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Estimating the changing burden of disease attributable to high body mass index in South Africa for 2000, 2006 and 2012

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Background. A high body mass index (BMI) is associated with several cardiovascular diseases, diabetes and chronic kidney disease, cancers, and other selected health conditions.

Objectives. To quantify the deaths and disability-adjusted life years (DALYs) attributed to high BMI in persons aged \geq 20 years in South Africa (SA) for 2000, 2006 and 2012.

Methods. The comparative risk assessment (CRA) methodology was followed. Meta-regressions of the BMI mean and standard deviation from nine national surveys spanning 1998 - 2017 were conducted to provide estimates by age and sex for adults aged \geq 20 years. Population attributable fractions were calculated for selected health outcomes using relative risks identified by the Global Burden of Disease Study (2017), and applied to deaths and DALY estimates from the second South African National Burden of Disease Study to estimate the burden attributed to high BMI in a customised Microsoft Excel workbook. Monte Carlo simulation-modelling techniques were used for the uncertainty analysis. BMI was assumed to follow a log-normal distribution, and the theoretical minimum value of BMI below which no risk was estimated was assumed to follow a uniform distribution from 20 kg/m² to 25 kg/m².

Results. Between 2000 and 2012, mean BMI increased by 6% from 27.7 kg/m² (95% confidence interval (CI) 27.6 - 27.9) to 29.4 kg/m² (95% CI 29.3 - 29.5) for females, and by 3% from 23.9 kg/m² (95% CI 23.7 - 24.1) to 24.6 kg/m² (95% CI 24.5 - 24.8) for males. In 2012, high BMI caused 58 757 deaths (95% uncertainty interval (UI) 46 740 - 67 590) or 11.1% (95% UI 8.8 - 12.8) of all deaths, and 1.42 million DALYs (95% UI 1.15 - 1.61) or 6.9% (95% UI 5.6 - 7.8) of all DALYs. Over the study period, the burden in females was ~1.5 - 1.8 times higher than that in males. Type 2 diabetes mellitus became the leading cause of death attributable to high BMI in 2012 (*n*=12 382 deaths), followed by hypertensive heart disease (*n*=12 146), haemorrhagic stroke (*n*=9 141), ischaemic heart disease (*n*=7 499) and ischaemic stroke (*n*=4 044). The age-standardised attributable DALY rate per 100 000 population for males increased by 6.6% from 3 777 (95% UI 2 639 - 4 869) in 2000 to 4 026 (95% UI 2 831 - 5 115) in 2012, while it increased by 7.8% for females from 6 042 (95% UI 5 064 - 6 702) to 6 513 (95% UI 5 597 - 7 033).

Conclusion. Average BMI increased between 2000 and 2012 and accounted for a growing proportion of total deaths and DALYs. There is a need to develop, implement and evaluate comprehensive interventions to achieve lasting change in the determinants and impact of overweight and obesity, particularly among women.

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The article in context

Evidence before this study. SA has a high prevalence of overweight and obesity among women. The first South African Comparative Risk Assessment Study (SACRA1) in 2000 estimated that the attributable burden due to excess body weight ranked fifth in terms of mortality and disability-adjusted life years (DALYs) among 17 risk factors evaluated, and accounted for 6.0 - 7.4% of total adult deaths and 2.4 - 3.0% of total adult DALYs.

Added value of this study. This study applied CRA methodology for three time points: 2000, 2006 and 2012. Nine national surveys were used to determine the trends in BMI, and an updated evaluation of the epidemiological evidence of the relative risks (RRs) of health outcomes was drawn from the Global Burden of Disease studies. The study revealed a steady increase in the prevalence of overweight and obesity between 2000 and 2012 and that high BMI resulted in 58 757 deaths in 2012, accounting for 11.1% of total deaths. The estimate for 2000 has been revised upwards, and the substantial difference between males and females has been confirmed.

Implications of the available evidence. A comprehensive strategy addressing fundamental systems will be required to stem the increasing prevalence of overweight and obesity in SA and reduce the burden of disease attributable to high BMI. The SA government has taken bold steps in introducing taxation of sugar-sweetened beverages, and is urged to implement the other strategies outlined in its 2015 Obesity Prevention and Control Strategy.

