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Estimating the changing burden of disease attributable to high systolic blood pressure in South Africa for 2000, 2006 and 2012

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Background. Ongoing quantification of trends in high blood pressure and the consequent disease impact are crucial for monitoring and decision-making. This is particularly relevant in South Africa (SA) where hypertension is well-established.

Objective. To quantify the burden of disease related to high systolic blood pressure (SBP) in SA for 2000, 2006 and 2012, and describe age, sex and population group differences.

Methods. Using a comparative risk assessment methodology, the disease burden attributable to raised SBP was estimated according to age, se, and population group for adults aged \geq 25 years in SA in the years 2000, 2006 and 2012. We conducted a meta-regression on data from nine national surveys (*N*=124 350) to estimate the mean and standard deviation of SBP for the selected years (1998 - 2017). Population attributable fractions were calculated from the estimated SBP distribution and relative risk, corrected for regression dilution bias for selected health outcomes associated with a raised SBP, above a theoretical minimum of 110 - 115 mmHg. The attributable burden was calculated based on the estimated total number of deaths and disability-adjusted life years (DALYs).

Results. Mean SBP (mmHg) between 2000 and 2012 showed a slight increase for adults aged \geq 25 years (127.3 - 128.3 for men; 124.5 - 125.2 for women), with a more noticeable increase in the prevalence of hypertension (31% - 39% in men; 34% - 40% in women). In both men and women, age-standardised rates (ASRs) for deaths and DALYs associated with raised SBP increased between 2000 and 2006 and then decreased in 2012. In 2000 and 2012, for men, the death ASR (339/100 000 v. 334/100 000) and DALYs (5 542/100 000 v. 5 423/100 000) were similar, whereas for women the death ASR decreased (318/100 000 v. 277/100 000) as did age-standardised DALYs (5 405/100 000 v. 4 778/100 000). In 2012, high SBP caused an estimated 62 314 deaths (95% uncertainty interval 62 519 - 63 608), accounting for 12.4% of all deaths. Stroke (haemorrhagic and ischaemic), hypertensive heart disease and ischaemic heart disease accounted for >80% of the disease burden attributable to raised SBP over the period.

Conclusion. From 2000 to 2012, a stable mean SBP was found despite an increase in hypertension prevalence, ascribed to an improvement in the treatment of hypertension and subsequent lowering of blood pressure. Nevertheless, the high mortality burden attributable to high SBP underscores the need for improved care for hypertension and cardiovascular diseases, particularly stroke, to prevent morbidity and mortality.

S Afr Med J 2022;112(8b):571-582. https://doi.org/10.7196/SAMJ.2022.v112i8b.16542

The article in context

Evidence before this study. The prevalence of hypertension in adult South Africans is high and associated with increased urbanisation coupled with the uptake of risk factors for raised blood pressure (BP) such as unhealthy diets, obesity and physical inactivity. Several national surveys have collected information on mean BP and the prevalence of hypertension. These have provided information on trends, as well as some understanding of the complex interplay of risk factors, demographics, equity and access to care. In 2000, the first South African Comparative Risk Assessment study (SACRA1) was conducted and assessed the attributable burden due to high BP. High BP ranked second in terms of mortality among 17 risk factors evaluated, and accounted for 9.0% of total adult deaths and 2.4% of total adult disability-adjusted life years (DALYs).

Added value of this study. This study applied the updated Global Burden of Diseases, Injuries and Risk Factors (GBD) methods to estimate the burden attributable to high systolic BP (SBP) from selected health-related outcomes in adults (aged \geq 25 years) for three time points, 2000, 2006 and 2012. The study produces comprehensive and comparable assessment of deaths, DALYs and their uncertainties attributable to raised SBP in SA. Data on SBP were extracted from nine national surveys and a pooled meta-regression analysis was conducted. The latter produced estimates of mean and standard deviation of the population distribution of SBP and prevalence of hypertension from 1998 until 2012, by population group, sex and age. In 2012, high SBP caused an estimated 62 314 deaths (95% uncertainty interval 62 519 - 63 608), accounting for 12.4% of all deaths in SA. Stroke, hypertensive heart disease and ischaemic heart disease accounted for the majority of the disease burden attributable to raised BP over the period.

Implications of the available evidence. Despite an increase in the prevalence of hypertension over the study period, there was no change in mean SBP. This may be related to the treatment of hypertension. The burden attributable to high BP remained substantial and unacceptably high, particularly in adults <60 years old. This underscores the need for improved care of hypertension and cardiovascular diseases, the main sequelae of high BP, to prevent morbidity and mortality.

The worldwide prevalence of hypertension or high blood pressure (HBP) is high, with approximately 22% of the adult population having the condition.^[1] Notably, over the last few decades, the burden of HBP has progressively shifted from high-income countries to low- and middle-income countries (LMICs).^[2] Among the estimated 1.13 billion adults with hypertension globally, about two-thirds reside in LMICs.^[3] Even the World Health Organization (WHO) African Region, with a high burden of infectious diseases, has a hypertension prevalence of 27%, which is the highest globally.^[3]

HBP is responsible for considerable morbidity, contributing to cardiovascular diseases such as heart attack, stroke and heart failure, and kidney failure, among other complications.^[4] Furthermore, HBP is the largest contributor to premature mortality worldwide,^[5,6] making it a major public health concern.

Appropriate treatment for HBP is available and is key to preventing complications and curbing hypertension-related morbidity and mortality. Nevertheless, hypertension management in LMICs is currently suboptimal, with HBP contributing substantially to morbidity and mortality.^[7] For example, in Africa, HBP accounts for more than half the number of incident acute stroke events. With a substantial burden occurring in working-age adults <60 years old, HBP is a major cause of considerable financial impoverishment on the continent, thereby affecting sustainable development.

