[30] For HHD, the hazard ratio decreased with older age, and ranged from 1.63 to 2.86 per 10 mm Hg increase in SBP.[31]

Confidence intervals were derived for hypertension-related complications and population attributable fractions by probabilistically sampling hypertension rates from a Dirichlet distribution based on the NIDS 2017 analysis outlined above and IHD, stroke, CKD, and HHD rates from Gamma distributions of the data described in **Supplementary Table 3**. We produced 1,000 probabilistic estimates reported 95% confidence intervals for complications and PAFs.

Hypertension-Related Complications – Costs

To estimate the cost of IHD, stroke, and CKD, published literature was reviewed to produce itemized lists of the costs associated with acute and chronic events. For acute events, we itemized costs for one hospitalisation. For chronic events, we itemized costs for one year of treatment. Unit costs were assigned to these items from publicly available data.

A cost-effectiveness analysis[32] from South Africa combined clinical guidelines with expert opinion to create 'impact inventories' which list the different types of resource use associated with chronic conditions including IHD, stroke, and renal disease. These inventories included resource use for acute and chronic care and informed resource use in our model (**Table 1, Supplementary Tables 4-5**). Unit costs were estimated with contemporary data which included the UPFS 2020, the Government Employee Medical Scheme 2019 tariffs, and public contracts for pharmaceutical products.[17,20,33] Estimated costs for IHD and stroke hospitalisations were around ZAR 16,400 (USD 1,160) and ZAR 23,900 (USD 1,680), respectively. Corresponding annual chronic care costs were ZAR 1,550 (USD 110) and ZAR 1,240 (USD 87).

In its early stages, CKD is largely treated through management of other CVD risk factors.[34] A proportion of patients with hypertension-related CKD will develop end-stage renal disease (ESRD). The South African Renal Registry provided information on the prevalence of ESRD and the proportion of CKD patients receiving haemodialysis, peritoneal dialysis, and kidney transplantation in the public healthcare system (**Supplementary Table 6**).[35] Itemized lists of resource use for dialysis and kidney transplant patients were taken from the cost-effectiveness paper described above (**Table 1, Supplementary Table 7**).[32] Resource use for kidney transplantation was derived from a cost-of-illness study of type-2 diabetes in South Africa.[36] Estimated annual costs for haemodialysis and peritoneal dialysis were ZAR 302,000 (USD 21,300) and ZAR 86,200 (USD 6,080), respectively. The cost of kidney transplantation was estimated to be around ZAR 139,000 (USD 9,770).

Societal Costs

A human capital approach was used to calculate the societal cost of hypertension. This approach assumes that all healthy time lost due to illness leads to lost productivity.[37] Every DALY experienced by an individual aged 20 to 65 years attributable to hypertension was

assigned the value of one gross domestic product (GDP) per capita (**Table 1**).[38] Societal costs were only included for the population without private health insurance. The per capita GDP for South Africa was estimated to be ZAR 85,100 (USD 6,000).[39,40]

Sensitivity Analysis

The effect of key modelling parameters on cost estimates was examined with one-way sensitivity analysis. Epidemiologic model inputs were systematically altered between upper and lower bounds derived from the NIDS 2017 analysis and the secondary data analysis outlined in **Supplementary Table 3** and **Supplementary Table 8**. The resulting change in direct, societal, and overall costs were recorded. Results from the sensitivity analysis were presented in a tornado diagram.

General Cost Assumptions

The price of healthcare goods and services may vary across time and setting.[41] Costs indexed in years prior to 2020 were inflated using SSA's regularly updated consumer price index (CPI) estimates for medical services and medical products.[42] In addition, costs derived from private healthcare sources were deflated using the ratio of prices paid in private versus public healthcare settings.[36] All costs were converted to U.S. dollars to provide international context for results.[40]

This study followed the Consolidated Health Economic Evaluation Reporting Standards reporting guideline (**Supplementary Table 9**).

Patient and public involvement

Patients and the general public were not directly involved in this study. We used publicly available data to conduct our analysis.

Results

Burden of Disease

We estimated that around 8.4 million (30.8%, 95% CI: 29.3-32.5%) adults aged ≥20 years without private health insurance have hypertension (**Table 2**). This proportion increased to 53.7% (95% CI: 51.2-56.6%) for adults aged ≥40 years. The prevalence of hypertension and antihypertensive medication use both increased with age (**Table 3, Supplementary Table 8**, **Supplementary Table 10**). Around 56.4% (95% CI: 54.5-58.2%) of hypertension was diagnosed, 84.5% (95% CI: 82.8-86.2%) of diagnosed hypertension was treated, and 54.7% (95% CI: 52.2-57.3%) of treated hypertension was controlled (**Supplementary Table 10**). Diagnosis of existent hypertension and likelihood of receiving treatment increased with age.

Hypertension leads to a significant burden of disease which increases with age. It was responsible for around 17.9% (95% CI: 15.3-20.4%) of IHD incidence, 27.8% (95% CI: 24.1-

31.0%) of stroke incidence, and 83.1% of HHD incidence (95% CI: 79.6-85.5%) (**Supplementary Table 11**). It caused around 31,200 hypertensive crises, 14,100 new cases of IHD, 13,600 new strokes, and 6,100 new cases of CKD annually (**Table 2, Supplementary Table 12**). Many individuals suffer from chronic health conditions caused by hypertension, leading to around 542,000 DALYs.

Cost of Hypertension

Total direct medical costs associated with hypertension were estimated to be around ZAR 10,834 million (USD 764 million). Direct hypertension screening and management costs accounted for ZAR 9,486 million (USD 669 million) (**Table 4**). Stroke was responsible for the largest amount of hypertension-related complication costs (ZAR 483 million; USD 34 million), followed by IHD (ZAR 451 million; USD 32 million) and hypertensive crises (ZAR 396 million; USD 28 million). The societal cost of hypertension was estimated to be ZAR 23,175 million (USD 1,634 million). This was 68.1% of the total cost of hypertension (ZAR 34,010 million; USD 2,398 million).

Sensitivity analysis showed that the proportion of the population with private health insurance, the societal cost of a DALY, the proportion of care that takes place in the public versus the private healthcare system, and the prevalence of hypertension had the largest impact on total cost estimates (**Figure 1**). Substantial reductions in direct medical and societal costs could be achieved if the prevalence of hypertension were to be reduced.

Discussion

To our knowledge, this is the first study of the economic burden of hypertension in South Africa. Hypertension exerts a heavy economic burden. The estimated direct cost represents 4.7% of the combined projection for national and provincial public health expenditure in 2020.[43] The total cost of ZAR 34,010 million (USD 2,398 million) represents around 0.65% of South Africa's GDP.[44] The management of hypertension must be considered in the context of other healthcare spending priorities. Previous studies have assessed the direct medical cost of type-2 diabetes in the public healthcare system (USD 162 million),[36] the total annual cost of smoking (USD 2,540 million),[45] and the costs associated with alcohol abuse (USD 2,270 million).[46]

We estimated that around 30.8% of adults aged ≥20 years without private health insurance have hypertension. This is lower than previous studies, but is based on more contemporaneous data.[1–3,47,48] We also estimated that hypertension leads to 542,000 DALYs annually. This is substantially more than a previous burden of disease study.[49]

Further research should establish optimal, cost-effective strategies to control BP. The results from this analysis may help inform inputs for cost-effectiveness models. Hypertension tends to

cluster with a number of other prominent risk factors for NCDs (e.g. obesity, diabetes and high cholesterol).[50,51] Healthcare decision-makers may take advantage of this clustering effect to efficiently target legislative or regulatory levers to reduce behaviours which lead to high BP and other NCDs. Some such legislative actions have already taken place in South Africa (e.g. mandatory salt regulations, a tax on sugary beverages).[52,53] Healthier foods and eating habits could be promoted with the advent of food labels, banning the marketing unhealthy foods and beverages, provision of healthy foodstuffs to vulnerable populations, and other interventions already in place globally.[54]

Limitations

As with many health economic evaluations conducted in low- and middle-income countries, data availability was a considerable limitation for this study. We synthesized data on the epidemiology of hypertension and costs of health services from multiple sources. Uncertainty from these sources will necessarily have propagated into our estimates. We explored this uncertainty with deterministic and probabilistic sensitivity analyses.

There is no system for the routine collection of national or subnational data in the South African public healthcare system. A 2015 governmental White Paper on NHI stated that a diagnosis-related grouping system will be developed for healthcare reimbursement along with an integrated national health information repository and data system.[7] This system could inform future costing and cost-effectiveness studies. Despite data limitations, a key strength of our analysis was that model inputs regarding the prevalence of hypertension, healthcare utilization, and the price of healthcare resources were all derived from South African data.

When estimating societal costs, we assumed that GDP accounts for the total value of all goods and services made within a country. Gross domestic product may underestimate activity in the 'informal' labour market and informal work (e.g. housekeeping, caretaking).[55] Around 3.0 million South Africans work in the informal sector.[56] Sensitivity analysis found that the way we valued DALYs greatly affected overall estimates of the societal cost of hypertension.

Finally, this costing analysis commenced during the Coronavirus 2019 (COVID-19) pandemic. Many healthcare resources have been redirected towards the prevention and treatment of this virus in South Africa. Much is still to be learned about the relationship between COVID-19 and hypertension. Some studies suggest that hypertension is predictive of severe illness.[57,58] Moreover, disruption in access to blood pressure screening and management may have led to an increase in uncontrolled hypertension and its complications.

Conclusion

Hypertension is highly prevalent in South Africa. A large proportion of public healthcare budgets are spent screening, treating, and controlling hypertension. An even greater economic burden is caused by reduced productivity attributable to the condition. Research is required to establish priority cost-effective strategies for lowering rates of hypertension and preventing complications.

Contributorship statement

CNKL developed the costing model, conducted the data analysis, interpreted results, and wrote the first draft of the manuscript. AE and KJH developed the idea for the study, secured the funding, and contributed to results interpretation, data analysis, and manuscript revisions. BLR contributed to results interpretation, data analysis, and manuscript revisions. All authors approved the final version of the manuscript.

Conflicts of Interest

Authors have no conflict of interest to declare.

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Data sharing statement

We used publicly available data to conduct our analysis. Access to the Microsoft Excel-based hypertension costing model is available by contacting ciaran.kohli-lynch@northwestern.edu.

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Table 1: Cost inputs
Derivation of costs outlined in text and Supplementary Tables 3-10

Parameter	Cost (ZAR 2020)	Sources
Visit costs		
Screening visit	144.00	17
Check-up visit	229.00	17
Medication, cost per day		
Hydrochlorothiazide 12.5 mg	0.14	20
Hydrochlorothiazide 25 mg	0.12	20
Enalapril 10 mg	0.16	20
Enalapril 20 mg	0.23	20
Amlodipine 5 mg	0.12	20
Amlodipine 10 mg	0.16	20
Spironolactone 25 mg	0.46	20
Hypertensive crises		
Urgencies	2,499.66	17,20
Emergencies	17,571.66	17,20
Hypertension-related complications		
Acute ischemic heart disease	16,407.20	17,20,32,59
Chronic ischemic heart disease	1,554.21	17,20,32,59
Acute stroke	23,883.23	17,20,32,59
Chronic stroke	1,235.21	17,20,32,59
Hemodialysis for end-stage renal disease	301,694.92	17,20,32,59
Peritoneal dialysis for end-stage renal disease	86,227.42	17,20,32,59
Transplant for end-stage renal disease	138,523.75	36
Societal costs		
Disability-adjusted life year	99,983.00	39
Physician visit (1.5 hours)	17.11.00	17,44
Hypertensive crisis (2 days)	54,748.00	17,20,44

Table 2: Hypertension-related complications treated in South African public healthcare system

Hypertension-Related Condition	Counts of conditions per year (95% CI)
Total number with hypertension* (% of age-group, 95% CI)	
Ages ≥20 years	8,360,000 (30.8%, 29.3-32.5%)
Ages ≥40 years	6,590,000 (53.7%, 51.2-56.6%)
Hypertensive crises	
Hypertensive urgencies	10,059 (8,449-11,797)
Hypertensive emergency	21,098 (17,846-24,772)
Ischemic heart disease	
Ischemic heart disease, incidence	14,059 (10,896-17,323)
Ischemic heart disease, prevalence	125,780 (103,881-148,572)
Ischemic heart disease, DALYs	99,573 (83,662-115,543)
Stroke	
Stroke, incidence	13,559 (10,883-16,274)
Stroke, prevalence	115,167 (96,547-133,525)
Stroke, DALYs	159,204 (135,174-180,341)
Chronic kidney disease	
Chronic kidney disease, incidence	6,135 (5,019-7,451)
Chronic kidney disease, prevalence	120,209 (109,714-131,898)
Chronic kidney disease, DALYs	89,333 (72,408-107,807)
Hypertensive heart disease	
Hypertensive heart disease, DALYs	173,234 (149,835-195,683)

* HTN grades 1-3 or currently receiving antihypertensive medication
CI – confidence interval, DALY – disability-adjusted life year

Table 3: Prevalence of SBP categories in SA adults without private health insurance

Population	Hypertension Category				
	Normotensive	Grade 1a	Grade 1b	Grade 2	Grade 3
Proportion of population (95% CI)					
Overall population	77.7 (76.8-78.5)	4.3 (3.8-4.7)	10.4 (9.8-11.0)	5.2 (4.8-5.7)	2.5 (2.2-2.8)
Young adults (age 20-39 years)	87.1 (86.1-88.0)	5.0 (4.4-5.6)	4.9 (4.3-5.5)	2.2 (1.8-2.6)	0.9 (0.7-1.2)
Middle adults (age 40-69 years)	67.1 (65.5-68.6)	3.8 (3.1-4.6)	16.5 (15.3-17.7)	8.4 (7.5-9.3)	4.2 (3.6-4.9)
Older adults (age ≥70 years)	54.8 (50.6-59.0)	n/a	24.3 (20.9-27.9)	14.2 (11.3-17.6)	6.7 (4.9-8.8)
SBP (mm Hg) within category, mean (95% CI)					
Overall population	113 (90-137)	137 (117-156)	139 (116-158)	155 (126-177)	178 (142-220)
Young adults (age 20-39 years)	112 (90-135)	137 (117-156)	133 (112-154)	147 (122-172)	164 (142-191)
Middle adults (age 40-69 years)	116 (92-137)	137 (119-156)	141 (119-158)	158 (131-177)	181 (142-219)
Older adults (age ≥70 years)	122 (98-139)	n/a	146 (127-160)	166 (152-177)	194 (178-225)

Normotension: SBP <140 mm Hg and DBP <90 mm Hg, Grade 1a: SBP 140-159 mm Hg or DBP 90-99 mm Hg with no other CVRFs, Grade 1b: SBP 140-159 mm Hg or DBP 90-99 mm Hg with another CVRF, Grade 2: SBP 160-179 mm Hg or DBP 100-109 mm Hg, Grade 3: SBP ≥180 mm Hg. Individuals who met two criteria (e.g., SBP <140 mm Hg and DBP 95 mm Hg) were included in the more severe hypertension category. Additional cardiovascular risk factors: smoking, diabetes, men aged ≥55 years, women aged ≥65 years, men waist circumference ≥94 cm, women waist circumference ≥80 cm.

CI – confidence interval, CVRF – cardiovascular risk factor, DBP – diastolic blood pressure, SBP – systolic blood pressure

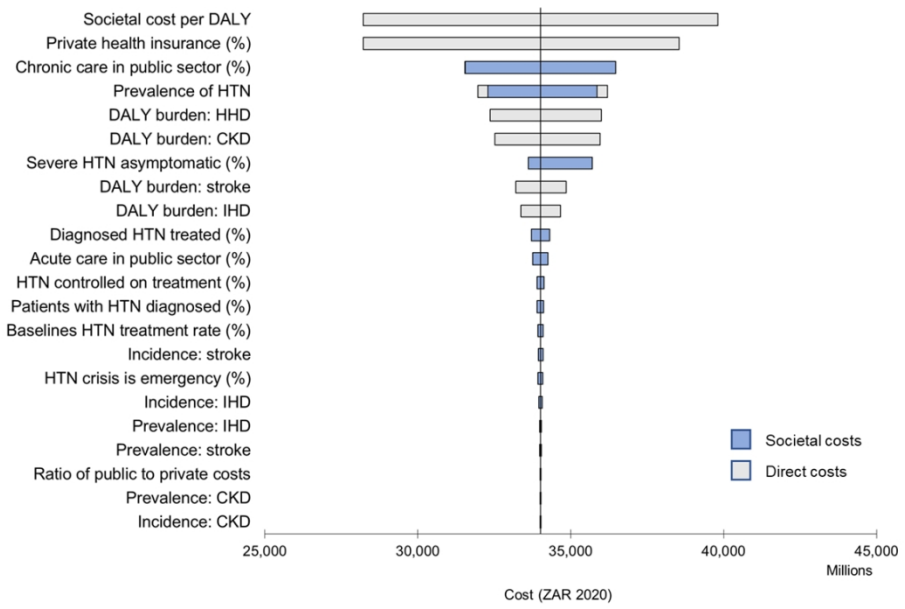
Table 4: Cost of hypertension in South African population with no private insurance

Cost Type	Cost, Millions (ZAR 2020)	Costs, Millions (USD 2020)
Direct costs	10,698	754
Age-group		
Young adults (age 20-39 years)	1,316	93
Middle adults (age 40-69 years)	6,985	492
Older adults (age ≥70 years)	2,396	169
Type of cost		
Screening	1636	115
Management	7718	544
Complications	1,344	95
Hypertensive crises	396	28
Ischemic heart disease	448	32
Stroke	481	34
Chronic kidney disease	19	94
Hypertensive heart disease	-	-
Societal costs	23,175	1,634
Age-group		
Young adults (age 20-39 years)	2,564	181
Middle adults (age 40-69 years)*	20,611	1,453
Type of cost		
Management	26	2
Complications	23,149	1,632
Hypertensive crises	-	-
Ischemic heart disease	4,010	283
Stroke	5,897	416
Chronic kidney disease	4,781	337
Hypertensive heart disease	8,461	597

*Societal costs incurred until age 65

Figure 1

Title: Tornado diagram showing results of sensitivity analyses
Legend: Tornado diagram shows impact of changing listed model parameters on the estimated overall cost of hypertension. Grey and blue bars indicate changes in the direct medical and societal cost of hypertension, respectively.
Abbreviations: CKD – chronic kidney disease, DALY – disability-adjusted life year, HHD – hypertensive heart disease, HTN – hypertension, IHD – ischaemic heart disease



Tornado diagram showing results of sensitivity analyses. CKD – chronic kidney disease, DALY – disability-adjusted life year, HHD – hypertensive heart disease, HTN – hypertension, IHD – ischaemic heart disease

546x355mm (59 x 59 DPI)

Supplementary Online Content

Title: Hypertension in the South African Public Healthcare System: Health and Economic Burden of Disease

Short title: Health and Economic Burden of Hypertension in South Africa

Table of Contents

Title: Hypertension in the South African Public Healthcare System: Health and Economic Burden of Disease

Short title: Health and Economic Burden of Hypertension in South Africa

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Key words: Economic burden; Cost-of-illness; Hypertension; Blood pressure; Non-communicable disease; South Africa.

