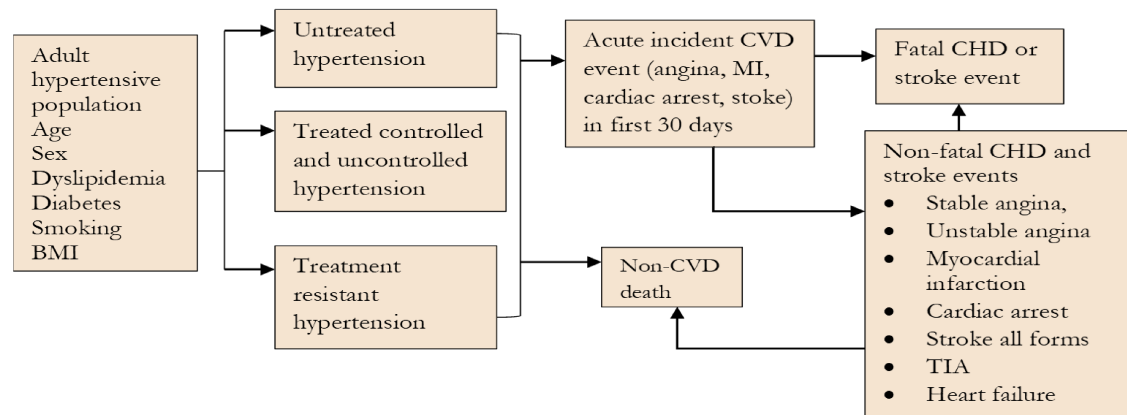


**Supplementary materials:** Economic burden of hypertension at selected Hospitals in Southern Ethiopia; a patient level analysis

### Cardiovascular disease policy model



**Supplementary Figure 1:** Cardiovascular disease policy model adapted for Sub-Saharan African perspective (1).

**Supplementary Table 1:** Age and sex specific distribution of Ethiopian population 2020 estimate, prevalence of hypertension and adult mortality rate

Age structure	Male	Female	Total	Estimated prevalence of hypertension	Mortality rate		Data Source
					Men	Women	
<b>Prevalence of hypertension</b>							(2-8)
0-14 years	21,657,152	21,381,628	43,038,780	NA	-	-	
15-19	5,572,330	5,464,174	11,036,504	19.6	0.00286	0.00222	
20-24	5,930,683	5,816,173	11,746,856	19.6	0.00319	0.00223	
25-29	4,889,739	4,802,450	9,692,189	19.6	0.00293	0.00232	
30-34	3,761,349	3,757,544	7,518,893	23.0	0.00397	0.00368	
35-39	3,091,148	3,182,837	6,273,985	23.0	0.00411	0.00222	
40-44	2,445,523	2,488,422	4,933,945	25.9	0.00584	0.00385	
45-49	2,071,480	2,033,228	4,104,708	25.9	0.00360	0.00457	
50-54	1,567,789	1,660,957	3,228,746	41.9	0.00354	0.00274	
55-59	1,159,002	1,316,318	2,475,320	41.9	0.00354	0.00274	
60-64	946,594	1,109,670	2,056,264	41.9	0.00354	0.00274	
≥ 65 years	1,676,478	1,977,857	3,654,335	41.9	0.00354	0.00274	
<b>Total</b>	<b>54,769,267</b>	<b>54,991,258</b>	<b>109,760,525</b>				
				Prevalence of untreated hypertension			
For all ages (15 +)				13.25			(9)

**Supplementary Table 2.** Model Parameters, Cohort Setting, and Probability of Transition between states and Disability weights for hypertension and related complications the Global Burden of Disease 2013 study and WHO Global Health Estimates

Parameter	Data	Source
Relative risk of hypertension treatment		
Relative risk of CHD event on hypertension treatment	0.683 (95% CI, 0.633–0.717)	(10-13)
Relative risk of a cerebrovascular event on hypertension treatment	0.633 (95% CI, 0.526–0.717)	(14)
Relative risk of CHD event on normotensive men and women	0.49 (95% CI 0.458–0.513) and 0.32 (0.292–0.342)	(15)
<b>Transition probabilities to death</b>		
<b>Health state</b>	<b>Disability weight Estimate</b>	<b>Source</b>
<b>Hypertension</b>		<b>(16)</b>
Treated	0.246	
Untreated	0.323	
Treated and controlled	0.171	
<b>Myocardial Infarction (MI)</b>		<b>(17)</b>
Day 1-2	0.432	
Days 3-28	0.074	
<b>Angina Pectoris</b>		
Mild	0.033	
Moderate	0.080	
Severe	0.167	
<b>Heart failure</b>		
Mild	0.041	
Moderate	0.072	
<b>Diabetes, digestive, and genitourinary disease</b>		
<b>Diabetes</b>	0.015 (0.012 - 0.018)	<b>(18-20)</b>
<b>Treated</b>	0.033	
<b>Untreated</b>	0.012	