Even in South Africa (SA), with a high burden of hypertension (men: 44%, women: 47%),^[8] hypertension control remains poor.^[9,10] It is therefore unsurprising that among the 17 risk factors evaluated in the first SA Comparative Risk Assessment (SACRA1) study,^[11] conducted by the SA Medical Research Council (SAMRC), HBP ranked second in 2000 (after unsafe sex/sexually transmitted disease) in terms of mortality. HBP accounted for 9.0% of total adult deaths and 2.4% of total adult disability-adjusted life years (DALYs).

Much of the disease burden for continuous risk variables such as blood pressure (BP) occurs at modestly raised measurements, which may not include the cut-points for a clinical diagnosis of hypertension.^[12] The association of BP with cardiovascular mortality is a continuous log-linear relationship arising from BP in the normal range of above 115/75 mmHg. Moderately raised BP, and not necessarily at measurements above the hypertension cut-point, are responsible for most of the disease burden.^[12] This has been reported in a meta-analysis of prospective observational studies from several countries,^[13] with the association found to be consistent across population groups, age and sex. Consequently, many studies report the effects of raised SBP above 115 mmHg when examining outcomes related to HBP, including SACRA1 and the WHO Comparative Risk Assessment Study for 2000.^[12] As HBP is a major public health issue in SA, ongoing quantification of the disease burden attributable to HBP is important to highlight the problem and improve management of hypertension in the country. The current, second SA Comparative Risk Assessment study (SACRA2), therefore, aims to estimate the burden of disease attributable to raised SBP in adults aged ≥25 years by population group and sex in SA for 2000, 2006 and 2012. The focus of this analysis on SBP only, rather than in conjunction with diastolic BP (DBP), is because of the stronger association of SBP with coronary heart disease mortality, stroke, and heart and kidney diseases compared with DBP.^[14] Further, DBP tends to decrease after middle age, while SBP continues to increase, with the latter contributing to morbidity and mortality.

Methods

With approximately 59 million people, SA has a diverse population. According to the 2011 census, 79% were black African, 9% were coloured, 3% were Asian and 9% were white (see disclaimer).^[15] Population group data in this study are based on self-report according to the categories used by Statistics SA.

Comparative risk assessment

The WHO comparative risk assessment methodology^[16,17] was used in this study. The disease burden attributable to a particular risk factor was estimated by comparing the current local health status with a theoretical minimum counterfactual with the lowest possible risk. We used a uniform theoretical minimum level (TMREL) distribution between 110 and 115 mmHg for all age and sex groups, based on the GBD approach, initially obtained through metaregression of pooled prospective studies.^[18] The analyses included participants aged \geq 25 years to enable comparisons with the SACRA1 study and the GBD study.

Exposure estimation

Data on individual SBP levels were extracted from nine population surveys conducted in SA between 1998 and 2017, namely: the three SA Demographic and Health Surveys (SADHS),^[19-21] five waves of the National Income Dynamics Study (NIDS)^[22-26] and the SA National Health and Nutrition Examination Survey (SANHANES-1).^[27] No individual was included in every survey, because the samples used in the three SADHSes and the single SANHANES-1 were independent. The samples in the five waves of the NIDS, however, overlap partially, with individuals included in more than one wave, because of the (partial) longitudinal design. The total sample size in terms of unique individuals was ~70 000. Within each survey, BP measurements were performed by trained field workers using validated models of Omron digital monitors and standardised techniques. A description of the data sources can be found in Tables S1 and S2 in the appendix (https://www.samedical.org/file/1842). A total of 124 350 individual measurements were further analysed from a total of 125 038.

We adopted a meta-regression approach for the estimated mean and standard deviation (SD) of the population distribution of SBP, by sex, age (25 - 34, 35 - 44, 45 - 54, 55 - 64, \geq 65 years) and population group (black African, coloured, white and Asian). Generalised additive models were fitted separately by sex and population group for the mean value and SD for year, age category and their interaction as predictors. In defining the structure of the models, we assumed a linear temporal trend for both mean SBP and its variance, but we left unspecified the shape of the relationship between each variable and age (modelled as a thin-plate spline).

We fitted the models with R statistical software v. 3.6.0 (R Core Team, Austria), and weighted the input estimates according to the quality weight approach by Doi *et al.*^[28] The latter combines, in a principled manner, information on the relative precision of the survey-specific estimates (as conveyed by their standard error) with information on the relative quality of the data sources (summarised by the risk of bias score shown in Table S3 in the appendix: https://www.samedical.org/file/1842).^[29] Table S4 in the appendix summarises the estimated mean and standard deviation of SBP, and the prevalence of hypertension.

The estimated coefficients were used to predict the values of the variables of interest (and their standard error) and recover sex-, ageand race-specific temporal trends in mean (SD) SBP.

Relative risks for selected risk-outcome pairs

The GBD 2017 study recently updated its SACRA1 methods, including a revision of the relative risks (RRs) of raised SBP from published systematic reviews.^[30] Thirteen outcomes were selected for this risk factor based on GBD 2017, and are listed in Table 1, along with the range of the RRs for each 10 mmHg above the TMREL. The RRs for each age group can be found in Table S5 in the appendix (https://www. samedical.org/file/1842).