Supplement

I. The National Income Dynamic Survey 2017

The National Income Dynamics Survey 2017 is the most contemporary national survey for South Africa. It contains individual-level blood pressure (BP), other health, and demographic information. The NIDS is a government-funded national household panel survey which is conducted every two years. It commenced in 2008, collecting data from more than 28,000 individuals on health, education, income, poverty, well-being, mortality, and migration. A 'top-up sample' was added in 2017 to account for attrition in recent waves.[1] Each wave of the survey has assigned cross-sectional sample weights which allow researchers to calibrate results to be representative of the contemporary South African population.[2] These weights were applied in our analyses.

Household surveys and individual surveys were completed for NIDS 2017. Respondents provided information through face-to-face interviews. Individuals were asked if they had ever been diagnosed with a list of health conditions which included hypertension and diabetes. They were also asked if they were currently taking medication for high BP. In addition, anthropometric measurements were taken alongside all individual questionnaires. Fieldworkers measured participants' height, weight, waist circumference, pulse, systolic blood pressure (SBP) and diastolic blood pressure (DBP). Blood pressure was measured twice. In our analyses, we used the average of these two measurements. Blood pressure was measured in the participant's left arm, after they had been seated for a minimum of 5 minutes. Blood pressure was recorded with an automated oscillometric devices (Omron M7 BP Monitor) which used standard multi-size cuffs.[3] Readings for SBP were excluded if <70 mm Hg and ≥270 mm Hg. Readings for DBP were excluded if <30 mm Hg and ≥180 mm Hg. Readings were also excluded if the differences between SBP and DBP was <15 mm Hg. These exclusions were enforced to ensure plausible BP readings were obtained, as defined by the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group. Fieldworkers received special training sessions in anthropometric measurement techniques from qualified nurses. Daily assessments were conducted to ensure the quality of fieldworker measurements.

II. Treatment to Manage Hypertension

Estimating the cost of treatment to manage hypertension involved three steps. First, the National Department of Health's Adult Primary Care (APC) 2019-20 hypertension treatment guidelines were reviewed and cost elements were itemized. Next, prices were applied to these costs. Finally, a decision tree was constructed to predict the number of patients receiving each stage of treatment suggested by the APC 2019-20, based on assumptions regarding hypertension control on medication. As BP treatment is not generally recommended for children or adolescents, costs were not incurred in these individuals.

There are seven BP management 'steps' outlined in the APC 2019-20 guidelines, involving increasing treatment intensity. Hypertensive patients start at a different level of treatment dependent on their hypertension grade. The steps are listed below:

- Step 1: Manage hypertension and cardiovascular risk through lifestyle advice. Reassess BP after three months, if uncontrolled move to Step 2.
- Step 2: Add hydrochlorothiazide 12.5mg daily. Reassess BP after one month, if uncontrolled move to Step 3.
- Step 3: Add enalapril 10mg daily. Reassess BP after one month, if uncontrolled move to Step 4.
- Step 4: Increase enalapril to 20mg daily. Reassess BP after one month, if uncontrolled move to Step 5.
- Step 5: Add amlodipine 5mg daily. Reassess BP after one month, if uncontrolled move to Step 6.
- Step 6: Increase amlodipine to 10mg daily. Reassess BP after one month, if uncontrolled move to Step 7.
- Step 7: Add spironolactone 25mg daily and increase HCTZ to 25mg daily. Reassess BP weekly until controlled.

Individuals with Grade 1a hypertension commence at Step 1. Individuals with Grade 1b and Grade 2 hypertension start on Step 2, and those with Grade 3 start on Step 3. A final, end-of-year, visit is recommended for all hypertensive patients. Step 7 was only recommended for patients with Grade 3 hypertension.

A decision tree was produced to estimate costs associated with different treatment steps. The tree predicted the number of steps required to control hypertension in different subgroups of patients. Probabilities of hypertension control while on treatment **(Supplementary Table 1)** were converted to rates in order to achieve observed rates of control after six potential increases in treatment intensity.

The structure of the decision tree is presented in **Supplementary Figure 1**. This example specifically models the scenario where patients begin with Grade 1a hypertension. Individuals receive lifestyle advice upon presenting with BP of 140-159/90-99 mm Hg and no other cardiovascular disease risk factors. All patients incur a visit cost at 3 months, at which point a proportion of patients will have achieved BP control. Individuals who have achieved control and remain uncontrolled incur the cost of one outpatient visit at this point. For patients who remain uncontrolled, they are prescribed Step 2 treatment (hydrochlorothiazide 12.5mg daily) and re-evaluated one month later. Again, a proportion of these patients will be controlled after one month. These patients are assumed to remain on Step 2 treatment for the remainder of the year. Uncontrolled patients incur the cost of one month of Step 2 treatment and progress to Step 3 (add enalapril 10mg daily). This process repeats itself until the highest step of treatment has been tried for a month, at which stage uncontrolled patients are considered to have treatment-resistant hypertension.[4] All patients incur a final visit cost at 12 months. Similar decision trees were constructed for patients who started at different steps in the treatment cascade.

Supplementary Table 1: Cost items for hypertension screening and management

Parameter	Unit price (ZAR 2020)	Source
Screening		
Level 1 facility visit fee	78.00	5
Nurse practitioner visit	66.00	5
Medication		
Hydrochlorothiazide 12.5 mg	0.14	6
Hydrochlorothiazide 25 mg	0.12	6
Enalapril 10 mg	0.16	6
Enalapril 20 mg	0.23	6
Amlodipine 5 mg	0.12	6
Amlodipine 10 mg	0.16	6
Spironolactone 25 mg	0.46	6
Check-ups		
Level 1 facility visit fee	114.00	5
Physician visit	115.00	5

Total cost per check-up visit: ZAR 229.00

Supplementary Table 2: Cost items for treatment of hypertensive crises

Parameter	Units required	Unit price (ZAR 2020)	Source
Hypertensive urgency, total cost: ZAR 2,499.66			
Inpatient (general ward) - level 2 facility	2	1,073.00	[5]
Inpatient (general ward) – physician	2	175.00	[5]
Step 5 medication, 1 day	2	1.83	[6]
Hypertensive emergency, total cost: ZAR 8,787.66			
Inpatient (intensive care) - level 2 facility	2	8,580.00	[5]
Inpatient (intensive care) - physician	2	204.00	[5]
Step 5 medication	2	1.83	[6]

Supplementary Table 3: Numbers of ischaemic heart disease, stroke, chronic kidney disease due to hypertension, and hypertensive heart disease events in Global Burden of Disease Study 2019

Complication	Incidence 95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischaemic heart disease				
Young adults (age 20-39 years)	9,066 (6,115-12,665)	41,853 (34,540-50,937)	48,391 (33,450-65,940)	
Middle adults (age 40-69 years)	59,012 (42,770-77,314)	509,656 (428,965-606,031)	380,846 (323,507-439,742)	7,8
Older adults (age ≥70 years)	41,154 (33,628-49,840)	397,252 (342,850-458,918)	235,801 (213,109-253,859)	
Stroke				
Young adults (age 20-39 years)	4,947 (3,386-7,154)	113,669 (91,317-136,831)	63,641 (47,179-82,664)	
Middle adults (age 40-69 years)	36,227 (27,391-47,103)	341,940 (288,580-403,696)	349,518 (305,321-395,223)	7,8
Older adults (age ≥70 years)	26,534 (21,701-32,774)	189,793 (157,234-227,130)	272,536 (247,839-292,139)	
Chronic kidney disease due to hypertension				
Young adults (age 20-39 years)	454 (249-695)	20,651 (15,737-26,822)	15,658 (9,366-24,479)	
Middle adults (age 40-69 years)	4,782 (3,341-6,467)	78,094 (65,860-92,056)	56,912 (40,757-77,525)	7,8
Older adults (age ≥70 years)	3,345 (2,793-3,951)	71,282 (63,613-79,662)	24,287 (28,523-40,484)	
Hypertensive heart disease				
Young adults (age 20-39 years)	-	-	15,114 (9,793-21,543)	
Middle adults (age 40-69 years)	-	-	133,912 (110,311-162,646)	7,8
Older adults (age ≥70 years)	-	-	106,319 (85,787-112,368)	

Supplementary Table 4: Acute and chronic care costs, ischaemic heart disease

Parameter	Units required	Unit price (ZAR 2020)	Source
Acute care, total cost: ZAR 16,407 (USD 1,157)			
Inpatient (general ward) – level 2 facility	2.5	1,073.00	[5,9]
Inpatient (general ward) – physician	2.5	175.00	[5,9]
Morphine	10.0	2.73	[6,9]
Aspirin	7.5	0.39	[6,9]
Prochlorperazine	2.5	167.53	[6,9]
Streptokinase	1.0	3,471.13	[6,9]
Enoxaparin	2.0	19.38	[6,9]
Clopidogrel	5.5	933.39	[6,9]
Daily drawing blood (test)	2.5	41.00	[5,9]
Echocardiography (test)	1.0	1,285.15	[6,9]
Daily electrolytes and urea (test)	2.5	108.96	[9,10]
Daily blood count (test)	2.5	74.10	[9,10]
Daily blood glucose (test)	2.5	38.76	[9,10]
Daily liver function (test)	2.5	359.21	[9,10]
Daily lipid (test)	2.5	132.16	[9,10]
Daily thyroid function (test)	2.5	409.62	[9,10]
Chronic care, total cost: ZAR 1,554 (USD 110)			
Nurse visit - level 1 facility	6.0	78.00	[5,9]
Nurse visit – nurse fees	6.0	59.00	[5,9]
Physician visit - level 1 facility	1.0	114.00	[5,9]
Physician visit - physician fees	1.0	115.00	[5,9]
Aspirin, daily	365	0.43	[6,9]
Statin, daily	365	0.94	[6,9]

Supplementary Table 5: Acute and chronic care costs, stroke

Parameter	Units required	Unit price (ZAR 2020)	Source
Acute care, total cost: ZAR 23,883 (USD 1,684)			
Inpatient (general ward) – Level 2 facility	14.0	1,073.00	[5,9]
Inpatient (general ward) – physician	14.0	175.00	[5,9]
Physiotherapy	1.0	1,080.97	[6,9]
Occupational therapy	1.0	401.88	[6,9]
Aspirin	14.0	0.41	[6,9]
Streptokinase	1.0	3,471.13	[6,9]
CT scan (test)	5.0	175.00	[6,9]
Drawing blood (test)	5.0	41.00	[6,9]
Blood count (test)	5.0	74.10	[5,9]
Chronic care, total cost: ZAR 1,235 (USD 87)			
Nurse visit - level 1 facility	2.0	78.00	[5,9]
Nurse visit – nurse fees	2.0	59.00	[5,9]
Physician visit - level 1 facility	2.0	114.00	[5,9]
Physician visit - physician fees	2.0	115.00	[5,9]
Aspirin, daily	365	0.43	[6,9]
Statin, daily	365	0.94	[6,9]

Supplementary Table 6: Proportion of chronic kidney disease patients in public healthcare system with end-stage renal disease and type of treatment

Parameter	Value	Source
Number with chronic kidney disease	4,749,648	[7]
Number receiving haemodialysis	1,282	[11]
Number receiving peritoneal dialysis	814	[11]
Number receiving transplant	1,038	[11]
Proportion CKD receiving haemodialysis	0.00027	[7,11]
Proportion CKD receiving peritoneal dialysis	0.00017	[7,11]
Proportion CKD receiving kidney transplant	0.00022	[7,11]

CKD – chronic kidney disease

Supplementary Table 7: Cost of treating end-stage renal disease

Parameter	Units required, annual	Unit price (ZAR 2020)	Source
Haemodialysis, total cost: ZAR 301,695 (USD 21,272)			
Haemodialysis - Level 2 facility	156.00	1,643.00	5,9
Haemodialysis - nurse practitioner	156.00	252.00	5,9
Physician visit - Level 1 facility	4.00	114.00	5,9
Physician visit - physician	4.00	115.00	5,9
Occupational therapy	1.00	391.04	9,12
Drawing blood (test)	1.00	41.00	5,9
Electrolyteres and urea (test)	4.00	108.96	9,10
Parathyroid hormone (test)	4.00	195.16	9,10
Blood count (test)	4.00	74.10	9,10
Liver function tests (test)	4.00	359.21	9,10
Calcium test (test)	4.00	38.76	9,10
Alkaline phosphosate test (test)	4.00	354.12	9,10
Albumin (test)	4.00	51.40	9,10
Peritoneal dialysis, total cost: ZAR 86,227 (USD 6,080)			
Peritoneal dialysis - Level 1 facility	156.00	254.00	5,9
Peritoneal dialysis - nurse practitioner	156.00	252.00	5,9
Physician visit - Level 1 facility	4.00	114.00	5,9
Physician visit - physician	4.00	115.00	5,9
Occupational therapy	4.00	401.88	6,9
Drawing blood (test)	1.00	41.00	5,9
Electrolyteres and urea tests (test)	4.00	108.96	9,10
Parathyroid hormone (test)	4.00	195.16	9,10
Blood count (test)	4.00	74.10	9,10
Liver function tests (test)	4.00	359.21	9,10
Calcium test (test)	4.00	38.76	9,10
Kidney transplant, total cost: ZAR 138,524 (USD 9,767)			
Procedure	1.00	4,886.73	13
Hospitalisation: recipient	1.00	24,439.80	13
Hospitalisation: donor	1.00	15,552.60	13
Follow-Up outpatient consultation	1.00	392.67	13
Post-transplant dietitian consultation	1.00	383.80	13
Post-transplant physiotherapist	1.00	383.80	13

Supplementary Table 8: Prevalence of SBP categories in National Income Dynamics Survey 2017

Population	Hypertension Category				
	Normotensive	Grade 1a	Grade 1b	Grade 2	Grade 3
Population with no private health insurance					
Proportion of population (95% CI)					
Overall population	77.7 (76.8-78.5)	4.3 (3.8-4.7)	10.4 (9.8-11.0)	5.2 (4.8-5.7)	2.5 (2.2-2.8)
Young adults (age 20-39 years)	87.1 (86.1-88.0)	5.0 (4.4-5.6)	4.9 (4.3-5.5)	2.2 (1.8-2.6)	0.9 (0.7-1.2)
Middle adults (age 40-69 years)	67.1 (65.5-68.6)	3.8 (3.1-4.6)	16.5 (15.3-17.7)	8.4 (7.5-9.3)	4.2 (3.6-4.9)
Older adults (age ≥70 years)	54.8 (50.6-59.0)	n/a	24.3 (20.9-27.9)	14.2 (11.3-17.6)	6.7 (4.9-8.8)
Mean SBP within category (mm Hg)					
Overall population	114 (91-137)	136 (117-156)	132 (114-152)	144 (123-162)	162 (140-197)
Young adults (age 20-39 years)	112 (90-135)	137 (117-156)	133 (112-153)	147 (120-159)	165 (140-191)
Middle adults (age 40-69 years)	117 (92-138)	138 (119-139)	142 (116-153)	158 (125-174)	182 (141-194)
Older adults (age ≥70 years)	122 (92-138)	n/a	146 (118-139)	166 (125-176)	190 (142-158)
Population with no private health insurance and no antihypertensive medication					
Proportion of population (95% CI)					
Overall population	81.5 (80.6-82.4)	4.7 (4.2-5.2)	8.1 (7.5-8.8)	3.9 (3.5-4.4)	1.7 (1.5-2.1)
Young adults (age 20-39 years)	87.8 (86.9-88.7)	4.9 (4.4-5.5)	4.5 (4-5.1)	2 (1.6-2.4)	0.8 (0.5-1)
Middle adults (age 40-69 years)	71.5 (69.6-73.3)	4.7 (3.8-5.7)	13.6 (12.3-15)	7.1 (6.1-8.1)	3.2 (2.5-4)
Older adults (age ≥70 years)	56.8 (50.8-62.6)	n/a	26.1 (20.7-32.2)	9.9 (6.8-13.9)	7.2 (4.6-10.6)
Mean SBP within category (mm Hg)					
Overall population	113 (90-137)	137 (117-156)	139 (116-158)	155 (126-177)	178 (142-220)
Young adults (age 20-39 years)	112 (90-135)	137 (117-156)	133 (112-154)	147 (122-172)	164 (142-191)
Middle adults (age 40-69 years)	116 (92-137)	137 (119-156)	141 (119-158)	158 (131-187)	181 (142-219)
Older adults (age ≥70 years)	122 (98-139)	n/a	146 (127-160)	166 (152-187)	194 (178-225)

Normotension: SBP <140 mm Hg and DBP <90 mm Hg, Grade 1a: SBP 140-159 mm Hg or DBP 90-99 mm Hg with no other CVRFs, Grade 1b: SBP 140-159 mm Hg or DBP 90-99 mm Hg with another CVRF, Grade 2: SBP 160-179 mm Hg or DBP 100-109 mm Hg, Grade 3: SBP ≥180 mm Hg. Individuals who met two criteria (e.g., SBP <140 mm Hg and DBP 95 mm Hg) were included in the more severe hypertension category. Additional cardiovascular risk factors: smoking, diabetes, men aged ≥55 years, women aged ≥65 years, men waist circumference ≥94 cm, women waist circumference ≥80 cm.