The state of being either under- or overweight throughout the life course is associated with adverse health outcomes.^[1] The public health challenge associated with increasing overweight and obesity has been recognised globally: during the last quarter of the 20th century, the world transitioned from an era when the prevalence of underweight was more than double that of obesity, to one in which more people are obese than are underweight.^[2] The development of overweight and obesity during the life course reflects, among other things, environmental and genetic interactions, and - partly due to fetal and postnatal imprinting - individuals from disadvantaged communities seem to have greater risks of these states than more affluent individuals.^[3] The growing trend in obesity is associated with progressive secular and age-related decreases in physical activity, together with substantial dietary changes with passive over-consumption of energy, despite the neurobiological processes controlling food intake.[3]

Over time, the complex mechanisms by which obesity promotes cardiovascular disease and diabetes are being revealed.^[4-8] White fat cells release bioactive mediators that result in chronic inflammation and insulin resistance, causing dyslipidaemia, high blood pressure, atherosclerosis and fibrinolysis and affecting coagulation. In addition, chronic inflammation has been found to affect tumour progression.^[8] Harmful renal effects of obesity may be mediated by hypertension or diabetes mellitus, as well as direct effects resulting in specific pathological changes in the kidneys. These include the development of glomerular hypertension, ectopic lipid accumulation and increased glomerular permeability caused by hyperfiltrationrelated glomerular filtration barrier injury, and ultimately the development of glomerulomegaly and glomerulosclerosis.^[9] A recent study by the Global BMI Mortality Collaboration $^{\scriptscriptstyle [10]}$ has demonstrated that overweight and moderate obesity are clearly associated with increased mortality.

BMI is a weight-for-height index of body fat, calculated as a person's weight in kilograms (kg) divided by the square of his/her height in metres (m²).^[11] BMI is not a direct measurement of body fat content, but is highly correlated with direct measures of body fat, including those obtained from underwater weighing, skinfold thickness measurements, dual-energy X-ray absorptiometry, and other methods.^[12,13] Furthermore, BMI has been strongly correlated with various adverse health outcomes consistent with such direct measures of body fatness.^[12,14,15]

Concerns about the health and economic burden of increasing BMI have led to overweight and obesity being included among the global non-communicable disease targets of the Sustainable Development Goals.^[16] It is therefore essential for countries to track their progress on major modifiable risk exposures, and to identify whether the burden of disease attributable to such risk is declining, increasing or stagnating. In the first comparative risk factor assessment for SA, high BMI was associated with 7% of adult mortality in 2000, placing it among the top five leading causes of adult deaths in the country at that stage.^[17] Approximately 87% of type 2 diabetes mellitus (T2DM) deaths, 68% of hypertensive disease deaths, 61% of endometrial cancer deaths, 45% of ischaemic stroke deaths, 38% of ischaemic heart disease deaths, 31% of kidney cancer deaths, 24% of osteoarthritis deaths, 17% of colon cancer deaths of persons aged ≥30 years, and 13% of postmenopausal breast cancer deaths in females aged ≥45 years were attributable to having a BMI $\geq 21 \text{ kg/m}^2$.^[17]

With systematically evaluated weight and height data available from nine quality-assessed national surveys, the aim of the research reported in this article was to estimate national trends in BMI, as well as the disease and injury burden attributable to high BMI in adults aged \geq 20 years for the years 2000, 2006 and 2012, incorporating improved methods, updated information on levels of exposure, and revised RRs. The updated findings for 2000 are compared with those from SACRA1^[17] and findings from 2012 – the latest year for which there are reliable national burden of disease estimates.^[18] We selected 2006, as this was when deaths due to HIV/AIDS peaked, representing a definitive point in national mortality trends. The results presented here supersede all previously published SACRA estimates.

Methods

The estimation of attributable burden from high BMI followed the general framework established for CRAs, as used in the Global Burden of Diseases, Injuries, and Risk Factors studies since 2002.^[19,20] The population attributable fraction (PAF) was calculated for selected health outcomes identified through systematic assessments conducted for the Global Burden of Disease (GBD) studies and applied to local estimates of the mean BMI, based on a meta-regression of national surveys and burden of Disease estimates from the second South African National Burden of Disease Study (SANBD2) for the respective years.^[21]

Estimation of population exposure

We used data from nine national surveys conducted in SA which measured the height and weight of representative samples of the adult population, namely the three South Africa Demographic and Health Surveys (SADHSs) from 1998 to 2016, [22-24] the five waves of the National Income Dynamics Study (NIDS) from 2008 to 2017,^[25-29] and the South African National Health and Nutrition Examination Survey (SANHANES-1) of 2012.^[30] We used the cut-offs shown in Table S1 in the appendix (https://www.samedical.org/file/1814) to identify implausible values of weight and height and BMI, which we excluded from the analysis. For surveys recording replicated measurements of height and/or weight, the multiple values were averaged, based on the measurement protocol of the survey (Table S2 in the appendix: https://www.samedical.org/file/1814), and the result was considered as the individual's height and weight, respectively. The number of records with non-missing values of BMI before and after applying the cleaning procedure is shown in Table S3 in the appendix (https://www.samedical.org/file/1814).