Estimation of population-attributable fraction and attributable burden

The population-attributable fraction (PAF) of disease burden in a population is determined by the distribution of the exposure to the risk factor in the population, and the RR of the disease occurrence given the exposure, calculated as:

$$PAF = \frac{\int_{50}^{250} RR(x) P(x) dx - \int_{50}^{250} RR(x) P'(x) dx}{\int_{50}^{250} RR(x) P(x) dx}$$

where 250 mmHg is the maximum exposure level, and 50 mmHg is the lowest exposure level. P(x) is the population distribution of exposure, P'(x) is the counterfactual distribution of exposure and RR(x) is the relative risk at exposure x. Customised Excel (Microsoft Corp., USA) spreadsheets were developed to calculate the attributable burden. The integral function of EpigearXL was used to calculate the PAF, which takes the integral of the product of the risk factor distribution and the corresponding RR function. The theoretical minimum risk distribution was assumed to follow a uniform distribution with a lower limit of 110 mmHg and upper limit of 115 mmHg. To get the total burden attributable to high SBP, the age- and sex-specific burden of disease estimates (deaths and DALYs) were multiplied by the PAFs and summed. Numbers of deaths and years of life lost (YLL) from premature mortality were obtained from the second SA National Burden of Disease Study (SANBD2).^[31] Years of life lived with disability (YLD) were calculated by applying the ratio between non-fatal and fatal burden from the GBD study^[30] to the SA mortality burden to extrapolate the non-fatal component.

Summary population measures related to high SBP exposure

For men, women and total persons, the percentages of the total number of deaths and DALYs were calculated. Age-standardised rates (ASRs) were also computed for deaths and DALYs for men, women and total persons in each age group, for those aged \geq 25 years, using population estimates^[32] for age-specific rates and the WHO world standard population weights.^[33]

Uncertainty analysis

Monte Carlo simulation techniques were used to present the uncertainty around the point estimates. These were applied using Ersatz software version 1.35 (EpiGear, Australia) which allows for uncertainty to be reflected in all the calculations. Separately for each year, sex, age group and health outcome, we drew 2 000 random samples from the distributions of the parameters of the exposure distribution, the RR functions and the TMREL and repeated the calculation of the PAFs, YLLs, YLDs, DALYs and ASTs. We used the 2.5th and 97.5th percentiles as the bounds of the 95% uncertainty interval (UI). In drawing the samples, a normal distribution was specified for the mean and SD estimates of SBP. For RR estimates, we used the Ersatz function ErRelative Risk. The ErRelative Risk function assumes a lognormal uncertainty distribution for the RR and introduces a correction to eliminate the upward bias in the mean of the randomly drawn values.

Results

Mean SBP

Mean SBP for the years 2000, 2006 and 2012 for women and men is shown in Table 2. There was no clear change in mean SBP over time; however, there were differences between men and women. The mean SBP was consistently higher in men than women across population groups and time points. In 2000, the mean SBP was 127.3 mmHg for men and 124.5 mmHg for women and increased slightly in 2012 (128.3 mmHg and 125.2 mmHg for men and women, respectively).

In 2012, mean SBP <115 mmHg was found only in 25 - 34-year-old black African, white and Asian women. It was higher in all other age, sex and population groups (Fig. S1 in appendix). Mean SBP increased across age categories in men and women of all population groups. Coloured men and women had the highest mean SBP by population group within age categories, except in \geq 65-year-old men. In the latter, mean SBP in coloured (145.0 mmHg) and Asian (145.3 mmHg) men were similar.

By population group and sex, mean SBP increased with older age (Figs. S2 - S5 in appendix). These patterns were consistent between 1998 and 2017 for each population group by sex across age categories. However, there were no clear patterns when comparing population groups by sex within age categories. The greatest increases in mean SBP within age categories between 1998 and 2017 were demonstrated in black African men (Fig. S2 in appendix) and coloured women (Fig. S3 in appendix). In contrast, there was a sharp decline in mean SBP within age categories in Asian men between 1998 and 2017 (Fig. S5 in appendix). Mean SBP either increased slightly or plateaued within age categories for other subgroups by population group and sex.

Table 1. Relative risks per 10 mmHg above the systolic blood pressure theoretical minimum level for cardiovascular and chroni	ic
kidney disease outcomes	

Disease outcomes	ICD code	Range across age groups
Rheumatic heart disease	I00-I09	1.104 - 1.631
Hypertensive heart disease	I11	1.619 - 2.862
Ischaemic heart disease	I20-I25	1.266 - 1.972
Endocarditis and other cardiomyopathy	I33, I38-I42	1.128 - 1.755
Ischaemic stroke	G45-G46.8, I63-I63.9, I65-I66.9,	1.201 - 1.854
	I67.2-I67.8, I69.3-I69.4	
Haemorrhagic stroke	I60-I62, I62.1-I62.9, I67.0-I67.1,	1.279 - 2.134
	I68.1-I68.2, I69.0-I69.2	
Atrial fibrillation and flutter	I48	1.134 - 1.76
Aortic aneurysm	I71	1.119 - 1.544
Peripheral vascular disease	I73	1.095 - 1.728
Other cardiovascular and circulatory diseases	I27, I28, I30-I31, I34-I37, I44-I45, I47,	1.137 - 1.744
	172, 177-178, 180, 182-184, 186-189,	
	I95-I98	
Chronic kidney disease due to hypertension, and glomerulonephritis	I12-I13.9; N03-N06	1.281*
Chronic kidney disease due to other and unspecified causes	N02, N07-N08, N18	1.282*
Chronic kidney disease due to diabetes mellitus	E10.2, E11.2	1.283*
*Relative risk was the same for all ages. Adapted from GBD 2017. ¹²⁹		

Table 2. Estimated mean (standard deviation) systolic blood pressure (mm Hg) for South African adults (≥25 years) by population group for 2000, 2006 and 2012.