CVRF – cardiovascular risk factor, DBP – diastolic blood pressure, SBP – systolic blood pressure

Supplementary Table 9. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Page 1 Line 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Page 2, Lines 1-33
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	Page 4, Lines 5-10
		Present the study question and its relevance for health policy or practice decisions.	Page 4, Lines 19-29
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 4, Lines 34-35 Page 5, Lines 10-18
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 5, Lines 10-18
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 4, Line 34 Page 5, Lines 10-18
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	n/a
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 4, Line 38
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 4, Lines 38-39
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 6, Lines 4-40 Page 7, Lines 1-5
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	n/a
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	n/a
Measurement and valuation of preference-based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n/a

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 6, Lines 11-30 Page 8, Lines 7-32
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 4, Line 38
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	n/a
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Page 4, Line 38 Supplementary Tables 4-5 Supplementary Table 7
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 5, Lines 1-8 Page 6, Lines 4-9 Page 8, Lines 35-40 Page 9, lines 2-6 Supplementary Material
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Methods Table 1
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-	n/a

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
		effectiveness ratios.	
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Page 10, Lines 7-11 Figure 1 Table 2 Table 3
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Page 9, Lines 22-35 Table 2 Table 3 Table 4
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Page 10, Lines 13-41 Page 11, Lines 1-41
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 12, Lines 4-8
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 12, Lines 1-2

Supplementary Table 10: Hypertension diagnosis, treatment, and control rates in National Income Dynamics Survey 2017

Population	Hypertension diagnosed† (95% CI)	Diagnosed hypertension treated† (95% CI)	Treated hypertension controlled‡ (95% CI)
Overall population	56.4 (54.5-58.2)	84.5 (82.8-86.2)	54.7 (52.2-57.3)
Young adults (age 20-39 years)	21.5 (18.6-24.5)	72.6 (65.8-78.6)	55.8 (46.4-65.0)
Middle adults (age 40-69 years)	65.4 (63.1-67.7)	85.6 (83.5-87.5)	55.0 (52.1-57.9)
Older adults (age ≥70 years)	84.9 (81.0-88.2)	86.9 (82.8-90.4)	53.2 (47.1-59.2)

Values given are proportions

*Denominator: Individuals with hypertension (SBP≥140 mm Hg or DBP ≥90 mm Hg or on antihypertensive medication)

†Denominator: Individuals with diagnosed hypertension

‡Denominator: Individuals receiving antihypertensive medication

Supplementary Table 11: Population-attributable fractions for hypertension-related complications

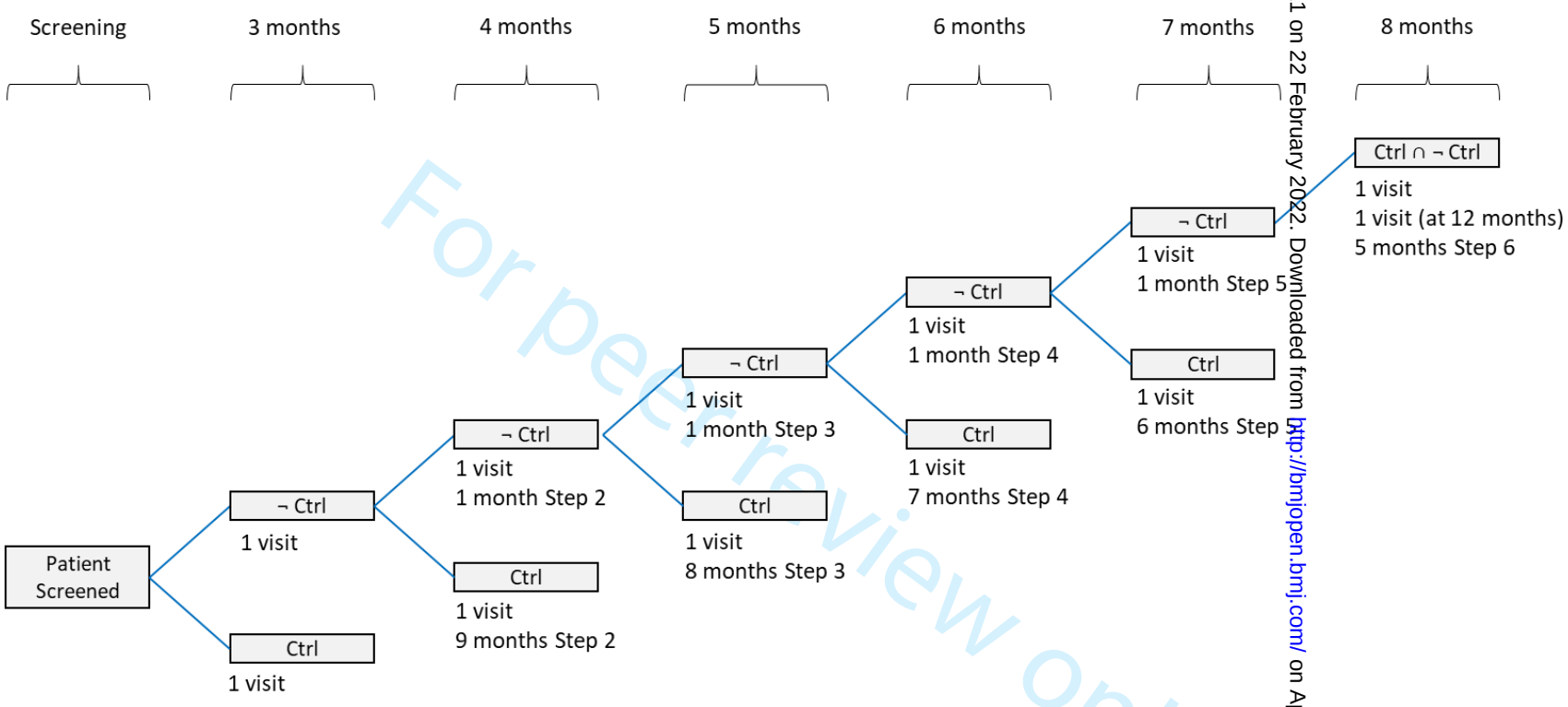
Parameter	Population-attributable fraction (%, 95% CI)
Ischaemic heart disease	
Overall	17.9 (15.3-20.4)
Young adults (age 20-39 years)	5.6 (4.8-6.5)
Middle adults (age 40-69 years)	15.6 (13.6-17.7)
Older adults (age ≥70 years)	24.2 (18.3-30.0)
Stroke	
Overall	27.8 (24.1-31.0)
Young adults (age 20-39 years)	9.0 (7.8-10.5)
Middle adults (age 40-69 years)	24.4 (21.5-27.3)
Older adults (age ≥70 years)	36.5 (28.5-43.6)
Hypertensive heart disease	
Overall	83.1 (79.6-85.5)
Young adults (age 20-39 years)	78.4 (74.2-82.0)
Middle adults (age 40-69 years)	88.3 (86.1-90.1)
Older adults (age ≥70 years)	76.9 (69.0-82.0)

CI – confidence interva

Supplementary Table 12: Numbers of hypertension-related complications

Complication	Incidence 95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischaemic heart disease				
Overall	14,059 (10,896-17,323)	125,780 (103,881-148,572)	99,573 (83,662-115,543)	7,8,15
Young adults (age 20-39 years)	364 (234-509)	1,662 (1,372-2,207)	2,273 (1,510-3,156)	
Middle adults (age 40-69 years)	6,562 (4,699-8,837)	56,040 (47,601-87,276)	49,518 (40,593-59,341)	
Older adults (age ≥70 years)	7,132 (4,904-9,383)	68,078 (44,886-68,938)	47,783 (35,323-59,772)	
Stroke				
Overall	13,559 (10,883-16,274)	115,167 (96,547-133,525)	159,204 (135,174-180,341)	7,8,15
Young adults (age 20-39 years)	319 (204-457)	7,253 (5,535-9,218)	4,802 (3465-6,582)	
Middle adults (age 40-69 years)	6,314 (4,661-8,513)	58,926 (47,660-71,697)	71,222 (60,144-83,919)	
Older adults (age ≥70 years)	6,926 (4,866-8,978)	48,988 (35,700-63,743)	83,180 (62,551-100,541)	
Chronic kidney disease due to hypertension				
Overall	6,135 (5,019-7,451)	120,209 (109,714-131,898)	89,333 (72,408-107,807)	7,8
Young adults (age 20-39 years)	324 (184-502)	14,600 (10,660-18,611)	13,090 (7,589-20,282)	
Middle adults (age 40-69 years)	3,419 (2,435-4,662)	55,213 (46,627-65,024)	47,578 (33,622-64,424)	
Older adults (age ≥70 years)	2,391 (1,995-2,829)	50,397 (45,085-55,781)	28,664 (23,975-34,082)	
Hypertensive heart disease				
Overall	-	-	173,234 (149,835-195,683)	7,8,16
Young adults (age 20-39 years)	-	-	9,909 (6,412-13,952)	
Middle adults (age 40-69 years)	-	-	96,849 (80,049-116,828)	
Older adults (age ≥70 years)	-	-	64,476 (53,056-73,805)	

Supplementary Figure 1: Decision tree for hypertension treatment



Associated resource use listed below each state, costs are cumulative
Ctrl – Hypertension controlled

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Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Title: Hypertension in the South African Public Healthcare System: Health and Economic Burden of Disease

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Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	n/a
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Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	n/a
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included	n/a

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
		studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference-based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n/a
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 6, Lines 11-30 Page 8, Lines 7-32
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Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Page 4, Line 38 Supplementary Tables 4-5 Supplementary Table 7
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Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty	Methods Table 1

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
		where appropriate. Providing a table to show the input values is strongly recommended.	
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	n/a
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Page 10, Lines 7-11 Figure 1 Table 2 Table 3
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Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Page 10, Lines 13-41 Page 11, Lines 1-41
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 12, Lines 4-8
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 12, Lines 1-2

BMJ Open

Hypertension in the South African Public Healthcare System: A Cost-of-Illness and Burden of Disease Study

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Title: Hypertension in the South African Public Healthcare System: A Cost-of-Illness and Burden of Disease Study

Short title: Health and Economic Burden of Hypertension in South Africa

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Abstract

Objectives

To quantify the health and economic burden of hypertension in the South African public healthcare system.

Setting

All inpatient, outpatient, and rehabilitative care received in the national public healthcare system.

Participants

Adults, aged ≥20 years, who receive care in the public healthcare system.

Outcomes

Worksheet-based models synthesized data from multiple sources to estimate the burden of disease, direct healthcare costs, and societal costs associated with hypertension. Results were disaggregated by sex.

Results

Approximately 8.22 million (30.8%, 95% confidence interval [CI]: 29.5-32.1%) South African adults with no private health insurance have hypertension. Hypertension was estimated to cause 14,000 (95% CI: 11,100-17,200) ischemic heart disease events, 13,300 (95% CI: 10,600-16,300) strokes, and 6,100 (95% CI: 4,970-7,460) cases of chronic kidney disease annually. Rates of hypertension, hypertension-related stroke, and hypertension-related chronic kidney disease were greater for women compared to men.

The direct healthcare costs associated with hypertension were estimated to be ZAR 10.1 billion (95% CI: 8.98-11.3 billion) or USD 0.711 billion (95% CI: 0.633-0.793 billion). Societal costs were estimated to be ZAR 29.4 billion (95% CI: 26.0-33.2 billion) or USD 2.08 billion (95% CI: 1.83-2.34 billion). Direct healthcare costs were greater for women (ZAR 6.11 billion or USD 0.431 billion) compared to men (ZAR 3.97 billion or USD 0.280 billion). Conversely, societal costs were lower for women (ZAR 10.5 billion or USD 0.743 billion) compared to men (ZAR 18.9 billion or USD 1.33 billion).

Conclusion

Hypertension exerts a heavy health and economic burden on South Africa. Establishing cost-effective best practice guidelines for hypertension treatment requires further research. Such research will be essential if South Africa is to make progress in its efforts to implement universal healthcare.

Key questions

What is already known?

- While the proportion of the South African population with uncontrolled hypertension has fallen in recent years, rates of diagnosis, treatment, and control remain concerning.
- Previous studies have produced varied estimates of the cost of hypertension in low- and middle-income countries; however, they have consistently found that the annual cost of hypertension-related care exceeds per capita annual healthcare expenditure.
- No previous studies have estimated the economic burden of hypertension in South Africa.

What are the new findings?

- Around one third of South African adults (aged ≥20 years) without private health insurance have hypertension.
- Direct healthcare costs associated with hypertension exert a heavy burden on public health budgets.
- The societal costs associated with hypertension, caused by reduced productivity in the workplace, account for a large proportion of the total cost of illness.
- Direct healthcare costs of hypertension are higher and societal costs are lower for women compared to men.

What do the new findings imply?

- To develop a sustainable universal healthcare programme, South Africa must establish priority cost-effective strategies for lowering rates of hypertension and preventing complications.

Strengths and limitations of this study

- This is the first study of the economic burden of hypertension in South Africa.
- A bottom-up approach was used for estimating direct costs.
- A human capital approach with disability-adjusted life year indexing was used to calculate societal costs.
- Despite data limitations, model inputs regarding the prevalence of hypertension, healthcare utilization, and the price of healthcare resources were all derived from South African data.
- Our estimate of societal costs may underestimate activity in the 'informal' labour market and informal work (e.g., housekeeping, caretaking).

Hypertension in the South African Public Healthcare System: A Cost-of-Illness and Burden of Disease Study

Background

High blood pressure (BP), or hypertension, caused an estimated 10.7 million deaths worldwide in 2015 and rates were higher in low- and middle-income countries.[1] Hypertension was responsible for around 47,000 deaths in South Africa in 2000. Since then, its prevalence has grown from 25% to greater than 40%.[2]

South Africa is an upper middle-income country in which hypertension is a highly prevalent condition.[2–5] While the proportion of the population with uncontrolled hypertension has fallen in recent years,[4] rates of diagnosis, treatment, and control remain low.[3] These rates are lower for low-income individuals, those with fewer years of education, and those who receive care in the public healthcare system.[2,6] Funding prevention, public screening, and treatment campaigns may improve population health and reduce health disparities.

Around 85% of the South African population has no private health insurance,[7] yet private healthcare accounts for more than half of the country's health-related expenditure.[8] The government is in the process of creating a National Health Insurance (NHI) program to address inequalities in access to comprehensive healthcare.[9] The NHI program will produce a centralized financing source for public healthcare which aims to improve the quality of public healthcare and increase its allotted budget.

There are considerable knowledge gaps related to the health and economic cost of hypertension and cardiovascular disease (CVD) in low- and middle-income countries.[10] No previous studies have considered the economic burden of hypertension in South Africa. Calculating the cost of hypertension and the prevalence of its complications will help decision-makers target public healthcare resources more efficiently, improving the sustainability of the NHI program.

The first objective of this study was to estimate the incidence and prevalence of hypertension and hypertension-related complications amongst individuals who receive care in the South African public healthcare system. The second objective was to calculate the annual healthcare and societal costs associated with hypertension in these individuals.

Methods

This study followed the Consolidated Health Economic Evaluation Reporting Standards reporting recommendations (**eTable 1**).

Ethics Statement

In accordance with University of the Witwatersrand guidelines on research ethics, this study did not require institutional review board approval as it was a secondary analysis of publicly available and de-identified data.

Study Parameters

We adopted a public healthcare sector perspective. The population of interest was adults aged ≥20 years receiving healthcare in the public health sector. We estimated prevalence of hypertension, number of hypertension-related complications, and costs associated with hypertension in this population. Costs were disaggregated into two categories: direct healthcare and societal costs. A time horizon of one year was adopted. No discount rate was applied.