We used standard statistical methods (weighted averages with robust standard errors) to take into account the complex sampling design of each survey, to calculate the mean and the standard deviation (SD) of the BMI distribution in each subpopulation defined by sex and 5-year age groups (15 - 19, ..., 75 - 79, ≥80 years). These estimates were used as inputs of a linear meta-regression model, fitted using a weighted ordinary least-square estimator, with weights calculated as a combination of the variance of each estimate and a survey 'quality score' derived through systematically reviewing the methodology and implementation^[31] using quality effect weighting, as described by Doi *et al.*^[32,33] The model has the form:

$$BMI_{s,g} = \beta_o + \beta_1 \cdot YEAR_s + \sum_{i=1}^{27} \beta_{i+1} \cdot GROUP_{g,i} + \sum_{i=1}^{27} \beta_{i+28} \cdot GROUP_{g,i} \cdot YEAR_s + \varepsilon_{s,g}$$

where s = 1,...9 is the survey indicator; g = 1,...28 is the indicator of the 28 age-sex groups (14 age categories for each sex); BMI_{sg} is the BMI for age-gender group g estimated from survey s; $YEAR_s$ is the median year of data collection of survey s; $GROUP_{gi}$; i = 1,...27 are the 27 dummy variables indicating group membership ($GROUP_{gi} = 1$ for I = g + 1, 0 otherwise); ε_{sg} is the estimation error for survey s and group g, and we assume that $\varepsilon_{sg} \sim N(0,\sigma)$ for each g and s; and β_0 to β_{55} are model coefficients.

To assess whether a non-linear trend would fit the data significantly better, a generalised additive model was also fitted to the data. This model relaxes the assumption of a linear trend and allows the average BMI (in each age-gender group) to be a smooth function of time. The smooth trend has been modelled with a thin-plate spline. As there were no strong statistical considerations to support the choice of the flexible model, considerations regarding data quality and the presence of implausible trends, especially in older age groups, led to the decision to apply linear time trends for each age and sex group. We used a similar approach to model the change in the SD of the BMI distribution.

The models were used to predict the age- and sex-specific mean and SD of the BMI distribution for the years 2000, 2006 and 2012 and age ≥ 20 years for use in this study. The method of moments was applied to derive parameters for the log-normal distribution, as it provided a better fit to the data than a normal distribution, particularly in the lower range of BMI values. The proportions of the population in six BMI classes including three grades of obesity (30.0 - <35.0 kg/m², 35.0 - <40.0 kg/m², and 40.0 - <60.0 kg/m²) (Table S4 in the appendix: https://www.samedical.org/file/1814)) were also estimated from the log-normal distribution.

Table 1. Disease outcome, ICD-10 cod	es, and RRs per 5-unit	increase in bo	dy mass index l	by age and sex		
			RR constant w	ith age		
Disease outcome	ICD-10 code	Age (yrs)	Male		Female	
Oesophageal cancer	C15	≥20	1.391		1.351	
Colorectal cancer	C18 - C21	≥20	1.177		1.059	
Liver cancer	C22	≥20	1.289		1.176	
Gallbladder and biliary tract cancers	C23 - C24	≥20	1.155		1.344	
Pancreas cancer	C25	≥20	1.071		1.210	
Breast cancer (premenopausal)	C50	20 - 49	-		0.890	
Breast cancer (postmenopausal)	C50	≥50	-		1.089	
Uterine cancer	C54 - C55	≥20	-		1.613	
Ovarian cancer	C56	≥20	-		1.038	
Kidney cancer	C64 - C66, C68	≥20	1.240		1.320	
Thyroid cancer	C73	≥20	1.221		1.136	
Non-Hodgkin's lymphoma	C82 - C85, C96	≥20	1.089		1.068	
Multiple myeloma	C88, C90	≥20	1.089		1.092	
Leukaemia	C91 - C95	≥20	1.086		1.131	
Atrial fibrillation and flutter	I48	≥20	1.344		1.346	
Asthma	J45 - J46	≥20	1.409		1.402	
Gallbladder and bile tract disease	K80 - K83	≥20	1.464		1.729	
Alzheimer's disease and other dementias	F00 - F03, G30 - G31	≥20	1.218		1.214	
Cataracts	H25 - H26, H28	≥20	1.104		1.104	
Low back pain	M47 - M54	≥20	1.100		1.100	
Gout	M10	≥20	1.628		1.493	
Osteoarthritis of the hip and knee	M13, M15 - M19	≥20	1.110		1.112	
		RR chan	ges with age (low	v and high valu	e)	
Disease outcome	ICD-10 code	Age (yrs)	Male low	Male high	Female low	Female high
Hypertensive heart disease	I11	≥20	1.697	3.122	1.697	3.122
Ischaemic heart disease	I20 - I25	≥20	1.170	2.274	1.170	2.274
Ischaemic stroke	G45 - G46.8,	≥20	1.068	2.472	1.068	2.472
	I63 - I63.9,					
	I65 - I66.9,					
	I67.2 - I67.8,					
	I69.3 - I69.4					
Haemorrhagic stroke	I60 - I62,	≥20	1.070	3.066	1.070	3.066
	I62.1 - I62.9,					
	I67.0 - I67.1,					
	I68.1 - 68.2,					
	I69.0 - I69.2					
T2DM (excluding CKD)	E11.0, E11.1,	≥20	1.461	3.547	1.461	3.547
	E11.3 - E11.9					
CKD due to T2DM	E11.2	≥35	1.431	2.036	1.431	2.036
CKD due to hypertension	I12 - I13	≥35	1.437	2.044	1.437	2.044
CKD due to glomerulonephritis	N03 - N06	≥35	1.452	2.044	1.452	2.044
CKD due to other and unspecified causes	N02, N07 - N08	≥35	2.044	2.032	2.044	2.032