Year	Sex	Black African	Coloured	Asian	White	National
2000	Men	124.7 (19.3)	130.8 (18.1)	128.5 (16.2)	127.6 (18.0)	127.3 (20.3)
	Women	123.5 (22.8)	126.5 (22.8)	120.2 (19.1)	122.1 (18.6)	124.5 (23.0)
2006	Men	125.8 (19.7)	131.3 (18.5)	127.1 (15.5)	128.8 (17.5)	127.8 (20.5)
	Women	123.8 (22.7)	128.6 (22.6)	121.7 (19.7)	123.5 (18.4)	124.9 (22.8)
2012	Men	126.6 (19.8)	131.6 (18.8)	125.5 (14.7)	129.4 (16.8)	128.3 (20.6)
	Women	123.8 (22.4)	130.5 (22.2)	122.9 (20.2)	124.8 (18.3)	125.2 (22.6)

The prevalence of hypertension (defined as BP \geq 140/90 mmHg and/or on antihypertensive medication) for 2000, 2006 and 2012 by sex, shown in Fig. 1, demonstrated a marked increase from 2000 to 2012. For men, the prevalence of hypertension increased from 31.1% to 38.9%, and for women the prevalence increased from 34.4% to 40.0%. Hypertension prevalence, in contrast to the mean SBP measurements, was higher in women than men throughout the study period.

Notably, the trends for hypertension prevalence between 1998 and 2015 differed by population group (Figs. S6 - S9 in appendix: https://www.samedical.org/ file/1842). Hypertension prevalence increased consistently within age categories in black African and coloured men and women, and in white women across two decades. Hypertension prevalence plateaued within age categories over time in Asian men and women, and white men.

The ASRs for deaths and DALYs attributable to raised SBP for men and women aged ≥ 25 years for the years 2000, 2006 and 2012 are shown in Fig. 2. In 2000 and 2012, for men, the death ASR (339/100 000

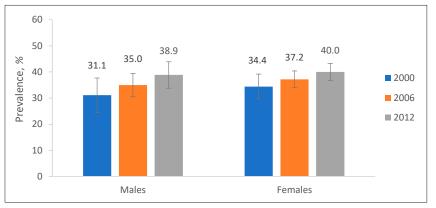


Fig. 1. *Prevalence of hypertension in males and females* (\geq 25 years) *in South Africa for 2000, 2006 and 2012.*

v. 334/100 000) and DALYs (5 542/100 000 v. 5 423/100 000) were similar, whereas for women the death ASR decreased (318/100 000 v. 277/100 000) as did age-standardised DALYs (5 405/100 000 v. 4 778/100 000).

Burden attributable to raised SBP

The estimated PAFs for raised SBP for 2000, 2006 and 2012 are shown for males, females and persons in Table 3 for all

related outcomes. The table shows that deaths and DALYs attributable to high SBP were substantial and increased slightly over time. In 2000, raised SBP caused an estimated 55 895 deaths (95% UI 49 717 - 56 588), accounting for 11.1% of total deaths. This increased to 62 314 deaths (95% UI 62 519 - 63 608), accounting for 12.4% of all deaths in 2012. PAFs were higher for females throughout the study

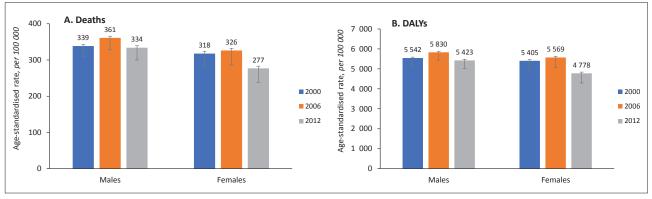


Fig. 2. Age-standardised (A) death and (B) disability-adjusted life year (DALY) rates attributable to high systolic blood pressure in South African adults aged \geq 25 years for 2000, 2006 and 2012.

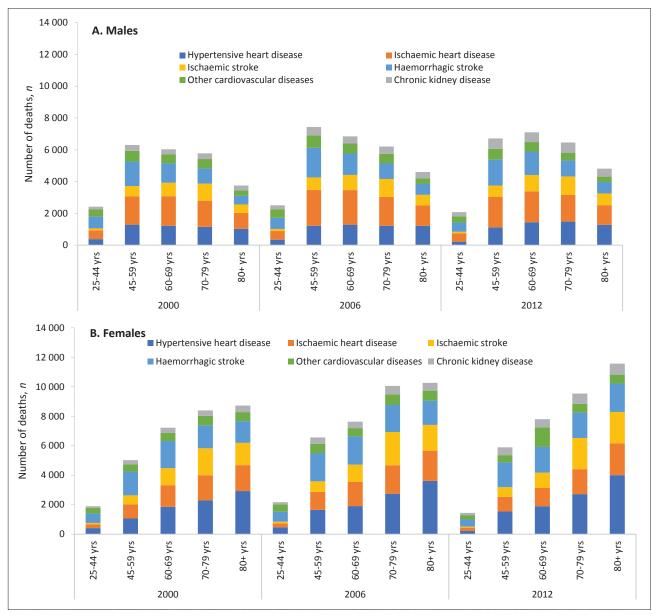


Fig. 3. Mortality attributable to systolic blood pressure >115 mmHg in (A) males and (B) females (aged \geq 25 years) in South Africa for 2000, 2006 and 2012.

period. The attributable fraction for raised SBP accounted for 13.3% deaths in females compared with 9.1% in males in 2000. By 2012, this increased to 14.8% and 10.2%, respectively.