Approach

Two worksheet-based costing models were developed in Microsoft Excel to synthesize data from multiple sources. One model was produced for men and another for women, due to previously observed sex differences in the age distribution of these populations, rates of hypertension and hypertension-related complications, and employment rates.[2,11,12]

The costing models accept a range of epidemiologic and cost inputs, which are described below, and output rates of hypertension-related complications, direct healthcare costs, and societal costs associated with hypertension. Confidence intervals were derived for hypertension-related complications and costs through probabilistic analysis. We probabilistically sampled epidemiologic model input parameters and produced 1,000 estimates of hypertension-related health and cost outcomes. We reported mean and 95% confidence intervals for all model outputs.

After communication with the National Department of Health, non-governmental research institutions, and examination of the open data portal for health services research,[13] it was established that no national dataset exists which details public healthcare expenditure disaggregated by disease type. It was determined that a bottom-up costing approach with secondary data sources was necessary. Analysis was disaggregated by sex and age-group (young adults – aged 20-39 years, middle adults – aged 40-69 years, and older adults – aged ≥70 years).

Population Size and Public Healthcare Utilization

Population size was informed by Statistics South Africa (SSA) mid-year estimates, disaggregated by sex.[14] Care-seeking behaviour was informed by recent national surveys. The proportion of screening and other outpatient care that occurs in the public healthcare system (70.7%) was derived from the Demographic and Health Survey 2016.[15] The proportion of acute care that occurs in the public healthcare system (71.5%) and the proportion of the population who have

no private health insurance (83.6%) were derived from the General Household Survey 2018.[7] In both cases, the 'public healthcare system' referred to healthcare provided in government hospitals, government clinics, community health centres, and other public sector facilities.

Hypertension Rates

Hypertension prevalence, diagnosis, treatment, and control were estimated in the National Income Dynamics Survey (NIDS) 2017, a largescale national survey of population health which is publicly available.[16] Analysis was conducted in the subset of respondents without private health insurance. All NIDS 2017 analysis was completed in the *R* programming language (Version 4.0.4, R Core Team). Participants were asked about hypertension diagnosis, medications, and CVD risk factors.[17] In addition, respondents had systolic blood pressure (SBP) and diastolic blood pressure (DBP) measured twice. We used the average of these values in our analysis. Individuals without SBP readings were omitted from the analysis. Cross-sectional sample weights were used to ensure results were representative of the contemporary South African population.[18] Further information on NIDS 2017 and the way participants' blood pressure was recorded is contained in the **supplementary material**.

Hypertension was split into five categories, in accordance with the National Department of Health's Adult Primary Care (APC) Guidelines 2019-20.[19] These were: normotension (SBP <140 mm Hg and DBP <90 mm Hg), Grade 1a (SBP 140-159 mm Hg or DBP 90-99, with no other cardiovascular risk factors), Grade 1b (SBP 140-159 mm Hg or DBP 90-99, with another cardiovascular risk factor), Grade 2 (SBP 160-179 mm Hg or DBP 100-109 mm Hg), and Grade 3 – or 'severe' hypertension (SBP ≥180 or DBP ≥110 mm Hg). If an individual had differential grades of systolic and diastolic BP, they were assigned the more severe of the two categories. For example, an individual with SBP 150 mm Hg (Grade 1) and DBP 105 mm Hg (Grade 2) would be assigned Grade 2 hypertension. 'Other cardiovascular risk factors' considered in the APC guidelines were smoking, diabetes, age ≥55 years for men, age ≥65 years for women, waist circumference ≥94 cm for men, and waist circumference ≥80 cm for women.

Prevalence of SBP categories was estimated in two subsets of the population: all individuals and individuals not currently receiving antihypertensive medication. Overall prevalence was calculated as the sum of hypertensive individuals not currently receiving antihypertensive medication plus the number receiving antihypertensive medication. Hypertension prevalence, diagnosis, treatment, and control rates were estimated for the overall population and separately for men and women. Confidence intervals for these rates were computed using incomplete beta functions with sample size based on the estimated variance of the proportion.[20]

Screening Costs

Costing for facility use and healthcare worker time came from the Uniform Patient Fee Schedule (UPFS) 2020.[21] The UPFS is a set of tariffs for public health services, including both

health practitioner and facility fees. The tariffs are updated annually and apply to all patients using public services.[22] There are three types of facility in the public healthcare system, which generally increase in price: district, regional, and tertiary.

There is limited guidance regarding screening in the APC 2019-20 or the South African Hypertension Society (SAHS) practice guidelines.[23] It was assumed that all screening would be undertaken by a nurse practitioner in a district-level health facility. The cost of a screening visit was estimated to be ZAR 144 (USD 10) (**Table 1**, **eTable 2**).

Management Costs

To estimate the cost of hypertension management, recommended resource use in the APC 2019-20 guideline was itemized. Resource use included medication, testing, and check-up visit costs (**Table 1**, **eTable 2**). The proportion of the population that reported antihypertensive medication use in NIDS 2017 received ongoing treatment. We assumed a proportion of the population with untreated hypertension would commence treatment over the course of a year. Specifically, we assumed that new treatment would commence according to the overall treatment rate of individuals with hypertension in the wider population.

The treatment steps contained in the APC guidelines are described in the **supplementary material**. Initial treatment intensity depended on untreated BP and treatment intensified with failure to control BP on lower treatment steps. A decision tree was constructed to predict the number of patients receiving each treatment step (**eFigure 1**). The tree predicted the number of steps required to control hypertension in different subgroups of patients. Probability of successful BP control during treatment was estimated in NIDS 2017. We were not able to estimate clinician compliance to APC guidelines. We assumed that all treated patients received guideline-compliant care and expert opinion was elicited to validate this assumption.

Unit costs for antihypertensive medications were derived from National Treasury contracts.[24] Outpatient visit costs came from the UPFS 2020. It was assumed that all check-ups would be administered by physicians in district-level facilities. The overall cost for a check-up visit was ZAR 229 (USD 16).

Hypertensive Crises

Most patients with severe hypertension are asymptomatic.[23,25] Some will experience hypertensive crises and require acute medical care. Hypertensive crises can be classified as urgencies or emergencies. The latter are more severe and involve ongoing organ damage. Published studies were used to estimate the proportion of patients with severe hypertension that experience a hypertensive crisis (5.5%) and the proportion of crises that are emergencies (32%).[26–28] Optimal treatment for hypertensive crises are outlined in the SAHS 2014 guidelines.[23] These guidelines were itemized and costed (**Table 1**, **eTable 3**), producing costs of around ZAR 2,500 (USD 176) for urgencies and ZAR 17,600 (USD 1,239) for emergencies.

Complications – Event Rates

We estimated the proportion of complications attributable to hypertension along with their acute and chronic costs. Five types of complication were considered: ischemic heart disease (IHD), stroke, chronic kidney disease (CKD), heart failure (HF), and hypertensive heart disease (HHD). While this is not an exhaustive list of conditions affected by hypertension, they were the complications most commonly included in previous costing studies[10,29] and there is strong evidence that hypertension is causative in their incidence.[30] We estimated the population-attributable fraction for each of these conditions associated with hypertension.

Overall rates of conditions which may be caused by hypertension were derived from the Global Burden of Disease Survey (GBDS) 2019, which combined multiple national surveys of demographics and health to produce sex-disaggregated estimates of incidence, prevalence, and disability-adjusted life years (DALYs) for different illnesses in South Africa.[31] This is a publicly available dataset.[32] Disability-adjusted life years are a metric which combine both the years of life lost from a health-related condition alongside the years of healthy life lost due to disability.[33] We took age-specific data from the GBDS and adjusted them with SSA population data (**eTable 4**). Due to perceived issues with HF coding, GBDS researchers decided to distribute its morbidity and mortality among multiple conditions. The majority of HF events are redistributed to IHD, stroke, and HHD.[34]

The GBDS provides direct estimates for the proportion of CKD events caused by hypertension. The population-attributable fraction (PAF) of IHD, stroke, and HHD associated with hypertension were estimated separately.[35] The PAF quantifies the proportion of events attributable to a given risk factor. It is estimated by predicting how many events would have occurred in subgroups of a population if a risk factor had been eliminated and comparing that number to actuality. We estimated the number of complications that would be prevented if mean SBP values in hypertensive subgroups were lowered to the mean value for normotensives. Hazard ratios of 1.24 and 1.16 per 10 mm Hg increase in SBP were employed for IHD and stroke, respectively.[36] For HHD, the hazard ratio decreased with older age, and ranged from 1.63 to 2.86 per 10 mm Hg increase in SBP.[37]

For the probabilistic analysis, we sampled hypertension rates from a Dirichlet distribution based on the NIDS 2017 analysis outlined above and IHD, stroke, CKD, and HHD rates from Gamma distributions of the GBDS 2019 data.

Complications – Costs

To estimate the cost of IHD, stroke, and CKD, published literature was reviewed to produce itemized lists of the costs associated with acute and chronic events. For acute events, we itemized costs for one hospitalisation and subsequent rehabilitative services (i.e., physiotherapy and occupation therapy for stroke and transplant patients). For chronic events,

we itemized costs for one year of treatment. Unit costs were assigned to these items from publicly available data.

A cost-effectiveness analysis[38] from South Africa combined clinical guidelines with expert opinion to create 'impact inventories' which list the different types of resource use associated with chronic conditions including IHD, stroke, and renal disease. These inventories included resource use for acute and chronic care and informed resource use in our model (**Table 1**, **eTables 5-6**). Unit costs were estimated with contemporary data which included the UPFS 2020, the Government Employee Medical Scheme 2019 tariffs, and public contracts for pharmaceutical products.[21,24,39] Estimated costs for IHD and stroke hospitalisations were around ZAR 16,400 (USD 1,160) and ZAR 23,900 (USD 1,680), respectively. Corresponding annual chronic care costs were ZAR 1,550 (USD 110) and ZAR 1,240 (USD 87).

In its early stages, CKD is largely treated through management of other CVD risk factors.[40] A proportion of patients with hypertension-related CKD will develop end-stage renal disease (ESRD). The South African Renal Registry provided information on the prevalence of ESRD and the proportion of CKD patients receiving haemodialysis, peritoneal dialysis, and kidney transplantation in the public healthcare system (**eTable 7**).[41] Itemized lists of resource use for dialysis and kidney transplant patients were taken from the cost-effectiveness paper described above (**Table 1**, **eTable 8**).[38] Resource use for kidney transplantation was derived from a cost-of-illness study of type-2 diabetes in South Africa.[42] Estimated annual costs for haemodialysis and peritoneal dialysis were ZAR 302,000 (USD 21,300) and ZAR 86,200 (USD 6,080), respectively. The cost of kidney transplantation was estimated to be around ZAR 139,000 (USD 9,770).

Societal Costs

A human capital approach was employed to calculate the societal cost of hypertension. This approach assumes that all healthy time lost due to illness (i.e., years of life lost and years of health life lost due to disability) leads to lost productivity.[43] Every DALY experienced by an individual aged 20 to 65 years attributable to hypertension was assigned the value of one gross domestic product (GDP) per worker, weighted by the proportion of the overall population who are currently employed (the "employment-to-population ratio").[44] Societal costs were only included for the population without private health insurance. The GDP per worker for South Africa was estimated to be ZAR 276,000 (USD 19,500).[45,46] The employment-to-population ratio was 43.3% for men and 33.2% for women.[12]

Sensitivity Analysis

The effect of key modelling parameters on cost estimates was examined with one-way sensitivity analysis. Epidemiologic model inputs were systematically altered between upper and lower bounds derived from the NIDS 2017 analysis and other secondary data analysis. The

resulting change in direct, societal, and overall costs were recorded. Results from the sensitivity analysis were presented in a tornado diagram.

General Cost Assumptions

The price of healthcare goods and services may vary across time and setting.[47] Costs indexed in years prior to 2020 were inflated using SSA's regularly updated consumer price index (CPI) estimates for medical services and medical products.[48] In addition, costs derived from private healthcare sources were deflated using the ratio of prices paid in private versus public healthcare settings.[42] All costs were converted to U.S. dollars to provide international context for results.[46]

Patient and Public Involvement

Patients and the general public were not directly involved in this study.

Results

Burden of Disease

We estimated that around 8.22 million (30.8%, 95% CI: 29.5-32.1%) adults aged ≥20 years without private health insurance have hypertension (**Table 2**). This proportion increased to 53.1% (95% CI: 50.7-55.7%) for adults aged ≥40 years. Rates of hypertension were greater for women and increased with age (**Table 3, eTable 9**). Around 51.1% (95% CI: 49.2-52.9%) of hypertension was diagnosed, 93.2% (95% CI: 91.6-94.5%) of diagnosed hypertension was treated, and 54.7% (95% CI: 52.2-57.3%) of treated hypertension was controlled (**eTable 10**). Diagnosis of existent hypertension, likelihood of receiving treatment, and likelihood of BP control on treatment were substantially higher for women and increased with age.

Hypertension leads to a significant burden of disease which increases with age. It was responsible for around 17.9% (95% CI: 15.4-20.5%) of IHD incidence, 27.6% (95% CI: 24.2-31.2%) of stroke incidence, and 82.8% of HHD incidence (95% CI: 79.5-85.6%) (**eTable 11**). Hypertension causes around 31,100 (95% CI: 29,000-36,9000) hypertensive crises, 14,000 (95% CI: 11,100-17,200) IHD events, 13,300 (95% CI: 10,600-16,300) strokes, and 6,110 (95% CI: 4,970-7,460) cases of CKD annually (**Table 2, eTable 12**). Many individuals suffer from chronic health conditions caused by hypertension, leading to around 517,000 DALYs. Women were estimated to experience more hypertensive crises, hypertension-related strokes, hypertension-related cases of CKD, and 50.6% of total hypertension-related DALYs (**eTable 13**).

Cost of Hypertension

The total cost of hypertension was ZAR 39.5 billion (95% CI: 35.0-44.5 billion) or USD 2.79 billion (95% CI: 2.47-3.31 billion). Total direct healthcare costs associated with hypertension were estimated to be ZAR 10.1 billion (95% CI: 8.98-11.3 billion) or USD 0.711 billion (95% CI: 0.633-0.793 billion) (**Table 4, eTable 14**). Direct hypertension screening and management costs

accounted for ZAR 8.75 billion (95% CI: 7.66 -9.88 billion) or USD 0.617 billion (95% CI: 0.541-0.697 billion). Stroke was responsible for the largest amount of hypertension-related complication costs, followed by IHD and hypertensive crises. The societal cost of hypertension was estimated to be ZAR 29.4 billion (95% CI: 26.0-33.2 billion) or USD 2.08 billion (95% CI: 1.83-2.34 billion). This was approximately 74.4% of the total cost of hypertension.

Direct healthcare costs of hypertension were higher for women (ZAR 6.11 billion or USD 0.431 billion) compared to men (ZAR 3.97 billion or USD 0.280 billion) (**eTable 14**). Conversely, societal costs of hypertension were lower for women (ZAR 10.5 billion or USD 0.743 billion) compared to men (ZAR 18.9 billion or USD 1.33 billion).

Sensitivity analysis showed that the proportion of the population with private health insurance, the societal cost of a DALY, the proportion of care that takes place in the public versus the private healthcare sector, and the overall prevalence of hypertension had the largest impact on total cost estimates (**Figure 1**). Substantial reductions in direct healthcare and societal costs could be achieved if the prevalence of hypertension were to be reduced.

Discussion

To our knowledge, this is the first study of the economic burden of hypertension in South Africa and it shows that hypertension exerts a heavy economic burden. Our estimate of hypertension's direct healthcare cost represents 4.4% of the combined projection for national and provincial public health expenditure in 2020.[49] The total cost of ZAR 39.5 billion or USD 2.79 billion represents around 0.76% of South Africa's GDP.[50] The management of hypertension must be considered in the context of other healthcare spending priorities. Previous studies have assessed the annual healthcare cost of type-2 diabetes in the public healthcare sector (USD 0.160 billion),[42] the annual cost of smoking (USD 2.54 billion),[51] and the annual cost associated with alcohol abuse (USD 2.27 billion).[52]

We estimated that around 30.8% of adults aged ≥20 years without private health insurance have hypertension. This is lower than previous studies, but is based on more contemporaneous data.[2–4,53,54] We also estimated that hypertension leads to 517,000 DALYs annually. This is substantially more than a previous burden of disease study which analysed data from 2000.[11]

While the majority of South Africans receive care in the public healthcare system, around 15% have private health insurance. We did not quantify the health and economic costs associated with hypertension in privately insured individuals. Previous studies have shown that income is not a significant predictor of elevated BP in South Africa but is a major determinant of hypertension awareness, treatment, and control.[4,55] Higher income individuals, including those with private health insurance, are more likely to receive treatment and are more likely to be employed. The average cost of hypertension management and the societal cost of

hypertension-related complications may be greater in this population. Conversely, rates of hypertension-related complications are likely lower in this population due to better BP control.