Diabetic neuropathy	0.133	
Chronic kidney disease (stage IV)	0.104	
End-stage renal disease: with kidney transplant	0.024	
End-stage renal disease: on dialysis	0.571	
Disutility due to daily medication	0.049 (0.031–0.072)	
<b>Acute Events</b>		
Myocardial Infarction	0.432 (0.288–0.579)	
Stroke	0.570 (0.377–0.707)	
Occurrence of second or later CVD event	0.985 (0.992–0.989)	
<b>Chronic States</b>		
Ischemic Heart Disease	0.08 (0.02–0.24)	
Stroke	0.135 (0.01–0.437)	
Alive post 2+ CVD Events	0.242 (0.11–0.437)	

CHD, coronary heart disease; SMR, standardized mortality ratio. \*Age and sex dependent †Applied multiplicatively to general population age- and sex-dependent utilities; CHD= Angina pectoris, coronary insufficiency, myocardial infarction, or coronary death.

**Supplementary table 3:** Simulation input parameters

Input parameter	Value	Source
Non-CVD death rate	0.005–0.176 (Age- and sex specific)#	Calculated from WHO lifetables and GBD 2017 (21)
Probability of first-time cardiovascular disease (CVD) event	Individual risk characteristic specific	Obtained from the Globorisk Office Calculator standardized for India [25]
<b>Acute CVD events</b>		
MI		
Probability of MI if CVD event occurs	37.6– 66.7% (Age- and sex specific)#	Calculated based on GBD 2017(21)
30-day fatality	0.01–0.13 (Age- and sex-specific)#	Calibrated based on findings of Huffman et al. 2018 (22)
Re-infarction (in 30 days)	0.0120 (0.0099–0.0141)ψ	ACS QUIK Study by Huffman et al. 2018 (22)
Acute Stroke (in 30 days)	0.0060 (0.0045–0.0075)ψ	ACS QUIK Study by Huffman et al. 2018 (22)
Stroke		
Probability of Stroke if CVD event occurs	33.2–62.3% (Age- and sex specific)#	Calculated based on GBD 2017 (21) And Jushua D. Bundry et al(23)
30-day fatality	0.12, 0.13 (Sex-specific)#	Calibrated based on a multi-site study by Pandian and Sudhan 2013 [30]
Repeat Stroke (in 30 days)	0.15 (0.1–0.2)ψ	Petty et al. 1998 (24)
Sudden cardiac death	0.10 per 100 patient-years (95% CI, 0.07–0.14) in a cohort of 33 of 3242 untreated hypertensive patients without evidence of coronary or cerebrovascular HD at entry and followed up for an average of 10.3 years	Heart disease and stroke statistics 2021 update
<b>Heart failure</b>		
Probability of AHF		
30-days fatality	0.0945	Obtained from the THESUS-HF registry (25) and Korean Acute Heart Failure Registry (KorAHF)(26, 27)