Note: Age details can be found in Table S7 in the appendix (https://www.samedical.org/file/1814). Source: Outcomes from the second South African National Burden of Disease Study^[38] and RR values from Global Burden of Disease 2017.^[34] RR = relative risk; CKD = chronic kidney disease; T2DM = type 2 diabetes mellitus.

RRs for selected risk-outcome pairs

There were 27 risk-outcome pairs included in this study for females, including cancers, cardiovascular diseases, chronic kidney disease, respiratory conditions, gallbladder and biliary disease, Alzheimer's disease and other dementias, T2DM, low back pain, gout and osteoarthritis (Table 1). For males, these risk-outcome pairs excluded ovarian cancer and uterine cancer. The RRs used were obtained from the GBD study for 2017^[34] (Table S5 in the appendix: https://www.samedical.org/ file/1814). The common RR or the lowest RR was used from conditions specified in the GBD study that needed to be grouped into a single condition from the SANBD2 list of conditions. For premenopausal females, high BMI was protective (RR = 0.890), while for females >50 years of age (postmenopausal), high BMI was harmful (RR = 1.089). The RR for osteoarthritis of the hip was used for osteoarthritis of the knee, since the burden estimate was not differentiated by hip and knee.

Estimation of the PAF and attributable burden

The attributable burden for each health outcome was calculated using a continuous distribution formulation of the general PAF:

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

where x is the BMI exposure level in kg/ m^2 ; *h* is the maximum exposure level, taken to be 60 kg/m²; and l is the lowest possible exposure level, assumed to be 10 kg/m². P(x)is the population distribution of exposure, P'(x) is the counterfactual distribution of exposure, and RR(x) is the relative risk. The integral function IntLognormalperunitRR of EpigearXL^[36] was used to effect the calculation in Excel (Microsoft Corp., USA). The theoretical minimum risk distribution was assumed to follow a uniform distribution with a lower limit of 20 kg/m² and upper limit of 25 kg/m2. The PAFs were multiplied by the burden of disease estimates from the SANBD2 for deaths, years of life lost (YLLs), years lived with disability (YLDs) and DALYs for the respective age and sex categories, and summed to provide the total disease burden attributable to high BMI.

Summary population measures related to high BMI exposure

The percentages of the total number of deaths and DALYs were calculated for males, females and persons. In addition, age-standardised rates (ASRs) were computed for deaths and DALYs for males, females and persons in each age group (\geq 20 years) using SA population $estimates^{[37]}$ for age-specific rates and the World Health Organization world standard population weights. $^{[38]}$

Uncertainty analysis

To present uncertainty around the point estimates, Monte Carlo simulation techniques were applied using Ersatz software version 1.35 developed by Barendregt.^[39] This allows for the uncertainty in all calculations to be reflected. A normal distribution was specified for the mean and standard error of the BMI estimates, and the function ErRelativeRisk was used for the RR input variables. The ErRelativeRisk function assumes a log-normal uncertainty distribution for the RR, and introduces a correction to eliminate the upward bias in the mean of the randomly drawn values.^[40] The attributable burden and the ASRs were taken as output variables, and 95% uncertainty intervals (UIs) were presented bounded by the 2.5th and 97.5th percentiles, using 2 000 iterations.