PAFs were highest for hypertensive heart disease (HHD) with 84% - 85% of HHD deaths attributable to raised SBP across the three time points. This was followed by haemorrhagic stroke with 60% - 62% of

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41 546 12014 39 446 10799 40 992 22 813 36 204 9 615 32 145 8 783 34 349 18 398 28 95 2 645 25 148 3 740 26 243 6 385 36 154 2 289 35 88 1 370 36 243 5 565	ronic kidney disease due to hypertension	42	928	20 882	40	1 315	27 955	41	2 243	48 837
36 204 9 615 32 145 8 783 34 349 18 398 28 95 2 645 25 148 3 740 26 243 6 385 36 154 2 289 35 88 1 370 36 242 3 659	rronic kidney disease due to other and specified causes	41	546	12 014	39	446	10 799	40	992	22 813
28 95 2645 25 148 3740 26 243 6385 36 154 2289 35 88 1370 36 242 3659	ortic aneurysm	36	204	9 615	32	145	8 783	34	349	18 398
36 154 2 289 35 88 1 370 36 242 3 659	eumatic heart disease	28	95	2 645	25	148	3 740	26	243	6 385
	nronic kidney disease due to	36	154	2 289	35	88	1 370	36	242	3 659
	omerulonephritis									:

		Males			Females	S		Total persons	rsons
Disease outcomes	AF (%)	Deaths	DALYs	AF (%)	Deaths	DALYs	AF (%)	Deaths	DALYs
Atrial fibrillation and flutter	39	90	4 580	38	149	4 732	38	239	9 312
Endocarditis	28	115	1 855	26	70	1 092	27	185	2 947
Peripheral vascular disease	45	70	1 447	47	106	2 276	46	176	3 723
Chronic kidney disease due to diabetes	38	86	1 796	34	51	983	37	137	2 779
mellitus									
Total attributable burden	ı	27 608	495 379	ı	36 683	628 421	,	64 290	1 123 800
95% UI		(25 494 - 27 842)	(466 577 - 498 253)	1	(32 156 - 37 351)	(571 001 - 635 392)		(57 738 -65 061)	(1 038 796 - 1 131 616)
% of total burden	ı	10.4	5.1	ı	15.4	6.7	ı	12.7	5.9
95% UI	ı	(9.6 - 10.4)	(4.8 - 5.1)	ī	(13.5 - 15.7)	(6.1 - 6.8)		(11.4 - 12.9)	(5.4 - 5.9)
2012									
DHH	85	5 550	87 250	85	10 365	16 0215	85	15 915	247 465
IHD	55	7 297	127 086	54	6 308	10 4036	55	13 605	231 122
Haemorrhagic stroke	63	5 414	96 047	60	7 556	128 966	62	12 970	225 012
Ischaemic stroke	55	3 732	55 867	52	6 018	87 119	53	9 750	14 2985
Other cardiomyopathy	46	1 733	37 399	47	1 859	4 3117	46	3 592	80 516
Other cardiovascular and circulatory diseases	40	1 249	26 063	35	971	20 053	37	2 220	46 115
Chronic kidney disease due to hypertension	43	734	18 750	40	981	23 760	42	1 715	42 510
Chronic kidney disease due to other and	44	663	16 066	42	577	15 866	43	1 240	31 931
unspecified causes									
Aortic aneurysm	39	191	12 985	35	118	12 493	37	309	25 478
Rheumatic heart disease	41	112	6 965	38	168	6 007	39	280	12 972
Chronic kidney disease due to glomerulonephritis	37	136	1 984	33	66	1 091	36	202	3 075
Atrial fibrillation and flutter	29	116	1 791	27	82	1 387	28	198	3 178
Endocarditis	29	67	1 760	26	120	3212	27	187	4 972
Peripheral vascular disease	40	86	1 813	35	44	819	38	130	2 632
Chronic kidney disease due to diabetes mellitus	46	84	1 955	48	122	3 231	47	206	5186
Total attributable burden		27 164	493 779		35 354	611 370		62 519	1 105 148
95% UI		(24 949 - 27 475)	(463 740 - 497 209)	,	(30 241 - 36 168)	(547 673 - 619 836)	ı	(55 327 - 63 608)	(1 013 871 - 1 115 666)
% of total burden	ı	10.2	5.1	ı	14.8	6.5	,	12.4	5.8
95% UI		(9.4 - 10.3)	(4.8 - 5.1)	,	(12.7 - 15.2)	(5.8 - 6.6)	,	(11.0 - 12.6)	(5.3 - 5.8)

mortality attributable to raised SBP, and ischaemic heart disease (IHD) (54% - 55%) and ischaemic stroke (52% - 53%).

The trends for DALYs were similar to those for deaths (Table 3). DALYs increased from 970 056 (UI 890 361 - 978 267) in 2000 to 1 105 148 (UI 1 013 871 - 1 115 666) in 2012. Attributable DALYs for raised SBP increased over the 12-year period and were higher in females (2000: 5.7%; 2012: 6.5%) than in males (2000: 4.5%; 2012: 5.1%).

Contribution of disease conditions to mortality attributable to high SBP

The attributable deaths for high SBP by the major causes and presented by age and sex between 2000 and 2012 are shown in Fig. 3. Interestingly, the trends across age categories differed in males and females. In 2000 and 2006, mortality attributable to high SBP peaked in 45 - 49-year-old working-age men, whereas in 2012 it peaked in 60 - 69-year-olds. In contrast, the mortality attributable to high SBP in females increased with age across all three years, peaking in the oldest women aged >80 years.

The estimated proportions of deaths attributable to high SBP are shown in Fig. 4 for major conditions in females and males for 2000 and 2012. Over 80% of mortality in males and females attributable to HBP was due to stroke, IHD and HHD across both time points. Stroke (haemorrhagic and ischaemic) was the predominant contributor to mortality in both males (2000: 33%; 2012: 34%) and females (2000: 40%; 2012: 38%). Mortality attributable to IHD was higher in males (27% - 28%) than females (17% - 20%), while the converse was true for HHD (males: 20% - 21%; females: 27% - 29%). From 2000 to 2012, deaths from chronic kidney disease increased in males from 6% to 10%, and in females from 5% to 7%, respectively.