Re-hospitalization	0.0736	Obtained from the THESUS-HF registry (25)
<b>Chronic events</b>		
Monthly risk of mortality	0.001–0.019 (Age- and sex-specific)#	Calibrated based on GBD 2017 (21)
Reinfarction	0.079 (0.073–0.085)ψ	Based on Steg et al. 2007 (28) and derived by Lin et al. 2019 (20)
Acute Stroke	0.014 (0.012–0.016)ψ	Based on Steg et al. 2007 (28) and derived by Lin et al. 2019 (20) Continue Or Stop post-Stroke Antihypertensives Collaborative Study (COSSACS) (29), BP reduction and secondary stroke prevention: systematic review(30)
<b>Stroke</b>		
Monthly risk of mortality	0.001–0.013 (Age- and sex specific)#	Calibrated based on GBD 2017 (21)  Stroke Risk in Treated Hypertension Based on Home Blood Pressure: the Ohasama Study(31)
Acute MI	0.043 (0.038–0.048)ψ	Based on Steg et al. 2007 (28) and derived by Lin et al. 2019 (20)
Acute Stroke	0.037 (0.033–0.041)	Based on Steg et al. 2007 (28) and derived by Lin et al. 2019 (20)
Relative risk of fatality for an individual with two or more CVD events	1.5	Smolina et al. 2012 (32)
<b>Heart failure</b>		
<b>Incidence</b>		Bulter J. et al (33, 34), and Davis BRK. et. al (35)
1 year mortality		
Re-hospitalization		<b>Moita B.eta al. 2019(36) and (37)</b>
<b>Effect of antihypertensive medication</b>		
Medication protocol for an individual	Initial SBP-specific#	Based on Ethiopian NCD control guideline
IHD relative risk due to medication	0.32–0.89 (Age- and initial SBP-specific)#	Based on findings by Law et al. 2009 (38) and Asayam Kei., 2017(39)
Stroke relative risk due to medication	0.20–0.89 (Age- and initial SBP-specific)#	Based on findings by Law et al. 2009(38)
IHD relative risk if partially adherent	0.66–0.95 (Age- and initial SBP-specific)	Calculated based on a linear relationship between adherence and efficacy as considered by Cherry et al. 2009(40)
Stroke relative risk if partially adherent	0.60–0.95 (Age- and initial SBP-specific)	Calculated based on a linear relationship between adherence and efficacy as considered by Cherry et al. 2009 (40) and Lisheng Liu, Zengwu Wang. et al(41)

**Supplementary Table 4:** Price of drugs, medical supplies, procedures and professional time used for management of hypertension in Southern Ethiopia, January, 2021

List of medicines	Unit	Price in 2021 Ethiopian birr		Price USD	Source
		Wholesale price	Retail price	Retail Price in 2021 USD	
Acetylsalicylic Acid - 81mg – Tablet (coated)	10x10	43.72	1.32	1.303	Ethiopian Pharmaceutical supply agency, Arba Minch Hub wholesale price 2021 and Arba Minch General hospital pharmacy retail price 2021
Adrenaline (Epinephrine)-0.1% in 1mL ampoule	Each	36.032	1.09	1.074	
Amiodarone - 100mg – Tablet	10x3	313.34	9.44	9.337	
Amlodipine - 10mg - Tablet	10x10	105.44	3.18	3.142	
Amlodipine - 5mg – Tablet	10x10	75.26	2.27	2.243	
Atenolol - 50mg – Tablet	10x10	58.70	1.77	1.749	
Atorvastatin - 20mg – Tablet	10x10	195.68	5.89	5.831	
Atorvastatin - 40mg – Tablet	10x3	140.76	4.24	4.195	
Beclomethasone Propionate -100mcg/dose – Aerosol	200 MD	131.85	3.97	3.929	
Candesartan - 8mg – Tablet	14x2	152.63	4.60	4.548	
Captopril - 12.5mg – Tablet	10x10	33.54	1.01	1.000	
Captopril - 25mg – Tablet	10x10	26.91	0.81	0.802	
Dexamethasone - 4mg/ml in 1ml Ampoule - Injection	10	3.95	0.12	0.118	
Captopril + HCT (50mg + 25mg)-Tablet	10x10	57.32	1.73	1.708	
Digoxin - 0.25mg – Tablet	10x10	202.18	6.09	6.025	
Enalapril Maleate - 10mg - Tablet	10x10	61.57	1.85	1.835	
Enalapril Maleate - 5mg – Tablet	10x10	63.92	1.93	1.905	
Enalapril Maleate – 2.5mg – Tablet	10x10	19.98	0.60	0.595	
Enalapril Maleate +HCT (10 mg + 25 mg)-tablet	10x10	78.22	2.36	2.331	
Glibenclamide - 5mg – Tablet	10x10	39.09	1.18	1.165	
Glucose 40% in 20 mL – IV infusion	Each	2.54	0.08	0.076	
Glyceryl Trinitrate - 0.4mg – Tablet (Sublingual)	100	487.21	14.67	14.518	
Hydralazine - 20mg/ml in 1ml ampoule - Injection	5	204.01	6.14	6.079	
Hydrochlorothiazide - 25mg – Tablet	25x4	48.05	1.45	1.432	
Insulin Isophane Biphasic (Soluble/Isophane Mixture)- (30 + 70)IU/ml in 10ml Vial -Injection(Suspension)	Each	85.20	2.57	2.539	
Insulin Isophane Human - 100IU/ml in 10ml Vial - Injection(Suspension)	Each	100.28	3.02	2.988	
Insulin Soluble Human - 100IU/ml in 10ml Vial	Each	106.21	3.20	3.165	
Lovastatin - 20mg – Tablet	10x10	84.59	2.55	2.521	
Metformin - 500mg – Tablet	10	27.78	0.84	0.828	
Methyldopa - 250mg – Tablet	100x10	51.75	1.56	1.542	
Metoprolol - 50mg – Tablet	10x10	94.43	2.84	2.814	
Morphine sulphate-30mg-tablet	110	410.71	12.37	12.239	
Nifedipine - 20mg – Tablet	10x10	58.70	1.77	1.749	
Prednisolone - 5 mg – Tablet	100x10	342.23	10.31	10.198	
Propranolol - 40mg – Tablet	10x10	67.54	2.03	2.013	
Propylthiouracil - 100mg - Tablet (Scored)	100	633.87	19.09	18.889	
Salbutamol - 0.1mg/dose - Aerosol (Oral Inhalation)	200 MD	117.20	3.53	3.492	
Spiroolactone - 25mg – Tablet	10x10	81.87	2.47	2.440	
Thyroxin Sodium - 0.1mg – Tablet	100	178.49	5.38	5.319	
Valsartan + HCT (80mg +12.5mg)	7*2	38.47	1.16	1.146	
<b>Laboratory and imaging costs</b>		<b>Price per test ETB</b>	Price in 2021 USD		
CBC		75.00		1.72	Arba Minch General Hospital Laboratory service price 2021
FBG/RBS		20.00		0.46	
Lipid profile (LDL, HDL, Total cholesterol, Triglyceride)		160.00		3.68	
ECG		120.00		2.76	
ECO		350.00		8.05	
CT-scan		1200		27.59	
RFT (bilirubin, creatinine)		80.00		1.84	
Chest-ray		726		16.69	
Urine analysis		15.00		0.34	
Body fluid analysis		100.00		2.30	
H. pylori		50.00		1.15	