We estimated that expenditure on hypertension management represents a large proportion of the direct healthcare costs associated with the condition. It is likely that guideline-concordant care will lead to better controlled hypertension which will reduce future hypertension-related complications. Dynamic state transmission models can estimate the long-term health and cost consequences of interventions which seek to better control hypertension. Previous studies have shown that scaling up current hypertension treatment guidelines would be cost-effective for the healthcare sector.[38] Programmes which train community health workers about hypertension to improve medication adherence are also cost-effective.[56] Such interventions are urgently required to save healthcare costs and ultimately improve population health. Further research should establish additional cost-effective strategies to upscale and improve hypertension care.

Hypertension tends to cluster with a number of other prominent risk factors for NCDs (e.g. obesity, diabetes and high cholesterol).[57,58] Healthcare decision-makers may take advantage of this clustering effect to efficiently target legislative or regulatory levers to reduce behaviours which lead to high BP and other NCDs. Some such legislative actions have already taken place in South Africa (e.g. mandatory salt regulations, a tax on sugary beverages).[59,60] Further cost-effectiveness studies could consider the advent of food labels to promote healthier diets, banning the marketing unhealthy foods and beverages, provision of healthy foodstuffs to vulnerable populations, and other interventions already in place globally.[61]

Limitations

As with many health economic evaluations conducted in low- and middle-income countries, data availability was a limitation for this study. We synthesized data on the epidemiology of hypertension and costs of health services from multiple sources. Uncertainty from these sources will necessarily have propagated into our estimates. We explored this uncertainty with deterministic and probabilistic sensitivity analyses.

There is no system for the routine collection of national or subnational data in the South African public healthcare system. A 2015 governmental White Paper on NHI stated that a diagnosis-related grouping system will be developed for healthcare reimbursement along with an integrated national health information repository and data system.[9] This system could inform future costing and cost-effectiveness studies. For example, our study would have benefited from information on clinical compliance to APC guidelines for hypertension management. Despite data limitations, a key strength of our analysis was that model inputs regarding the prevalence of hypertension, healthcare utilization, and the price of healthcare resources were all derived from South African data.

We used the GBDS 2019 to estimate hypertension-related complication rates. The GBDS is a wide-ranging study which estimates disease incidence, prevalence, and severity in 204 countries and territories. It accomplishes this by synthesizing local epidemiologic data using complex statistical models [62]. This multi-country approach to modelling in the GBDS survey may lead researchers to overlook important local insights. For example, Pillay-van Wyk et al. reformulated South African mortality data to correct for misclassified HIV/AIDS mortality.[63] They found that these adjustments led to significant variation between local and GBDS estimates of mortality and morbidity for several conditions including HHD and stroke.

When estimating societal costs, we assumed that GDP accounts for the total value of all goods and services made within a country. Gross domestic product may underestimate activity in the 'informal' labour market and informal work (e.g. housekeeping, caretaking).[64] Around 3.0 million South Africans work in the informal sector.[12] Sensitivity analysis found that the way we valued DALYs greatly affected overall estimates of the societal cost of hypertension.

Finally, this costing analysis commenced during the Coronavirus 2019 (COVID-19) pandemic. Many healthcare resources have been redirected towards the prevention and treatment of COVID-19 in South Africa. Much is still to be learned about the relationship between COVID-19 and hypertension. Some studies suggest that hypertension is predictive of severe illness.[65–67] Moreover, disruption in access to blood pressure screening and management may have led to an increase in uncontrolled hypertension and its complications.

Conclusion

Hypertension is highly prevalent in South Africa. A large proportion of public healthcare budgets are spent screening, treating, and controlling hypertension. An even greater economic burden is caused by reduced productivity attributable to the condition. Research is required to establish priority cost-effective strategies for lowering rates of hypertension and preventing complications.

Contributorship statement

CNKL developed the costing model, conducted the data analysis, interpreted results, and wrote the first draft of the manuscript. AE and KJH developed the idea for the study, secured the funding, and contributed to results interpretation, data analysis, and manuscript revisions. BLR contributed to results interpretation, data analysis, and manuscript revisions. All authors approved the final version of the manuscript.

Conflicts of Interest

Authors have no conflict of interest to declare.

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Data sharing statement

We used publicly available data to conduct our analysis. Access to the Microsoft Excel-based hypertension costing model is available by contacting ciaran.kohli-lynch@northwestern.edu.

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Table 1: Cost inputs
Derivation of costs outlined in text and eTables 3-10

Parameter	Cost (ZAR 2020)	Sources
Visit costs		
Screening visit	144.00	21
Check-up visit	229.00	21
Medication, cost per day		
Hydrochlorothiazide 12.5 mg	0.14	24
Hydrochlorothiazide 25 mg	0.12	24
Enalapril 10 mg	0.16	24
Enalapril 20 mg	0.23	24
Amlodipine 5 mg	0.12	24
Amlodipine 10 mg	0.16	24
Spironolactone 25 mg	0.46	24
Hypertensive crises		
Urgencies	2,499.66	21,24
Emergencies	17,571.66	21,24
Hypertension-related complications		
Acute ischemic heart disease	16,407.20	21,24,38,68
Chronic ischemic heart disease	1,554.21	21,24,38,68
Acute stroke	23,883.23	21,24,38,68
Chronic stroke	1,235.21	21,24,38,68
Hemodialysis for end-stage renal disease	301,694.92	21,24,38,68
Peritoneal dialysis for end-stage renal disease	86,227.42	21,24,38,68
Transplant for end-stage renal disease	138,523.75	42
Societal costs		
Disability-adjusted life year	99,983.00	45
Physician visit (1.5 hours)	17.11	21,50
Hypertensive crisis (2 days)	54,748.00	21,24,50

Table 2: Hypertension-related complications treated in South African public healthcare system

Hypertension-Related Condition	Counts of conditions per year (95% CI)
Total number with hypertension* (% of age-group, 95% CI)	
Ages ≥20 years	8,219,164 (30.8, 29.5-32.1)
Ages ≥40 years	6,428,960 (53.1, 50.7-55.7)
Hypertensive crises	
Hypertensive urgencies	10,033 (8,401-11,897)
Hypertensive emergency	21,068 (17,640-24,983)
Ischemic heart disease	
Ischemic heart disease, incidence	13,991 (11,082-17,193)
Ischemic heart disease, prevalence	125,974 (103,829-150,104)
Ischemic heart disease, DALYs	99,927 (83,936-118,119)
Stroke	
Stroke, incidence	13,308 (10,611-16,336)
Stroke, prevalence	113,056 (95,427-132,961)
Stroke, DALYs	156,813 (132,327-182,448)
Chronic kidney disease	
Chronic kidney disease, incidence	6,105 (4,974-7,459)
Chronic kidney disease, prevalence	119,814 (108,219-131,274)
Chronic kidney disease, DALYs	88,913 (71,937-107,987)
Hypertensive heart disease	
Hypertensive heart disease, DALYs	171,202 (144,414-198,969)

* HTN grades 1-3 or currently receiving antihypertensive medication
CI – confidence interval, DALY – disability-adjusted life year

Table 3: Prevalence of SBP categories in SA adults without private health insurance

Population	Hypertension Category				
	Normotensive	Grade 1a	Grade 1b	Grade 2	Grade 3
Proportion of population (95% CI)					
Overall population (≥20 years)	77.7 (76.8-78.5)	4.3 (3.8-4.7)	10.4 (9.8-11.0)	5.2 (4.8-5.7)	2.5 (2.2-2.8)
Young adults (age 20-39 years)	87.1 (86.1-88.0)	5.0 (4.4-5.6)	4.9 (4.3-5.5)	2.2 (1.9-2.6)	0.9 (0.7-1.2)
Middle adults (age 40-69 years)	67.1 (65.5-68.6)	3.8 (3.1-4.6)	16.5 (15.3-17.7)	8.4 (7.5-9.3)	4.2 (3.6-4.9)
Older adults (age ≥70 years)	54.8 (50.6-59.0)	n/a	24.3 (20.9-27.9)	14.2 (11.3-17.6)	6.7 (4.9-8.8)
SBP (mm Hg) within category, mean (95% CI)					
Overall population	114 (91-137)	136 (117-156)	132 (114-152)	144 (123-172)	162 (140-197)
Young adults (age 20-39 years)	112 (90-135)	137 (117-156)	133 (112-153)	147 (120-159)	165 (140-191)
Middle adults (age 40-69 years)	117 (92-138)	138 (119-139)	142 (116-153)	158 (125-174)	182 (141-194)
Older adults (age ≥70 years)	122 (92-138)	n/a	146 (118-139)	166 (125-156)	190 (142-158)

Normotension: SBP <140 mm Hg and DBP <90 mm Hg, Grade 1a: SBP 140-159 mm Hg or DBP 90-99 mm Hg with no other CVRFs, Grade 1b: SBP 140-159 mm Hg or DBP 90-99 mm Hg with another CVRF, Grade 2: SBP 160-179 mm Hg or DBP 100-109 mm Hg, Grade 3: SBP ≥180 mm Hg. If an individual had differential grades of systolic and diastolic BP, they were assigned the more severe of the two categories. Additional cardiovascular risk factors: smoking, diabetes, men aged ≥55 years, women aged ≥65 years, men waist circumference ≥94 cm, women waist circumference ≥80 cm.
CI – confidence interval, CVRF – cardiovascular risk factor, DBP – diastolic blood pressure, SBP – systolic blood pressure

Table 4: Cost of hypertension in South African population with no private insurance

Cost Type	Cost, Millions (ZAR 2020)	Cost, Millions (USD 2020)
Direct healthcare costs	10,080 (8,983-11,251)	711 (633-793)
Age-group		
Young adults (age 20-39 years)	1,244 (1,023-1,495)	88 (72-105)
Middle adults (age 40-69 years)	6,510 (5,687-7,428)	459 (401-524)
Older adults (age ≥70 years)	2,326 (1,733-2,999)	164 (122-211)
Type of cost		
Screening	1,462 (1,309-1,613)	103 (92-114)
Management	7,285 (6,366-8,264)	514 (449-583)
Complications	1,334 (1,129-1,552)	81 (69-93)
Hypertensive crises	395 (331-469)	28 (23-33)
Ischemic heart disease	447 (370-526)	32 (26-37)
Stroke	472 (391-560)	33 (28-39)
Chronic kidney disease	19 (17-21)	1.3 (1.2-1.4)
Societal costs	29,436 (25,979-33,200)	2,075 (1,832-2,341)
Age-group		
Young adults (age 20-39 years)	3,318 (2,516-4,272)	234 (177-301)
Middle adults (age 40-69 years)*	26,118 (22,805-29,733)	1,842 (1,608-2,096)
Type of cost		
Management	39 (32-45)	2.7 (2.2-3.2)
Complications	29,397 (25,940-33,161)	2,073 (1,829-2,338)
Ischemic heart disease	5,376 (4,344-6,583)	379 (306-464)
Stroke	7,481 (6,185-8,977)	527 (436-633)
Chronic kidney disease	6,107 (4,433-7,991)	431 (313-563)
Hypertensive heart disease	10,434 (8,190-12,778)	736 (577-901)

*Societal costs incurred until age 65

Figure 1: Tornado diagram showing results of sensitivity analyses

Legend: Figure indicates changes in direct healthcare and societal cost estimates associated with changing key model input parameters. CKD – chronic kidney disease, DALY – disability-adjusted life year, HHD – hypertensive heart disease, HTN – hypertension, IHD – ischemic heart disease

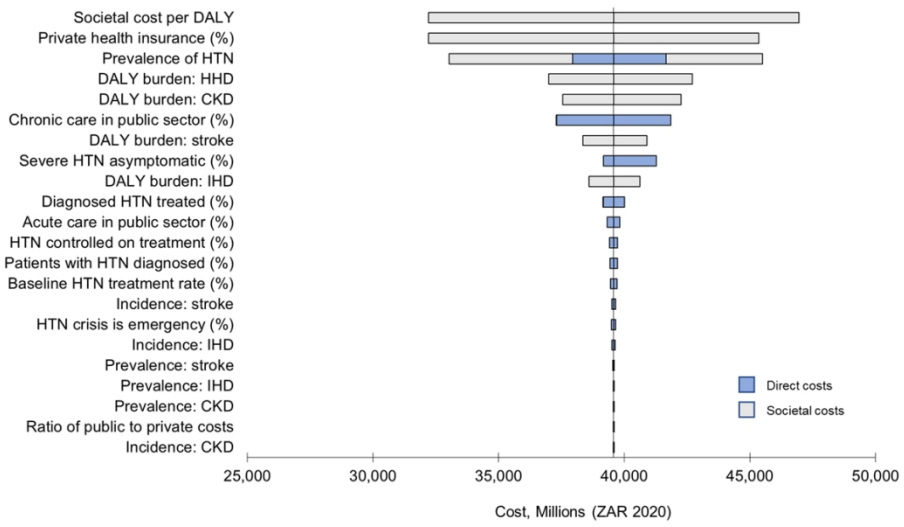

Figure indicates changes in direct healthcare and societal cost estimates associated with changing key model input parameters. CKD – chronic kidney disease, DALY – disability-adjusted life year, HHD – hypertensive heart disease, HTN – hypertension, IHD – ischemic heart disease

569x316mm (59 x 59 DPI)

Supplementary Online Content

Title: Hypertension in the South African Public Healthcare System: A Cost-of-Illness and Burden of Disease Study

Short title: Health and Economic Burden of Hypertension in South Africa

Table of Contents

Title: Hypertension in the South African Public Healthcare System: A Cost-of-Illness and Burden of Disease Study

Short title: Health and Economic Burden of Hypertension in South Africa

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Key words: Economic burden; Cost-of-illness; Hypertension; Blood pressure; Non-communicable disease; South Africa.

Supplement

I. The National Income Dynamic Survey 2017

The National Income Dynamics Survey 2017 is the most contemporary national survey for South Africa. It contains individual-level blood pressure (BP), other health, and demographic information. The NIDS is a government-funded national household panel survey which is conducted every two years. It commenced in 2008, collecting data from more than 28,000 individuals on health, education, income, poverty, well-being, mortality, and migration. A 'top-up sample' was added in 2017 to account for attrition in recent waves.[1] Each wave of the survey has assigned cross-sectional sample weights which allow researchers to calibrate results to be representative of the contemporary South African population.[2] These weights were applied in our analyses.

Household surveys and individual surveys were completed for NIDS 2017. Respondents provided information through face-to-face interviews. Individuals were asked if they had ever been diagnosed with a list of health conditions which included hypertension and diabetes. They were also asked if they were currently taking medication for high BP. In addition, anthropometric measurements were taken alongside all individual questionnaires. Fieldworkers measured participants' height, weight, waist circumference, pulse, systolic blood pressure (SBP) and diastolic blood pressure (DBP). Blood pressure was measured twice. In our analyses, we used the average of these two measurements. Blood pressure was measured in the participant's left arm, after they had been seated for a minimum of 5 minutes. Blood pressure was recorded with an automated oscillometric devices (Omron M7 BP Monitor) which used standard multi-size cuffs.[3] Readings for SBP were excluded if <70 mm Hg and ≥270 mm Hg. Readings for DBP were excluded if <30 mm Hg and ≥180 mm Hg. Readings were also excluded if the differences between SBP and DBP was <15 mm Hg. These exclusions were enforced to ensure plausible BP readings were obtained, as defined by the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group. Fieldworkers received special training sessions in anthropometric measurement techniques from qualified nurses. Daily assessments were conducted to ensure the quality of fieldworker measurements.

II. Treatment to Manage Hypertension

Estimating the cost of treatment to manage hypertension involved three steps. First, the National Department of Health's Adult Primary Care (APC) 2019-20 hypertension treatment guidelines were reviewed and cost elements were itemized. Next, prices were applied to these costs. Finally, a decision tree was constructed to predict the number of patients receiving each stage of treatment suggested by the APC 2019-20, based on assumptions regarding hypertension control on medication. As BP treatment is not generally recommended for children or adolescents, costs were not incurred in these individuals.

There are seven BP management 'steps' outlined in the APC 2019-20 guidelines, involving increasing treatment intensity. Hypertensive patients start at a different level of treatment dependent on their hypertension grade. The steps are listed below:

- Step 1: Manage hypertension and cardiovascular risk through lifestyle advice. Reassess BP after three months, if uncontrolled move to Step 2.
- Step 2: Add hydrochlorothiazide 12.5mg daily. Reassess BP after one month, if uncontrolled move to Step 3.
- Step 3: Add enalapril 10mg daily. Reassess BP after one month, if uncontrolled move to Step 4.
- Step 4: Increase enalapril to 20mg daily. Reassess BP after one month, if uncontrolled move to Step 5.
- Step 5: Add amlodipine 5mg daily. Reassess BP after one month, if uncontrolled move to Step 6.
- Step 6: Increase amlodipine to 10mg daily. Reassess BP after one month, if uncontrolled move to Step 7.
- Step 7: Add spironolactone 25mg daily and increase HCTZ to 25mg daily. Reassess BP weekly until controlled.

Individuals with Grade 1a hypertension commence at Step 1. Individuals with Grade 1b and Grade 2 hypertension start on Step 2, and those with Grade 3 start on Step 3. A final, end-of-year, visit is recommended for all hypertensive patients. Step 7 was only recommended for patients with Grade 3 hypertension.

A decision tree was produced to estimate costs associated with different treatment steps. The tree predicted the number of steps required to control hypertension in different subgroups of patients. Probabilities of hypertension control while on treatment **(Supplementary Table 1)** were converted to rates in order to achieve observed rates of control after six potential increases in treatment intensity.