Interestingly, in 2000 and 2012, the contribution of stroke, IHD and HHD to mortality attributable to HBP differed by population groups (Fig. S9 in appendix: https://www.samedical.org/file/1842). IHD was the predominant contributor to mortality attributable to HBP in Asian and white males (60% - 63%) and females (46% - 49%). The rates of IHD and stroke mortality attributable to HBP were almost comparable in coloured males (stroke: 34% - 37%; IHD: 39%) and females (stroke: 36% - 37%; IHD: 32%). Stroke (haemorrhagic and ischaemic) predominated in black African males (37% - 38%) and females (41% - 42%), followed by HHD (men: 25% - 27%, females: 31% - 34%) and then IHD (males: 16% - 17%, females: 11% - 13%). Notably, within populations groups, IHD was consistently higher in males than females, as expected.

Fig. 5 shows that the ASRs for deaths and DALYs by population group in 2000 and 2006 were highest for Asians followed by coloureds, with these rates decreasing in 2012. Whites had the lowest death ASR across all years. In contrast to their counterparts who demonstrated declining rates from 2000 to 2012, in black Africans, these rates were higher in 2006 than 2000, but dropped in 2012. The patterns illustrated in Fig. 5 are reflected in the age-standardised trends of the predominant contributors to high SBP mortality (Table S6 in appendix: https://www.samedical.org/

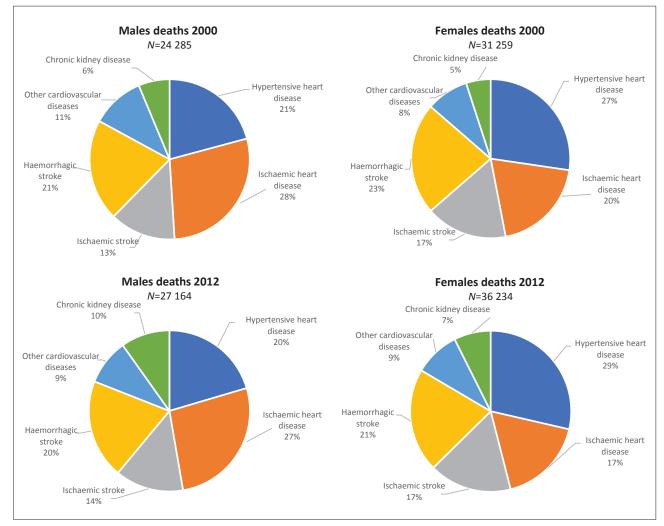


Fig. 4. Mortality attributable to systolic blood pressure >115 mmHg in South African adults aged \geq 25 years presented by sex for 2000 and 2012.

file/1842). For example, in Asian males, the age-standardised IHD deaths per 100 000 attributable to high SBP were the highest for any condition by population group across all time points. The fewer age-standardised IHD deaths attributable to high SBP in Asian males in 2012 (224.2/100 000) compared with 2000 (316.8/100 000) were mirrored in the decline in their death ASRs. A similar trend was found in Asian females.

Discussion

This study has described the trends in raised SBP and hypertension prevalence and quantified the burden of disease (ASRs for

deaths and DALYs) attributable to high SBP in 2000, 2006 and 2012. Although mean SBP remained stable but suboptimal over the study period, the prevalence of hypertension increased. Mortality and DALYs attributable to high SBP increased slightly between 2000 and 2012. There were differences by population group: the death ASRs were highest for Asians in 2000 and 2006, but decreased approximating that for black Africans in 2012. Stroke, HHD and IHD were the predominant causes of mortality attributable to high SBP with differences by population group and sex.

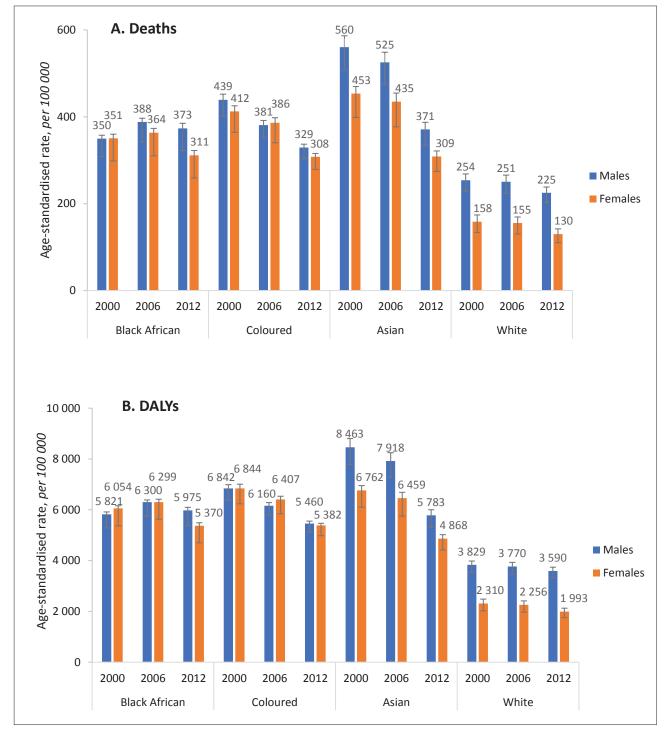


Fig. 5. Age-standardised (A) death and (B) disability-adjusted life year (DALY) rates attributable to systolic blood pressure >115 mmHg by population group and sex in South Africa for 2000, 2006 and 2012.