Liver function test (AST, ALT, ALP)	120.00	2.76	
Thyroid function test (T3, T4, TSH)	432.00	9.93	
<b>Hospital bed days</b>			
Primary hospital	52.52	1.21	WHO Choice (42) inflated to 2021
Secondary hospital	54.76	1.26	
Tertiary hospital	70.81	1.63	
<b>Health facility visit</b>		0.00	
Primary hospital	18.58	0.43	
Secondary hospital	21.17	0.49	
Tertiary hospital	22.06	0.51	
Health center visit	23.00	0.53	
PCI intervention	63,000.00	1448.28	
In-patient costs for MI	45240.00	1040.00	
In-patient costs for Stroke	40890.00	940.00	
Outpatient cost for IHD (per annum)	1957.50	45.00	
Outpatient cost for Stroke (per annum)	2914.50	67.00	
<b>Salary scale of human resource</b>		0.00	
Physician	21,100.00	485.06	MOH, Ethiopia 2012/2019
Acute care nurse	7470.00	171.72	
Pharmacy personnel	8047.00	184.99	
Laboratory technician	6460.00	148.51	
Program cost per person per annum	993.29	22.83	
<b>Antihypertensive treatment</b>			(43).
Antihypertensive medication (per individual per annum)	Drug costs based on national Drug supply agency wholesale price		
Out-patient consultations (per visit)	<b>\$43.36</b>	Annual outpatient visit cost (12*WHO cost per outpatient visit inflated to 2021) WHO Choice (42)	
One-time diagnostic tests		Based on Laboratory procedures and test price of Arba Minch General Hospital, 2021	
In-patient costs for MI	\$1040	WHO Choice (42) inflated to 2021	
In-patient costs for Stroke	\$940		
<b>Chronic CVD care</b>			
Secondary care medication in public sector (per individual per annum)	\$92, \$184 (Dosage-specific)§	MSH-2015 International Drug Price Indicator inflated to 2021(25)	
Outpatient cost for IHD (per annum)	\$45	WHO Choice (44) inflated to 2021	
Outpatient cost for Stroke (per annum)	\$67		
Average inflation rate Ethiopia	16.58%	<a href="https://take-profit.org/en/statistics/inflation-rate/ethiopia/">https://take-profit.org/en/statistics/inflation-rate/ethiopia/</a>	
Average inflation rate foreign	2.02%		
Percentage change	24.6%		
Exchange rate July 2021 (1USD)	43.5 ETB		
1USD = 20.999 ETB in 2016 and 43.5 in 2021; PPP= 12.1/8.1 = 1.5			
MD: metered Dose; MOH: Ministry of Health 1 USD = 43.5 January 2021			
<b>Note:</b> 30% mark-up at regional EPSA hub, 31% mark-up at Public Hospital level			