The structure of the decision tree is presented in **eFigure 1**. This example specifically models the scenario where patients begin with Grade 1a hypertension. Individuals receive lifestyle advice upon presenting with BP of 140-159/90-99 mm Hg and no other cardiovascular disease risk factors. All patients incur a visit cost at 3 months, at which point a proportion of patients will have achieved BP control. Individuals who have achieved control and remain uncontrolled incur the cost of one outpatient visit at this point. For patients who remain uncontrolled, they are prescribed Step 2 treatment (hydrochlorothiazide 12.5mg daily) and re-evaluated one month later. Again, a proportion of these patients will be controlled after one month. These patients are assumed to remain on Step 2 treatment for the remainder of the year. Uncontrolled patients incur the cost of one month of Step 2 treatment and progress to Step 3 (add enalapril 10mg daily). This process repeats itself until the highest step of treatment has been tried for a month, at which stage uncontrolled patients are considered to have treatment-resistant hypertension.[4] All patients incur a final visit cost at 12 months. Similar decision trees were constructed for patients who started at different steps in the treatment cascade.

eTable 1. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Page 1 Line 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Page 2, Lines 1-35
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	Page 5, Lines 6-23
		Present the study question and its relevance for health policy or practice decisions.	Page 5, Lines 25-35
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 5, Lines 34-35 Page 6, Lines 5-10
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 6, Lines 5-6
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 5, Line 34 Page 6, Line 5
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	n/a
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 4, Line 34
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 6, Lines 9-10
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 9, Lines 1-33
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	n/a
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	n/a
Measurement and valuation of preference-based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n/a
Estimating resources and	13a	*Single study-based economic evaluation:*	Not applicable

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
costs		Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 6, Lines 12-40 Page 7, Lines 38-41 Page 8, Lines 1-30 Page 9, Lines 35-41 Page 10, Lines 1-33
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 11, Line 1-7
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	n/a
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Page 8, Line 12 -Page 10, Line 34 eTables 5-6 eTable 8 eFigure 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 7, Lines 4-36 Page 8, Lines 9-30 Page 9, Lines 1-33 Page 10, lines 24-33 Supplementary Material
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Methods Table 1
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If	n/a

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
		applicable, report incremental cost-effectiveness ratios.	
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Results Figure 1 Table 2 Table 3 Table 4
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Results Table 2 Table 3 Table 4 eTables 9-14
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Page 12, Lines 15-39 Page 13, Lines 1-20
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 15, Lines 11-15
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 15, Lines 8-9

eTable 2: Cost items for hypertension screening and management

Parameter	Unit price (ZAR 2020)	Source
Screening		
Level 1 facility visit fee	78.00	5
Nurse practitioner visit	66.00	5
Medication		
Hydrochlorothiazide 12.5 mg	0.14	6
Hydrochlorothiazide 25 mg	0.12	6
Enalapril 10 mg	0.16	6
Enalapril 20 mg	0.23	6
Amlodipine 5 mg	0.12	6
Amlodipine 10 mg	0.16	6
Spironolactone 25 mg	0.46	6
Check-ups		
Level 1 facility visit fee	114.00	5
Physician visit	115.00	5

Total cost per check-up visit: ZAR 229.00

eTable 3: Cost items for treatment of hypertensive crises

Parameter	Units required	Unit price (ZAR 2020)	Source
Hypertensive urgency, total cost: ZAR 2,499.66 (USD 176)			
Inpatient (general ward) - level 2 facility	2	1,073.00	[5]
Inpatient (general ward) – physician	2	175.00	[5]
Step 5 medication, 1 day	2	1.83	[6]
Hypertensive emergency, total cost: ZAR 8,787.66 (USD 619)			
Inpatient (intensive care) - level 2 facility	2	8,580.00	[5]
Inpatient (intensive care) - physician	2	204.00	[5]
Step 5 medication	2	1.83	[6]

eTable 4A: Numbers of ischemic heart disease, stroke, chronic kidney disease due to hypertension, and hypertensive heart disease events in Global Burden of Disease Study 2019, women and men combined

Complication	Incidence (95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischemic heart disease				
Young adults (age 20-39 years)	9,060 (6,077-12,657)	41,796 (34,331-50,885)	48,279 (31,676-68,175)	7,8
Middle adults (age 40-69 years)	58,751 (42,438-77,283)	506,513 (425,280-603,082)	378,098 (311,347-448,191)	
Older adults (age ≥70 years)	41,071 (33,405-49,799)	395,931 (341,926-458,351)	235,392 (208,951-257,140)	
Stroke				
Young adults (age 20-39 years)	4,946 (3,363-7,184)	113,697 (90,942-138,124)	63,584 (45,020-85,740)	7,8
Middle adults (age 40-69 years)	36,205 (27,344-47,241)	341,901 (287,672-405,362)	348,281 (294,883-406,236)	
Older adults (age ≥70 years)	26,564 (21,642-32,577)	189,963 (157,097-226,793)	272,768 (244,413-296,115)	
Chronic kidney disease due to hypertension				
Young adults (age 20-39 years)	453 (249-706)	20,645 (15,580-26,890)	15,639 (8,974-24,899)	7,8
Middle adults (age 40-69 years)	4,762 (3,314-6,449)	77,889 (65,466-91,808)	56,577 (39,388-78,878)	
Older adults (age ≥70 years)	3,335 (2,758-3,982)	71,144 (63,224-79,930)	34,187 (28,152-40,878)	
Hypertensive heart disease				
Young adults (age 20-39 years)	-	-	15,100 (9,075-22,917)	7,8
Middle adults (age 40-69 years)	-	-	133,725 (102,977-170,355)	
Older adults (age ≥70 years)	-	-	100,514 (84,387-115,093)	

CI – confidence interval, DALY – disability adjusted life years

eTable 4B: Numbers of ischemic heart disease, stroke, chronic kidney disease due to hypertension, and hypertensive heart disease events in Global Burden of Disease Study 2019, women

Complication	Incidence (95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischemic heart disease				
Young adults (age 20-39 years)	3,396 (2,226-4,828)	14,212 (11,670-17,319)	13,110 (6,475-21,192)	7,8
Middle adults (age 40-69 years)	25,843 (18,552-33,963)	206,410 (174,297-243,197)	128,017 (103,671-153,349)	
Older adults (age ≥70 years)	23,271 (18,938-28,207)	206,437 (179,378-237,049)	133,704 (118,401-149,039)	
Stroke				
Young adults (age 20-39 years)	2,246 (1,483-3,356)	64,192 (51,413-77,963)	25,665 (16,229-36,993)	7,8
Middle adults (age 40-69 years)	19,423 (14,586-25,418)	190,775 (160,548-226,408)	163,629 (138,728-190,486)	
Older adults (age ≥70 years)	17,952 (14,599-21,983)	126,750 (105,083-150,732)	181,597 (161,965-197,300)	
Chronic kidney disease due to hypertension				
Young adults (age 20-39 years)	188 (100-298)	9,681 (7,310-12,528)	5,674 (3,032-9,489)	7,8
Middle adults (age 40-69 years)	2,246 (1,548-3,069)	38,344 (32,191-45,038)	22,156 (15,420-30,836)	
Older adults (age ≥70 years)	1,793 (1,490-2,141)	40,496 (36,040-45,576)	18,307 (15,091-21,716)	
Hypertensive heart disease				
Young adults (age 20-39 years)	-	-	7,039 (3,503-11,688)	7,8
Middle adults (age 40-69 years)	-	-	68,987 (53,370-86,912)	
Older adults (age ≥70 years)	-	-	70,699 (59,786-80,888)	

CI – confidence interval, DALY – disability adjusted life years

eTable 4C: Numbers of ischemic heart disease, stroke, chronic kidney disease due to hypertension, and hypertensive heart disease events in Global Burden of Disease Study 2019, men

Complication	Incidence (95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischemic heart disease				
Young adults (age 20-39 years)	5,664 (3,851-7,829)	27,584 (22,661-33,567)	35,169 (25,201-46,983)	[7,8]
Middle adults (age 40-69 years)	32,908 (23,887-43,320)	300,102 (250,983-359,884)	250,081 (207,676-294,842)	
Older adults (age ≥70 years)	17,799 (14,468-21592)	189,495 (16,2548-221,303)	99,688 (90,550-108,101)	
Stroke				
Young adults (age 20-39 years)	2,699 (1,880-3,828)	49,506 (39,529-60,161)	37,919 (28,791-48,747)	[7,8]
Middle adults (age 40-69 years)	16,782 (12,758-21,823)	151,126 (127,124-178,954)	184,652 (156,155-215,750)	
Older adults (age ≥70 years)	8,612 (7,044-105,95)	63,213 (52,014-76,062)	91,171 (82,449-98,815)	
Chronic kidney disease due to hypertension				
Young adults (age 20-39 years)	265 (149-407)	10,964 (8,271-14,363)	9,965 (5,942-15,410)	[7,8]
Middle adults (age 40-69 years)	2,516 (1,765-3,380)	39,545 (33,276-46,770)	34,421 (23,968-48,042)	
Older adults (age ≥70 years)	1,542 (1,268-1,841)	30,647 (27,183-34,354)	15,880 (13,061-19,162)	
Hypertensive heart disease				
Young adults (age 20-39 years)	-	-	8,061 (5,573-11,230)	[7,8]
Middle adults (age 40-69 years)	-	-	64,738 (49,606-83,443)	
Older adults (age ≥70 years)	-	-	29,816 (24,601-34,204)	

CI – confidence interval, DALYs – disability adjusted life years

eTable 5: Acute and annual chronic care costs, ischemic heart disease

Parameter	Units required	Unit price (ZAR 2020)	Source
Acute care, total cost: ZAR 16,407 (USD 1,157)			
Inpatient (general ward) – level 2 facility	2.5	1,073.00	[5,9]
Inpatient (general ward) – physician	2.5	175.00	[5,9]
Morphine	10.0	2.73	[6,9]
Aspirin	7.5	0.39	[6,9]
Prochlorperazine	2.5	167.53	[6,9]
Streptokinase	1.0	3,471.13	[6,9]
Enoxaparin	2.0	19.38	[6,9]
Clopidogrel	5.5	933.39	[6,9]
Daily drawing blood (test)	2.5	41.00	[5,9]
Echocardiography (test)	1.0	1,285.15	[6,9]
Daily electrolytes and urea (test)	2.5	108.96	[9,10]
Daily blood count (test)	2.5	74.10	[9,10]
Daily blood glucose (test)	2.5	38.76	[9,10]
Daily liver function (test)	2.5	359.21	[9,10]
Daily lipid (test)	2.5	132.16	[9,10]
Daily thyroid function (test)	2.5	409.62	[9,10]
Annual chronic care, total cost: ZAR 1,554 (USD 110)			
Nurse visit - level 1 facility	6.0	78.00	[5,9]
Nurse visit – nurse fees	6.0	59.00	[5,9]
Physician visit - level 1 facility	1.0	114.00	[5,9]
Physician visit - physician fees	1.0	115.00	[5,9]
Aspirin, daily	365	0.43	[6,9]
Statin, daily	365	0.94	[6,9]

eTable 6: Acute and annual chronic care costs, stroke

Parameter	Units required	Unit price (ZAR 2020)	Source
Acute care, total cost: ZAR 23,883 (USD 1,684)			
Inpatient (general ward) – Level 2 facility	14.0	1,073.00	[5,9]
Inpatient (general ward) – physician	14.0	175.00	[5,9]
Physiotherapy	1.0	1,080.97	[6,9]
Occupational therapy	1.0	401.88	[6,9]
Aspirin	14.0	0.41	[6,9]
Streptokinase	1.0	3,471.13	[6,9]
CT scan (test)	5.0	175.00	[6,9]
Drawing blood (test)	5.0	41.00	[6,9]
Blood count (test)	5.0	74.10	[5,9]
Annual chronic care, total cost: ZAR 1,235 (USD 87)			
Nurse visit - level 1 facility	2.0	78.00	[5,9]
Nurse visit – nurse fees	2.0	59.00	[5,9]
Physician visit - level 1 facility	2.0	114.00	[5,9]
Physician visit - physician fees	2.0	115.00	[5,9]
Aspirin, daily	365	0.43	[6,9]
Statin, daily	365	0.94	[6,9]

eTable 7: Proportion of chronic kidney disease patients in public healthcare system with end-stage renal disease and type of treatment

Parameter	Value	Source
Number with CKD	4,749,648	[7]
Number receiving haemodialysis	1,282	[11]
Number receiving peritoneal dialysis	814	[11]
Number receiving transplant	1,038	[11]
Proportion CKD receiving haemodialysis	0.00027	[7,11]
Proportion CKD receiving peritoneal dialysis	0.00017	[7,11]
Proportion CKD receiving kidney transplant	0.00022	[7,11]

CKD – chronic kidney disease

eTable 8: Cost of treating end-stage renal disease

Parameter	Units required, annual	Unit price (ZAR 2020)	Source
Haemodialysis, total cost (annual): ZAR 301,695 (USD 21,272)			
Haemodialysis - Level 2 facility	156.00	1,643.00	5,9
Haemodialysis - nurse practitioner	156.00	252.00	5,9
Physician visit - Level 1 facility	4.00	114.00	5,9
Physician visit - physician	4.00	115.00	5,9
Occupational therapy	1.00	391.04	9,12
Drawing blood (test)	1.00	41.00	5,9
Electrolytes and urea (test)	4.00	108.96	9,10
Parathyroid hormone (test)	4.00	195.16	9,10
Blood count (test)	4.00	74.10	9,10
Liver function tests (test)	4.00	359.21	9,10
Calcium test (test)	4.00	38.76	9,10
Alkaline phosphosate test (test)	4.00	354.12	9,10
Albumin (test)	4.00	51.40	9,10
Peritoneal dialysis, total cost (annual): ZAR 86,227 (USD 6,080)			
Peritoneal dialysis - Level 1 facility	156.00	254.00	5,9
Peritoneal dialysis - nurse practitioner	156.00	252.00	5,9
Physician visit - Level 1 facility	4.00	114.00	5,9
Physician visit - physician	4.00	115.00	5,9
Occupational therapy	4.00	401.88	6,9
Drawing blood (test)	1.00	41.00	5,9
Electrolytes and urea tests (test)	4.00	108.96	9,10
Parathyroid hormone (test)	4.00	195.16	9,10
Blood count (test)	4.00	74.10	9,10
Liver function tests (test)	4.00	359.21	9,10
Calcium test (test)	4.00	38.76	9,10
Kidney transplant, total cost: ZAR 138,524 (USD 9,767)			
Procedure	1.00	4,886.73	13
Hospitalisation: recipient	1.00	24,439.80	13
Hospitalisation: donor	1.00	15,552.60	13
Follow-Up outpatient consultation	1.00	392.67	13
Post-transplant dietitian consultation	1.00	383.80	13
Post-transplant physiotherapist	1.00	383.80	13

eTable 9A: Prevalence of SBP categories in National Income Dynamics Survey 2017, combined women and men

Population	Hypertension category				
	Normotensive	Grade 1a	Grade 1b	Grade 2	Grade 3
Population with no private health insurance					
Proportion of population (95% CI)					
Overall population (age ≥20 years)	77.7 (76.8-78.5)	4.3 (3.8-4.7)	10.4 (9.8-11.0)	5.2 (4.8-5.7)	2.5 (2.2-2.8)
Young adults (age 20-39 years)	87.1 (86.1-88.0)	5.0 (4.4-5.6)	4.9 (4.3-5.5)	2.2 (1.8-2.6)	0.9 (0.7-1.2)
Middle adults (age 40-69 years)	67.1 (65.5-68.6)	3.8 (3.1-4.6)	16.5 (15.3-17.7)	8.4 (7.5-9.3)	4.2 (3.6-4.9)
Older adults (age ≥70 years)	54.8 (50.6-59.0)	n/a	24.3 (20.9-27.9)	14.2 (11.3-17.6)	6.7 (4.9-8.8)
Mean SBP within category (mm Hg)					
Overall population (age ≥20 years)	114 (91-137)	136 (117-156)	132 (114-152)	144 (123-162)	162 (140-197)
Young adults (age 20-39 years)	112 (90-135)	137 (117-156)	133 (112-153)	147 (120-159)	165 (140-191)
Middle adults (age 40-69 years)	117 (92-138)	138 (119-139)	142 (116-153)	158 (125-174)	182 (141-194)
Older adults (age ≥70 years)	122 (92-138)	n/a	146 (118-139)	166 (125-176)	190 (142-158)
Population with no private health insurance and no antihypertensive medication					
Proportion of population (95% CI)					
Overall population (age ≥20 years)	81.5 (80.6-82.4)	4.7 (4.2-5.2)	8.1 (7.5-8.7)	3.9 (3.5-4.4)	1.7 (1.5-2.1)
Young adults (age 20-39 years)	87.8 (86.9-88.7)	4.9 (4.4-5.5)	4.5 (4-5.1)	2 (1.6-2.4)	0.8 (0.5-1)
Middle adults (age 40-69 years)	71.5 (69.6-73.3)	4.7 (3.8-5.7)	13.6 (12.3-15)	7.1 (6.1-8.1)	3.2 (2.5-4)
Older adults (age ≥70 years)	56.8 (50.8-62.6)	n/a	26.1 (20.7-32.2)	9.9 (6.8-13.9)	7.2 (4.6-10.6)
Mean SBP within category (mm Hg)					
Overall population (age ≥20 years)	113 (90-137)	137 (117-156)	139 (116-158)	155 (126-177)	178 (142-220)
Young adults (age 20-39 years)	112 (90-135)	137 (117-156)	133 (112-154)	147 (122-172)	164 (142-191)
Middle adults (age 40-69 years)	116 (92-137)	137 (119-156)	141 (119-158)	158 (131-187)	181 (142-219)
Older adults (age ≥70 years)	122 (98-139)	n/a	146 (127-160)	166 (152-187)	194 (178-225)