The burden of high SBP was considerable over the study period of more than a decade, accounting for 12.4% of mortality and 5.8% of DALYs in 2012 in SA. Globally, high SBP was the leading single risk factor for mortality, contributing to 9.4 million deaths and 7.0% of DALYs in 2010,^[18] and remained high in 2015 with DALYs increasing to 7.8% in women and 9.2% in men.^[34] This underscores the fact that greater attention needs to be focused on the prevention and management of high SBP and hypertension globally and in SA to curb the related morbidity and mortality. Preventive lifestyle measures include decreasing salt intake, increasing fruit and vegetable consumption, greater physical activity and avoiding harmful alcohol intake, while quitting tobacco decreases the risk of hypertension complications.[35] Addressing these behavioural risk factors together with the use of optimal antihypertensive medication can substantially reduce the adverse health burden associated with HBP.

Across all time points, population groups and sexes, mean SBP was higher than the clinically recommended optimal cut-point of 120 mmHg, with slight increases shown in many subgroups from 2000 to 2012. This is of concern considering that the adverse consequences of SBP have been demonstrated with lower SBP measurements of 115 mmHg, which fall into the clinically defined normal BP range. The current mean SBP measurements in this study do not warrant clinical drug intervention but could easily be lowered to optimal readings by adopting the lifestyle measures advocated above. This underscores the need for population-level interventions to improve the health of the nation. Such interventions may include the need for improved diets through reformulation of foods such as mandated reductions in salt, improving the built environment to encourage physical activity, tightening tobacco control legislation and introducing alcohol control initiatives, among other measures.

An increase in hypertension prevalence accompanied by a stable mean SBP was unexpected. However, this may be related to the treatment of hypertension with antihypertensive medication, which would have contributed to lower BP. This may be reflected in the higher hypertension prevalence but lower mean SBP in women than men across all time points. Although the management of hypertension is suboptimal in SA, women have been found to have better rates of controlled hypertension than men.^[8,36,37] These better control rates, despite the higher hypertension prevalence, could have contributed to lower BP measurements in women.

The exception, however, was Asian men, who were the only subgroup whose mean SBP decreased over time within all age categories, while their hypertension prevalence remained stable. The reason for this may be perhaps greater vigilance among their healthcare providers in treating their hypertension and lowering BP measurements, because of the known susceptibility to adverse outcomes and greater risk for IHD in Asian/Indian men.[38,39] Mortality from circulatory diseases is known to vary among ethnic/ population groups, with a considerable excess of IHD reported globally among people of Indian descent.^[40] This accords with the findings of the present study, where 60% - 62% of mortality attributed to high SBP in Asian men was because of IHD. Further, ASRs for deaths and DALYs in 2000 and 2006 were substantially higher in Asian men than other men, despite their comparable or even lower mean SBP measurements. The lowering of their mean SBP over time may have contributed to the decline in the death ASR in Asian men from >500/100 000 in 2000 and 2006 to <400/100 000 in 2012.

Owing to the complexity of the influences and interactions on mean SBP and adverse outcomes, there are likely to be other contributors to the high death ASRs and DALYs in both Asian men and women, compared with their counterparts, particularly in 2000 and 2006. These poorer outcomes, despite comparable or lower mean SBP, particularly in Asian women, may be attributed to more frequent comorbidities such as diabetes, or a greater genetic susceptibility, among other influences, in Asians. A multicentre SA study reported a greater likelihood for hypertension in Indian women,^[41] after adjusting for other hypertension risk factors, which may perhaps contribute to their poorer outcomes. Further research is required to explore the influences on ASRs for deaths and DALYs in SA, which is beyond the scope of the current study. The conditions contributing to mortality attributable to high SBP by population groups were in keeping with the literature. While IHD is common in Asians and whites, stroke is the most frequent sequela of high BP in black Africans.^[42] Nevertheless, delays in accessing care following a stroke are common, and a major impediment to successful outcomes. Considering the substantial burden associated with stroke in SA, awareness of the symptoms of stroke and the urgent need for early care should be highlighted via health education campaigns in the country.^[7]

The substantial mortality burden attributable to high SBP in <60-year-old adults in this study, i.e. premature mortality, is likely to be due to suboptimal hypertension control. These preventable early deaths are of grave concern because they affect the working-age SA population. The deaths of breadwinners in poor communities have farreaching social and financial repercussions, and frequently exacerbate poverty. This pattern reflects the high proportion of cardiovascular disease mortality, mainly due to IHD and stroke, that occurs in <60-year-old adults in LMICs, and which is likely linked to poor management of cardiovascular diseases and their risk factors.^[7]

The well-established rise in BP with older age was expected to be reflected in higher mortality attributable to high SBP with increasing age. However, across all time points, this trend was evident for women in this study, but not in men. A possible explanation may be the shorter lifespan in SA men (59.7 years) compared with women (65.1 years). The substantially fewer men than women >60 years of age may thus have contributed to the declining trend in mortality attributed to high SBP in men. Nonetheless, further research is required to understand the mortality patterns attributed to high SBP in SA men aged >60 years.

Mean SBP was higher in coloured women than in other women, and may be related, among other adverse influences, to their higher prevalence of severe obesity (25.7% v. 20.4% overall).^[8] Further, rates of harmful alcohol intake (defined as consuming \geq 5 drinks on at least one occasion in the past 30 days) were more than double in coloured women compared with the overall rate in women (10.2% v. 4.8%). Moreover, coloured women and men, compared with other population groups, were most likely to consume salty snacks daily (20.3% v. 12.8% overall). The daily consumption of fried foods, fast foods and processed meats was also highest in the coloured population compared with their counterparts. These unhealthy dietary habits in coloured men likely contributed to their higher mean SBP compared with their counterparts. This underscores the importance of avoiding unhealthy lifestyle behaviours to maintain optimal BP.