**Supplementary Table 5:** Risk of death across age and gender covariate categories stratified for hypertension

Variables	Categories	Incidence of death (%)		Relative risk in each category (CI)	Source
		High BP group	Normal		
Age	20-29	1.68%	0.54%	3.11 (1.16-8.36)	(8)
	30-39	1.71%	0.94%	1.82 (1.04-3.19)	
	40-49	2.43%	1.88%	1.29 (0.91-1.82)	
	50-59	6.30%	4.03%	1.56 (1.28-1.91)	
	60 and above	19.32%	15.9%	1.21 (1.12-1.31)	
Gender	Women	8.71%	1.1%	3.31 (2.98-3.68)	
	Men	15.47%	4.62%	3.34(3.02-3.70)	
<b>Risk of all case mortality</b>					
Gender	Treatment status	< 60 years	> 60 years	HR (95% CI)	(45)
Men	Normal	<b>0.0068</b>	<b>0.0214</b>	1.00 (Reference)	
	Treated controlled	<b>0.0188</b>	<b>0.0305</b>	1.20 (0.92-1.57)	
	Treated uncontrolled	<b>0.0252</b>	<b>0.0372</b>	1.55 (1.19-2.01)	
	Untreated	<b>0.0197</b>	<b>0.0336</b>	1.45 (1.23-1.72)	
Women	Normal	<b>0.00528</b>	<b>0.01870</b>	1.00 (Reference)	
	Treated controlled	<b>0.01675</b>	<b>0.02841</b>	1.11 (0.84-1.47)	
	Treated uncontrolled	<b>0.02533</b>	<b>0.03736</b>	1.63 (1.34-1.99)	
	Untreated	<b>0.02075</b>	<b>0.03471</b>	1.31 (1.06-1.61)	

**Supplementary Table 6:** Annual mortality rate in the total population, those with hypertension by treatment and control status and those without hypertension in Ethiopia in 2021 by age group and sex based on literature review of systematic reviews and clinical trials

Age group	Mortality rate in the total population	Mortality rate among people without hypertension	Mortality rate among people with treated and controlled hypertension	Mortality rate among people with treated but uncontrolled hypertension	Mortality rate among people with untreated hypertension	References
<b>Women</b>						
15-19	0.00222	0.00222	0.016746	0.025	0.02075	Ko, Min Jung. et al. 2016 (46), Mende Sorato, et al, 2021. (1, 23, 45, 47, 48).
20-24	0.00223	0.00223	0.016746	0.025	0.02075	
25-29	0.00232	0.00232	0.016746	0.025	0.02075	
30-34	0.00368	0.00368	0.016746	0.025	0.02075	
35-39	0.00222	0.00222	0.016746	0.025	0.02075	
40-44	0.00385	0.00385	0.016746	0.025	0.02075	
45-49	0.00457	0.00457	0.016746	0.025	0.02075	
50-54	0.00182	0.00182	0.016746	0.025	0.02075	
55-59	0.00182	0.00182	0.016746	0.025	0.02075	
60-64	0.00441	0.00441	0.028414	0.037	0.03471	
<b>Men</b>						
15-19	0.00286	0.00286	0.018783	0.025	0.01969	Kuriakose A. et al. 2014. (8), EDHS, 2016 (7, 45, 47-50)
20-24	0.00319	0.00319	0.018783	0.025	0.01969	
25-29	0.00293	0.00293	0.018783	0.025	0.01969	
30-34	0.00397	0.00397	0.018783	0.025	0.01969	
35-39	0.00411	0.00411	0.018783	0.025	0.01969	
40-44	0.00584	0.00584	0.018783	0.025	0.01969	
45-49	0.0036	0.0036	0.018783	0.025	0.01969	
50-54	0.00354	0.00354	0.018783	0.025	0.01969	
55-59	0.00354	0.00354	0.018783	0.025	0.01969	
60-64	0.00354	0.00354	0.030451	0.037	0.03365	



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