CI – confidence interval; Normotension: SBP <140 mm Hg and DBP <90 mm Hg, Grade 1a: SBP 140-159 mm Hg or DBP 90-99 mm Hg with no other CVRFs, Grade 1b: SBP 140-159 mm Hg or DBP 90-99 mm Hg with another CVRF, Grade 2: SBP 160-179 mm Hg or DBP 100-109 mm Hg, Grade 3: SBP ≥180 mm Hg. If an individual had differential grades of systolic and diastolic BP, they were assigned the more severe of the two categories. Additional cardiovascular risk factors: smoking, diabetes, men aged ≥55 years, women aged ≥65 years, men waist circumference ≥94 cm, women waist circumference ≥80 cm.
CVRF – cardiovascular risk factor, DBP – diastolic blood pressure, SBP – systolic blood pressure

eTable 9B: Prevalence of SBP categories in National Income Dynamics Survey 2017, women

Population	Hypertension Category				
	Normotensive	Grade 1a	Grade 1b	Grade 2	Grade 3
Population with no private health insurance					
Proportion of population (95% CI)					
Overall population (age ≥20 years)	78.7 (77.8-79.8)	1.1 (0.9-1.4)	12.3 (11.5-13.2)	5.2 (4.6-5.8)	2.6 (2.2-3.0)
Young adults (age 20-39 years)	89.7 (86.1-88)	1.3 (4.4-5.6)	6.1 (4.3-5.5)	1.9 (1.8-2.6)	1 (0.7-1.2)
Middle adults (age 40-69 years)	68.3 (65.5-68.6)	1.1 (3.1-4.6)	18.5 (15.3-17.7)	8.1 (7.5-9.3)	4 (3.6-4.9)
Older adults (age ≥70 years)	54.5 (50.6-59)	n/a	25 (20.9-27.9)	14 (11.3-17.6)	6.6 (4.9-8.8)
Mean SBP within category (mm Hg)					
Overall population (age ≥20 years)	112 (90-136)	133 (112-157)	139 (116-158)	157 (125-168)	180 (142-223)
Young adults (age 20-39 years)	109 (89-133)	129 (112-152)	131 (111-153)	143 (120-162)	162 (141-184)
Middle adults (age 40-69 years)	116 (92-137)	138 (123-158)	141 (119-159)	158 (130-178)	182 (143-223)
Older adults (age ≥70 years)	122 (97-139)	n/a	146 (125-159)	166 (142-178)	190 (148-222)
Population with no private health insurance and no antihypertensive medication					
Proportion of population (95% CI)					
Overall population (age ≥20 years)	84.1 (83.0-85.1)	1.3 (1.0-1.6)	9.5 (8.7-10.4)	3.6 (3.1-4.2)	1.6 (1.3-1.9)
Young adults (age 20-39 years)	90.6 (86.9-88.7)	1.3 (4.4-5.5)	5.6 (4.0-5.1)	1.8 (1.6-2.4)	0.8 (0.5-1)
Middle adults (age 40-69 years)	73.9 (69.6-73.3)	1.3 (3.8-5.7)	15.4 (12.3-15)	6.6 (6.1-8.1)	2.7 (2.5-4)
Older adults (age ≥70 years)	59.6 (50.8-62.6)	n/a	25.4 (20.7-32.2)	9.2 (6.8-13.9)	5.8 (4.6-10.6)
Mean SBP within category (mm Hg)					
Overall population (age ≥20 years)	111 (89-135)	132 (112-156)	137 (114-158)	153 (123-176)	177 (141-223)
Young adults (age 20-39 years)	109 (89-133)	129 (111-153)	131 (111-152)	142 (120-172)	161 (140-183)
Middle adults (age 40-69 years)	115 (92-137)	137 (123-157)	140 (118-159)	157 (128-186)	180 (141-225)
Older adults (age ≥70 years)	121 (98-139)	n/a	145 (127-160)	164 (142-187)	198 (181-224)

CI – confidence interval; Normotension: SBP <140 mm Hg and DBP <90 mm Hg, Grade 1a: SBP 140-159 mm Hg or DBP 90-99 mm Hg with no other CVRFs, Grade 1b: SBP 140-159 mm Hg or DBP 90-99 mm Hg with another CVRF, Grade 2: SBP 160-179 mm Hg or DBP 100-109 mm Hg, Grade 3: SBP ≥180 mm Hg. If an individual had differential grades of systolic and diastolic BP, they were assigned the more severe of the two categories. Additional cardiovascular risk factors: smoking, diabetes, men aged ≥55 years, women aged ≥65 years, men waist circumference ≥94 cm, women waist circumference ≥80 cm.
CVRF – cardiovascular risk factor, DBP – diastolic blood pressure, SBP – systolic blood pressure

eTable 9C: Prevalence of SBP categories in National Income Dynamics Survey 2017, men

Population	Hypertension Category				
	Normotensive	Grade 1a	Grade 1b	Grade 2	Grade 3
Population with no private health insurance					
Proportion of population (95% CI)					
Overall population (age ≥20 years)	76.1 (74.7-77.5)	8.4 (7.6-9.5)	7.8 (6.9-8.7)	5.2 (4.5-6.0)	2.3 (1.9-2.9)
Young adults (age 20-39 years)	84.0 (86.1-88.0)	9.4 (4.4-5.6)	3.4 (4.3-5.5)	2.4 (1.8-3.6)	0.8 (0.7-1.2)
Middle adults (age 40-69 years)	65.4 (65.5-68.6)	7.9 (3.1-4.6)	13.3 (15.3-17.7)	8.9 (7.5-9.3)	4.5 (3.6-4.9)
Older adults (age ≥70 years)	55.6 (50.6-59.0)	n/a	22.8 (20.9-27.9)	14.6 (11.3-17.6)	7 (4.9-8.8)
Mean SBP within category (mm Hg)					
Overall population (age ≥20 years)	117 (93-138)	139 (121-156)	143 (123-158)	158 (131-167)	181 (149-213)
Young adults (age 20-39 years)	117 (93-137)	139 (122-156)	140 (120-158)	151 (130-163)	168 (148-194)
Middle adults (age 40-69 years)	118 (93-138)	138 (120-157)	143 (124-158)	159 (133-176)	182 (151-214)
Older adults (age ≥70 years)	123 (97-139)	n/a	146 (131-159)	167 (155-187)	191 (175-214)
Population with no private health insurance and no antihypertensive medication					
Proportion of population (95% CI)					
Overall population (age ≥20 years)	78.5 (77.0-79.9)	8.9 (7.9-9.9)	6.5 (5.6-7.4)	4.2 (3.6-5.0)	1.9 (1.5-2.5)
Young adults (age 20-39 years)	84.5 (86.9-88.7)	9.2 (4.4-5.5)	3.3 (4-5.1)	2.3 (1.6-2.4)	0.7 (0.5-1.0)
Middle adults (age 40-69 years)	68.5 (69.6-73.3)	8.7 (3.8-5.7)	11.3 (12.3-15.0)	7.7 (6.1-8.1)	3.8 (2.5-4.0)
Older adults (age ≥70 years)	52.9 (50.8-62.6)	n/a	27.1 (20.7-32.2)	10.8 (6.8-13.9)	9.2 (4.6-10.6)
Mean SBP within category (mm Hg)					
Overall population (age ≥20 years)	117 (93-137)	139 (121-156)	142 (122-158)	157 (131-167)	179 (144-213)
Young adults (age 20-39 years)	117 (93-137)	139 (122-156)	140 (120-157)	151 (130-172)	167 (147-191)
Middle adults (age 40-69 years)	117 (93-138)	137 (119-156)	142 (124-158)	159 (133-167)	182 (143-215)
Older adults (age ≥70 years)	123 (102-139)	n/a	146 (128-157)	168 (155-187)	190 (168-220)

CI – confidence interval; Normotension: SBP <140 mm Hg and DBP <90 mm Hg, Grade 1a: SBP 140-159 mm Hg or DBP 90-99 mm Hg with no other CVRFs, Grade 1b: SBP 140-159 mm Hg or DBP 90-99 mm Hg with another CVRF, Grade 2: SBP 160-179 mm Hg or DBP 100-109 mm Hg, Grade 3: SBP ≥180 mm Hg. If an individual had differential grades of systolic and diastolic BP, they were assigned the more severe of the two categories. Additional cardiovascular risk factors: smoking, diabetes, men aged ≥55 years, women aged ≥65 years, men waist circumference ≥94 cm, women waist circumference ≥80 cm.
CVRF – cardiovascular risk factor, DBP – diastolic blood pressure, SBP – systolic blood pressure

eTable 10: Hypertension diagnosis, treatment, and control rates in National Income Dynamics Survey 2017

Population	Hypertension diagnosed† (95% CI)	Diagnosed hypertension treated† (95% CI)	Treated hypertension controlled‡ (95% CI)
Combined women and men			
Overall population (age ≥20 years)	51.1 (49.2-52.9)	93.2 (91.6-94.5)	54.7 (52.2-57.3)
Young adults (age 20-39 years)	20.2 (17.3-23.4)	77.1 (68.3-84.5)	55.8 (46.4-65.0)
Middle adults (age 40-69 years)	59.3 (57.0-61.7)	94.4 (92.8-95.7)	55.0 (52.1-57.9)
Older adults (age ≥70 years)	75.7 (71.1-79.9)	97.5 (95.7-98.6)	53.2 (47.1-59.2)
Women			
Overall population (age ≥20 years)	62.4 (60.3-64.7)	94.3 (92.7-95.6)	55.8 (53.0-58.7)
Young adults (age 20-39 years)	29.9 (25.3-34.8)	84.3 (77.0-90.0)	60.3 (49.8-70.2)
Middle adults (age 40-69 years)	69.1 (66.4-71.7)	94.7 (92.6-96.2)	56.6 (53.3-59.9)
Older adults (age ≥70 years)	79.4 (74.2-84.0)	98.4 (96.6-99.4)	50.7 (44.0-57.4)
Men			
Overall population (age ≥20 years)	34.0 (31.1-37.1)	90.0 (86.1-93.1)	51.5 (46.0-57.1)
Young adults (age 20-39 years)	11.7 (8.1-16.0)	60.9 (40.6-78.8)	41.9 (22.9-62.8)
Middle adults (age 40-69 years)	41.8 (37.7-46.0)	93.5 (90.6-95.8)	50.2 (43.8-56.7)
Older adults (age ≥70 years)	68.2 (58.5-76.9)	95.2 (90.5-98.0)	59.3 (46.2-71.4)

CI – confidence interval; Values given are proportions

*Denominator: Individuals with hypertension (SBP≥140 mm Hg or DBP ≥90 mm Hg or on antihypertensive medication)

†Denominator: Individuals with diagnosed hypertension

‡Denominator: Individuals receiving antihypertensive medication

eTable 11: Population-attributable fractions for hypertension-related complications

Parameter	Population-attributable fraction (%, 95% CI)		
	Combined Women and Men	Women	Men
Ischemic heart disease			
Overall (age ≥20 years)	17.9 (15.4-20.5)	17.8 (14.5-21.1)	18.3 (16.4-20.2)
Young adults (age 20-39 years)	5.6 (4.7-6.6)	4.4 (3.6-5.4)	6.6 (5.7-7.5)
Middle adults (age 40-69 years)	15.5 (13.6-17.6)	14.5 (12.5-16.5)	16.7 (14.8-18.8)
Older adults (age ≥70 years)	24.1 (18.1-30.8)	22.2 (16.0-28.6)	26.3 (20.9-32.1)
Stroke			
Overall (age ≥20 years)	27.6 (24.2-31.2)	27.0 (22.5-31.3)	27.9 (25.2-30.5)
Young adults (age 20-39 years)	9.0 (7.6-10.5)	7.1 (5.9-8.7)	10.5 (9.1-11.8)
Middle adults (age 40-69 years)	24.3 (21.5-27.2)	22.8 (19.9-25.8)	25.9 (23.2-28.8)
Older adults (age ≥70 years)	36.2 (28.2-44.6)	33.6 (25.2-41.8)	39.2 (32.2-46.2)
Hypertensive heart disease			
Overall (age ≥20 years)	82.8 (79.5-85.6)	80.1 (75.0-83.6)	85.2 (83.2-87.1)
Young adults (age 20-39 years)	78.2 (73.6-82.1)	76.8 (72.0-81.5)	78.2 (74.0-81.7)
Middle adults (age 40-69 years)	88.2 (86.1-90.0)	87.2 (84.5-89.3)	88.9 (87.2-90.5)
Older adults (age ≥70 years)	76.3 (68.7-82.7)	73.5 (64.0-80.7)	79.2 (73.6-83.8)

CI – confidence interval

eTable 12A: Hypertension-related complications treated in South African public healthcare system, women

Hypertension-Related Condition	Counts of conditions per year (95% CI)
Total number with hypertension* (% of age-group, 95% CI)	
Ages ≥20 years	4,503,460 (32.3, 30.7-34.2)
Ages ≥40 years	3,840,462 (57.5, 54.5-60.8)
Hypertensive crises	
Hypertensive urgencies	4,813 (3,899-5,845)
Hypertensive emergency	10,107 (8,188-12,273)
Ischemic heart disease	
Ischemic heart disease, incidence	6,452 (4,941-8,063)
Ischemic heart disease, prevalence	54,029 (43,158-66,120)
Ischemic heart disease, DALYs	41,173 (33,136-50,196)
Stroke	
Stroke, incidence	7,619 (6,021-9,446)
Stroke, prevalence	64,193 (53,195-76,392)
Stroke, DALYs	83,711 (68,996-98,780)
Chronic kidney disease	
Chronic kidney disease, incidence	3,027 (2,463-3,663)
Chronic kidney disease, prevalence	62,563 (57,074-68,218)
Chronic kidney disease, DALYs	38,512 (31,520-46,211)
Hypertensive heart disease	
Hypertensive heart disease, DALYs	98,333 (83,828-113,458)

*Hypertension Grades 1-3 or currently receiving antihypertensive medication
CI – confidence interval, DALY – disability-adjusted life year

eTable 12B: Hypertension-related complications treated in South African public healthcare system, men

Hypertension-Related Condition	Counts of conditions per year (95% CI)
Total number with hypertension* (% of age-group, 95% CI)	
Ages ≥20 years	3,715,705 (29.0, 27.1-31)
Ages ≥40 years	2,588,498 (47.7, 44-51.4)
Hypertensive crises	
Hypertensive urgencies	5,220 (4,501-6,052)
Hypertensive emergency	10,961 (9,452-12,709)
Ischemic heart disease	
Ischemic heart disease, incidence	7,539 (6,141-9,130)
Ischemic heart disease, prevalence	71,945 (60,671-83,984)
Ischemic heart disease, DALYs	58,754 (50,800-67,923)
Stroke	
Stroke, incidence	5,689 (4,590-6,890)
Stroke, prevalence	48,863 (42,232-56,569)
Stroke, DALYs	73,103 (63,331-83,668)
Chronic kidney disease	
Chronic kidney disease, incidence	3,077 (2,511-3,796)
Chronic kidney disease, prevalence	57,250 (51,146-63,056)
Chronic kidney disease, DALYs	50,401 (40,417-61,776)
Hypertensive heart disease	
Hypertensive heart disease, DALYs	72,870 (60,585-85,511)

*Hypertension Grades 1-3 or currently receiving antihypertensive medication
CI – confidence interval, DALY – disability-adjusted life year

eTable 13A: Numbers of hypertension-related complications, combined women and men

Complication	Incidence (95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischemic heart disease				
Overall (age ≥20 years)	13,991 (11,082-17,193)	125,974 (103,829-150,104)	99,927 (83,936-118,119)	7,8,14
Young adults (age 20-39 years)	377 (246-537)	1,736 (1,334-2,211)	2,427 (1,637-3,498)	
Middle adults (age 40-69 years)	6,566 (4,586-8,848)	56,456 (45,055-68,943)	50,367 (40,093-62,086)	
Older adults (age ≥70 years)	7,049 (5,049-9,422)	67,782 (49,171-87,613)	47,132 (35,073-60,509)	
Stroke				
Overall (age ≥20 years)	13,308 (10,611-16,336)	113,056 (95,427-132,961)	156,813 (132,327-182,448)	7,8,14
Young adults (age 20-39 years)	315 (203-452)	6,872 (5,199-8,909)	4,834 (3,314-6,606)	
Middle adults (age 40-69 years)	6,257 (4,531-8,313)	58,423 (47,068-70,724)	71,144 (57,641-86,288)	
Older adults (age ≥70 years)	6,736 (4,765-8,889)	47,761 (34,486-62,706)	80,836 (62,524-100,641)	
Chronic kidney disease due to hypertension				
Overall (age ≥20 years)	6,105 (4,974-7,459)	119,814 (108,219-131,274)	88,913 (71,937-107,987)	7,8
Young adults (age 20-39 years)	321 (181-508)	14,569 (10,790-19,076)	13,232 (7,427-20,134)	
Middle adults (age 40-69 years)	3,404 (2,365-4,603)	55,009 (46,370-64,541)	47,060 (32,094-64,439)	
Older adults (age ≥70 years)	2,380 (1,963-2,847)	50,236 (44,657-56,742)	28,621 (23,556-34,164)	
Hypertensive heart disease				
Overall (age ≥20 years)	-	-	171,202 (144,414-198,969)	7,8,15
Young adults (age 20-39 years)	-	-	9,744 (5,835-14,839)	
Middle adults (age 40-69 years)	-	-	98,228 (75,317-122,377)	
Older adults (age ≥70 years)	-	-	63,230 (52,453-75,230)	