SACRA2 builds on SACRA1, although the findings of the two studies are not directly comparable because of the different methodologies and outcomes used for analyses. The present study used an updated method to estimate the burden of disease, whereby data on individual SBP measurements were extracted from nine population surveys conducted in SA between 1998 and 2017. We adopted a meta-regression approach for the estimation of mean and SD of the population distribution of SBP, by sex, age and population group. Our study also included updated disease outcomes, as evidence has emerged to support the causality of high SBP in other diseases (e.g. rheumatic heart disease, endocarditis and other cardiomyopathies, atrial fibrillation and flutter, aortic aneurysm, peripheral vascular disease, other cardiovascular and circulatory diseases, chronic kidney disease due to hypertension, glomerulonephritis, chronic kidney disease due to other and unspecified causes, and chronic kidney disease due to diabetes mellitus). Hence we report a much higher number of deaths and DALYs attributable to high SBP in 2000 (55 895 deaths and 970 056 DALYs) compared with the same year in the previous study. The observed differences in the death and DALY rates can be accounted for by other circumstances, including the use of an upgraded methodology for estimating exposure.^[29]

Study limitations and strengths

Our study did not estimate the burden of high DBP nor the burden in adults <25 years of age. Estimates depended on extrapolating the quantitative effects of BP and the GBD RR values for SBP on cardiovascular diseases obtained from Cochrane reviews and the GBD 2017 study (mainly meta-analysis), which do not necessarily represent the risk of cardiovascular outcomes for the SA population. However, it may not affect the results of longitudinal comparison within the same region as well as horizontal comparison among a population with similar characteristics. Although many of these RRs have been adjusted for the major confounders (e.g. age, sex, smoking and physical activity), the possibility of residual confounding cannot be excluded.

The strength of this study includes the use of publicly available nationally representative surveys on prevalence of hypertension that include both self-reported information on the use of medication and standard measurement of SBP disaggregated by age, sex and population group over time. We used the RR from the GBD study derived from a meta-regression of studies from other countries reported in two recent Cochrane meta-analyses of 107 randomised trials on the effect of reduced sodium intake on BP. Since Cochrane reviews are considered the gold standard, we believe we are using strong data for our estimates. The use of GBD-approach methodology allows for comparisons under similar conditions.

Tracking mean SBP and the prevalence of hypertension are essential components of non-communicable disease (NCD) surveillance, and will contribute to an understanding of their effectiveness as well as provide information needed to develop policies and programmes to reduce the impact of HBP. However, the national NCD surveillance system is currently underdeveloped. Ideally, SBP should be monitored at a population level using a standardised protocol. Nevertheless, the pooled analysis of large population-based studies demonstrated very similar estimates of mean SBP and prevalence of hypertension for SA.^[43]

Conclusion

The overall mean SBP levels of men and women in the general population have remained high but constant, although the prevalence of hypertension has increased and the burden attributable to high SBP remains substantial. This is despite easily adoptable proven preventive measures and the availability of low-cost, effective antihypertensive medication. Our results support increased efforts at both the population level, i.e. prevention measures, and the individual level, i.e. optimal hypertension management, to curb the disease burden associated with high SBP.

Furthermore, the mortality burden attributable to high SBP in adults <60 years of age was unacceptably high. Together with optimal hypertension care, there needs to be timely and appropriate management of cardiovascular diseases. This is particularly true for stroke, which was responsible for over a third of the mortality attributable to high SBP. To prevent cardiovascular disease morbidity and mortality, particularly in younger working-age adults, widespread mass education campaigns for cardiovascular disease prevention and care in SA are crucial.

Disclaimer. The population group classification is based on self-reporting according to the groups defined by the Population Registration Act of 1950, i.e. black African, coloured (persons of mixed descent), Indian/Asian (persons of Indian descent) and white (persons of European descent). This classification is being used to highlight issues that reflect effects of historical disparities, and the authors do not subscribe to this classification for another purpose.

Declaration. None.

Acknowledgements. The survey review team, led by VPvW, conducted the risk of bias assessment of the national surveys. The following individuals are acknowledged for their contribution: DB, RAR, OA, ET, Pam Groenewald, Andiswa Zitho, BN, Jané D Joubert, Mmakamohelo Direko, Mweete Nglazi, Nomonde Gwebushe, Nomfuneko Sithole, AC, Linda Mbuthini, Lyn Hanmer, Akhona Ncinitwa, Nadine Nannan, Nada Abdelatif, Richard Matzopoulos, IN, Ali Dhansay and Ria Laubscher. The NBD team, led by VPvW, was responsible for mapping the NBD and GBD causes generating YLDS and DALYS estimates for national, province and population group. The following individuals are acknowledged for their contribution: William Msemburi, OA, AC, IN, Tracy Glass, Pam Groenewald and DB.

Author contributions. Conceived and designed the study: BN, RP, DB, VPvW. Prepared data for analysis: AC. Analysed the data: NA, AC. Interrogated and interpreted results: all. Drafted manuscript: BN, NA, VPvW, DB, AC. Edited manuscript for clinical significance: NP. Critical review of manuscript: all. Senior authors: DB, VPvW, RP. Agreed to final version: all.

Funding. This research and the publication thereof have been funded by the SA Medical Research Council's Flagships Awards Project (SAMRC-RFA-IFSP-01-2013/SA CRA 2). DB was principal investigator together with co-principal investigators VPvW and Jané D Joubert.

Conflicts of interest. None.

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Accepted 24 March 2022