CI – confidence interval; DALY – disability-adjusted life year

eTable 13B: Numbers of hypertension-related complications, women

Complication	Incidence (95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischemic heart disease				
Overall (age ≥20 years)	6,452 (4,941-8,063)	54,029 (43,158-66,120)	41,173 (33,136-50,196)	7,8,14
Young adults (age 20-39 years)	107 (66-156)	441 (329-585)	478 (247-821)	
Middle adults (age 40-69 years)	2,656 (1,817-3,640)	21,074 (16,691-25,702)	15,505 (12,053-19,457)	
Older adults (age ≥70 years)	3,689 (2,565-5,052)	32,514 (22,854-42,909)	25,190 (17,804-33,348)	
Stroke				
Overall (age ≥20 years)	7,619 (6,021-9,446)	64,193 (53,195-76,392)	83,711 (68,996-98,780)	7,8,14
Young adults (age 20-39 years)	114 (69-168)	3,232 (2,371-4,325)	1,537 (934-2,287)	
Middle adults (age 40-69 years)	3,169 (2,260-4,272)	30,791 (24,668-37,574)	31,218 (25,511-37,692)	
Older adults (age ≥70 years)	4,336 (3,003-5,776)	30,170 (21,514-40,097)	50,955 (38,489-64,869)	
Chronic kidney disease due to hypertension				
Overall (age ≥20 years)	3,027 (2,463-3,663)	62,563 (57,074-68,218)	38,512 (31,520-46,211)	7,8
Young adults (age 20-39 years)	134 (74-212)	6,808 (5,091-8,804)	4,786 (2,381-7,867)	
Middle adults (age 40-69 years)	1,611 (1,104-2,183)	27,119 (22,823-31,789)	18,376 (12,782-25,371)	
Older adults (age ≥70 years)	1,282 (1,060-1,532)	28,636 (25,428-32,384)	15,350 (12,714-18,212)	
Hypertensive heart disease				
Overall (age ≥20 years)	-	-	98,333 (83,828-113,458)	7,8,15
Young adults (age 20-39 years)	-	-	4,450 (2,218-7,505)	
Middle adults (age 40-69 years)	-	-	50,309 (38,606-62,209)	
Older adults (age ≥70 years)	-	-	43,573 (36,006-51,861)	

CI – confidence interval; DALY – disability-adjusted life year

eTable 13C: Numbers of hypertension-related complications, men

Complication	Incidence (95% CI)	Prevalence (95% CI)	DALYs (95% CI)	Source
Ischemic heart disease				
Overall (age ≥20 years)	7,539 (6,141-9,130)	71,945 (60,671-83,984)	58,754 (50,800-67,923)	7,8,14
Young adults (age 20-39 years)	270 (180-381)	1,295 (1,005-1,626)	1,950 (1,390-2,677)	
Middle adults (age 40-69 years)	3,910 (2,769-5,208)	35,382 (28,364-43,241)	34,862 (28,041-42,629)	
Older adults (age ≥70 years)	3,359 (2,484-4,370)	35,268 (26,316-44,705)	21,942 (17,270-27,161)	
Stroke				
Overall (age ≥20 years)	5,689 (4,590-6,890)	48,863 (42,232-56,569)	73,103 (63,331-83,668)	7,8,14
Young adults (age 20-39 years)	200 (134-284)	3,640 (2,828-4,584)	3,297 (2,380-4,319)	
Middle adults (age 40-69 years)	3,089 (2,271-4,042)	27,633 (22,400-33,150)	39,926 (32,130-48,597)	
Older adults (age ≥70 years)	2,400 (1,763-3,113)	17,591 (12,972-22,609)	29,880 (24,035-35,772)	
Chronic kidney disease due to hypertension				
Overall (age ≥20 years)	3,077 (2,511-3,796)	57,250 (51,146-63,056)	50,401 (40,417-61,776)	7,8
Young adults (age 20-39 years)	186 (108-297)	7,761 (5,698-10,272)	8,446 (5,046-12,267)	
Middle adults (age 40-69 years)	1,794 (1,261-2,419)	27,890 (23,547-32,752)	28,684 (19,312-39,067)	
Older adults (age ≥70 years)	1,097 (903-1,315)	21,599 (19,229-24,358)	13,270 (10,842-15,952)	
Hypertensive heart disease				
Overall (age ≥20 years)	-	-	72,870 (60,585-85,511)	7,8,15
Young adults (age 20-39 years)	-	-	5,294 (3,617-7,334)	
Middle adults (age 40-69 years)	-	-	47,919 (36,711-60,168)	
Older adults (age ≥70 years)	-	-	19,657 (16,447-23,369)	

CI – confidence interval; DALY – disability-adjusted life year

eTable 14A: Cost of hypertension in South African population with no private insurance, combined women and men

Cost Type	Cost, Thousands (ZAR 2020)	Cost, Thousands (USD 2020)
Direct healthcare costs	10,080,415 (8,983,387-11,250,697)	710,749 (633,400-793,263)
Age-group		
Young adults (age 20-39 years)	1,244,366 (1,023,478-1,495,007)	87,737 (72,164-105,410)
Middle adults (age 40-69 years)	6,510,072 (5,686,833-7,427,618)	459,012 (400,967-523,706)
Older adults (age ≥70 years)	2,325,977 (1,733,182-2,999,018)	164,000 (122,203-211,454)
Type of cost		
Screening	1,461,908 (1,309,207-1,612,555)	103,076 (92,310-113,698)
Management	7,284,858 (6,365,669-8,263,758)	513,641 (448,830-582,661)
Complications	1,333,649 (1,128,548-1,552,242)	80,663 (69,127-92,582)
Hypertensive crises	395,271 (330,962-468,726)	27,870 (23,335-33,049)
Ischemic heart disease	447,093 (370,480-526,443)	31,524 (26,121-37,118)
Stroke	472,452 (391,167-560,189)	33,312 (27,581-39,498)
Chronic kidney disease	18,833 (17,096-20,548)	1,328 (1,205-1,449)
Societal costs	29,435,883 (25,979,351-33,200,239)	2,075,463 (1,831,750-2,340,881)
Age-group		
Young adults (age 20-39 years)	3,318,085 (2,515,678-4,272,294)	233,951 (177,376-301,231)
Middle adults (age 40-69 years)*	9,515,739 (22,804,575-29,732,732)	1,841,512 (1,607,903-2,096,394)
Type of cost		
Management	38,506 (32,316-45,400)	2,715 (2,278-3,201)
Complications	29,397,377 (25,940,430-33,161,481)	2,072,748 (1,829,006-2,338,147)
Ischemic heart disease	5,375,841 (4,344,432-6,583,275)	379,039 (306,317-464,174)
Stroke	7,481,234 (6,184,815-8,977,342)	527,486 (436,078-632,974)
Chronic kidney disease	6,106,797 (4,433,138-7,991,449)	430,578 (312,571-563,460)
Hypertensive heart disease	10,433,505 (8,190,288-12,778,222)	735,645 (577,480-900,966)

*Societal costs incurred until age 65

eTable 14B: Cost of hypertension in South African population with no private insurance, women

Cost Type	Cost, Thousands (ZAR 2020)	Cost, Thousands (USD 2020)
Direct healthcare costs	6,112,592 (5,451,641-6,820,698)	430,986 (384384-480913)
Age-group		
Young adults (age 20-39 years)	841,227 (706,924-990,371)	59,313 (49,844-69,829)
Middle adults (age 40-69 years)	3,860,909 (3,380,621-4,400,701)	272,225 (238,361-310,284)
Older adults (age ≥70 years)	1,410,456 (1,026,146-1,837,643)	99,448 (72,351-129,568)
Type of cost		
Screening	990,353 (913,852-1,063,900)	69,828 (64,434-75,013)
Management	4,453,112 (3,904,677-5,053,643)	313,980 (275,311-356,322)
Complications	669,127 (542,146-805,010)	33,809 (27,781-39,896)
Hypertensive crises	189,627 (153,618-230,276)	13,370 (10,831-16,236)
Ischemic heart disease	199,863 (159,421-240,554)	14,092 (11,240-16,961)
Stroke	269,827 (220,115-323,526)	19,025 (15,520-22,811)
Chronic kidney disease	9810 (8,992-10,654)	692 (634-751)
Societal costs	10,540,988 (9,207,404-11,919,619)	743,223 (649,195-840,428)
Age-group		
Young adults (age 20-39 years)	1,041,868 (718,226-1,421,443)	73,460 (50,641-100,223)
Middle adults (age 40-69 years)*	9,499,120 (8,185,466-10,794,041)	669,763 (577,140-761,066)
Type of cost		
Management	23,122 (19,563-27,300)	1,630 (1,379-1,925)
Complications	10,517,866 (9,182,132-11,896,820)	741,593 (647,413-838,820)
Ischemic heart disease	1,318,193 (1,029,126-1,650,503)	92,943 (72,562-116,374)
Stroke	2,706,901 (2,250,344-3,239,393)	190,858 (158,667-228,403)
Chronic kidney disease	1,949,471 (1,416,024-2,612,944)	137,453 (99,841-184,233)
Hypertensive heart disease	4,543,301 (3,556,413-5,540,343)	320,339 (250,755-390,638)

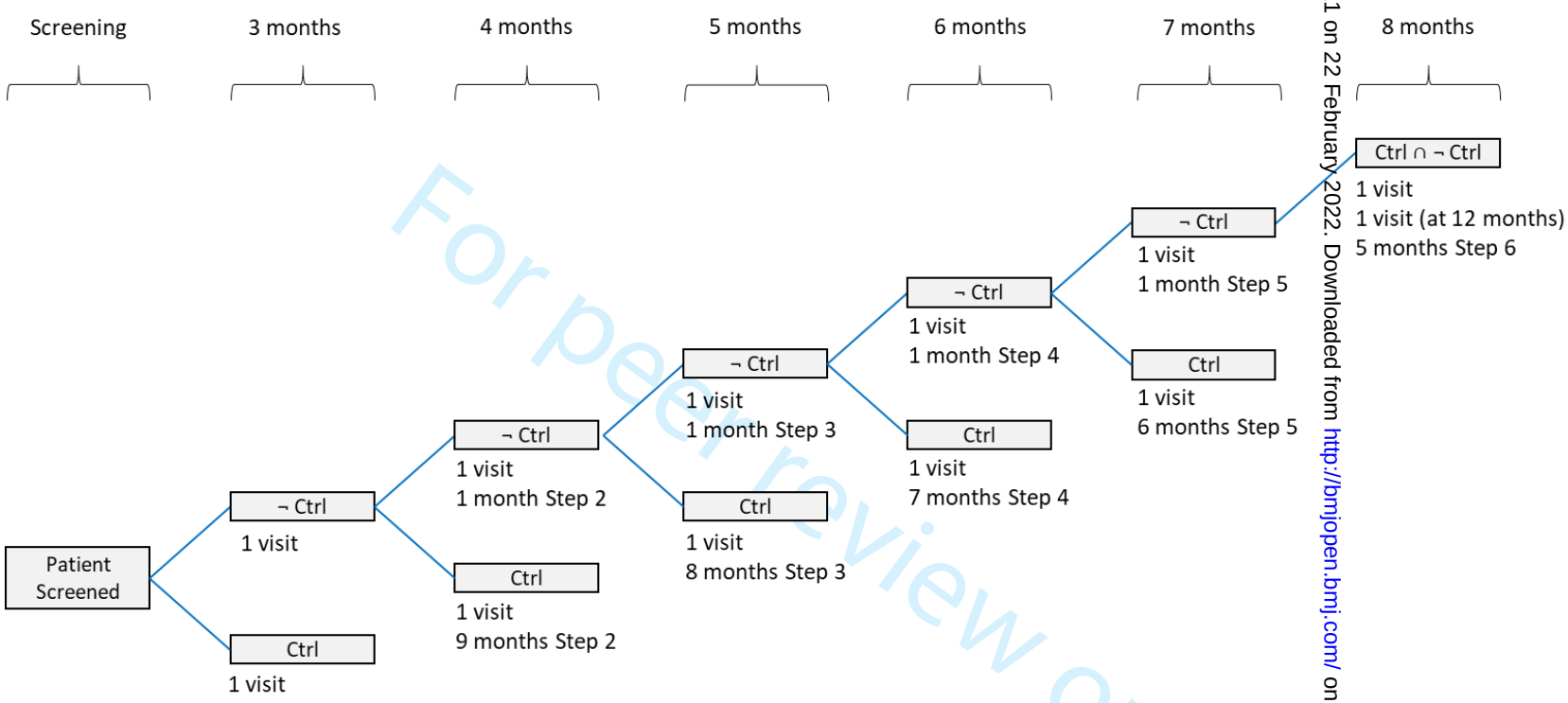
*Societal costs incurred until age 65

eTable 14C: Cost of hypertension in South African population with no private insurance, men

Cost Type	Cost, Thousand (ZAR 2020)	Costs, Thousand (USD 2020)
Direct healthcare costs	3,967,823 (3,531,746-4,429,999)	279,763 (249,016-312,350)
Age-group		
Young adults (age 20-39 years)	403,139 (316,554-504,636)	28,424 (22,320-35,581)
Middle adults (age 40-69 years)	2,649,163 (2,306,212-3,026,917)	186,787 (162,606-213,422)
Older adults (age ≥70 years)	915,521 (707,036-1,161,375)	64,552 (49,852-81,886)
Type of cost		
Screening	471,555 (395,355-548,655)	33,248 (27,876-38,685)
Management	2,831,746 (2460,992-3210,115)	199,661 (173,519-226,339)
Complications	664,522 (586,402-747,232)	46,854 (41,346-52,686)
Hypertensive crises	205,644 (177,344-238,450)	14,500 (12,504-16,813)
Ischemic heart disease	247,230 (211,059-285,889)	17,432 (14,881-20,157)
Stroke	202,625 (171,052-236,663)	14,287 (12,061-16,687)
Chronic kidney disease	9023 (8,104-9,894)	636 (571-698)
Societal costs	18,894,895 (16,771,947-21,280,620)	1,332,240 (1,182,555-1,500,453)
Age-group		
Young adults (age 20-39 years)	2,276,217 (1,797,452-2,850,851)	160,491 (126,735-201,008)
Middle adults (age 40-69 years)*	16,618,678 (14,619,109-18,938,691)	1,171,749 (1,030,763-1,335,328)
Type of cost		
Management	15,384 (12,753-18,100)	1,085 (899-1,276)
Complications	18,879,511 (16,758,298-21,264,661)	1,331,155 (1,181,593-1,499,327)
Ischemic heart disease	4,057,648 (3,315,306-4,932,772)	286,096 (233,755-347,800)
Stroke	4,774,333 (3,934,471-5,737,949)	336,628 (277,411-404,571)
Chronic kidney disease	4,157,326 (3,017,114-5,378,505)	293,125 (212,730-379,227)
Hypertensive heart disease	5,890,204 (4,633,875-7,237,879)	415,306 (326,725-510,328)

*Societal costs incurred until age 65

eFigure 1: Decision tree for hypertension treatment



Associated resource use listed below each state, costs are cumulative
Ctrl – Hypertension controlled

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Title: Hypertension in the South African Public Healthcare System: A Cost-of-Illness and Burden of Disease Study

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Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Page 1 Line 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Page 2, Lines 1-35
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	Page 5, Lines 6-23
		Present the study question and its relevance for health policy or practice decisions.	Page 5, Lines 25-35
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 5, Lines 34-35 Page 6, Lines 5-10
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 6, Lines 5-6
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 5, Line 34 Page 6, Line 5
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	n/a
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 4, Line 34
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 6, Lines 9-10
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 9, Lines 1-33
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	n/a
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included	n/a

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
		studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference-based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n/a
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 6, Lines 12-40 Page 7, Lines 38-41 Page 8, Lines 1-30 Page 9, Lines 35-41 Page 10, Lines 1-33
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 11, Line 1-7
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	n/a
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Page 8, Line 12 -Page 10, Line 34 eTables 5-6 eTable 8 eFigure 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 7, Lines 4-36 Page 8, Lines 9-30 Page 9, Lines 1-33 Page 10, lines 24-33 Supplementary Material
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for	Methods Table 1

Section/item	Item No	Recommendation	Reported on page, line number(s), figure, table
		distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	n/a
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Results Figure 1 Table 2 Table 3 Table 4
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Results Table 2 Table 3 Table 4 eTables 9-14
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Page 12, Lines 15-39 Page 13, Lines 1-20
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 15, Lines 11-15
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 15, Lines 8-9