Results

Estimates of the mean BMI from the metaregression are shown in Table 2 by age and sex for each study year. The mean BMI increased with age up to the age of 55 years and was consistently higher for females than males. The mean BMI increased between 2000 and 2012, from 27.7 kg/m² (95% CI 27.6 - 27.9) to 29.4 kg/m2 (95% CI 29.3 - 29.5) for females and from 23.9 kg/m2 (95% CI 23.7 - 24.1) to 24.7 kg/m² (95% CI 24.5 - 24.8) for males, accounting for a 6% and 3% increase for females and males, respectively. The proportional distribution of BMI categories is shown in Fig. 1, indicating noticeable increases in the proportions of grade 1, grade 2 and grade 3 obesity for females.

Fig. 2 shows the age-standardised death and DALY rates for the burden attributable to high BMI for males and females aged ≥20 years (values provided in Table S7 in the appendix: https://www.samedical.org/ file/1814). The ASR for deaths attributable to high BMI in those aged ≥ 20 years increased slightly for males, from 184 per 100 000 population (95% UI 127 - 240) in 2000 to 195/100 000 (95% UI 136 - 250) in 2012, i.e. a 6.2% increase in death rate. It showed a slight decrease for females (-3.9%), from 279/100 000 population (95% UI 229 - 314) in 2000 to 268/100 000 population (95% UI 218 - 305) in 2012. The age-standardised high BMIattributable DALY rate per 100 000 population for males increased by 6.6%, from 3 777 (95% UI 2 639 - 4 869) in 2000 to 4 026 (95% UI 2 831 - 5 115) in 2012, while it increased by 7.8% for females, from 6 042 (95% UI 5 064 - 6 702) to 6 513 (95% UI 5 597 - 7 033). In 2012, the female-to-male rate ratio was 1.4 for deaths and 1.6 for DALYs.

The estimated number of deaths and DALYs attributable to high BMI is reported in Table 3 for each disease outcome for males, females and persons for 2000, 2006 and 2012. The conditions are ranked from highest to lowest in terms of the number of person deaths in each year.

Hypertensive heart disease was the leading contributor to attributable deaths in 2000 and 2006, but T2DM became the leading disease associated with high BMI in 2012. In 2012, T2DM accounted for 21% of the deaths attributable to high BMI and 25% of the attributable DALYs, while hypertensive heart disease accounted for 21% of the deaths attributable to high BMI and 14% of the attributable DALYs.

Table 3 shows that high BMI accounted for 9.5% (95% UI 7.4 - 11.1) of all deaths

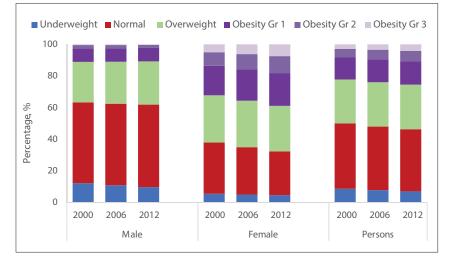


Fig. 1. Estimated body mass index category proportions for \geq 20-year-olds by sex in South Africa for 2000, 2006 and 2012.

in 2000 and increased to 11.1% (95% UI 8.8 - 12.8) in 2012, with a dip in 2006 to 8.6% (95% UI 6.8 - 10.0). This pattern was seen for males and females, although the proportions of deaths for females were substantially higher than those for males at each time point. In 2012, high BMI accounted for 15.4% (95% UI 12.8 - 17.0) of female deaths and 7.2% (95% UI 5.0 - 9.1) of male deaths. High BMI accounted for a lower proportion of total DALYs than total deaths for males and females, but followed identical temporal trends with a less pronounced dip in 2006.

The number of deaths attributable to high BMI is shown in Fig. 3 by disease outcome for 2000, 2006, and 2012 for males and females. The two younger age groups span 15 years each as there are fewer deaths in these age groups. Apart from the growth in numbers of deaths over time and the higher number of female deaths attributable to high BMI, there was a shift in the age distribution of the burden. In males, there was growth over time in the burden in those aged >50 years. Females displayed similar changes, with a noticeable increase in numbers of deaths in the 70 - 79-year age group. There were growing numbers of deaths from T2DM and chronic kidney disease in particular. Between 2000 and 2012, the death ASR per 100 000 population for T2DM increased by 21% for females (from 47.8 to 57.8) and by 40% for males (from 27.8 to 39.0) (Table 4). It also increased for chronic kidney disease, by 37% for females (from 18.5 to 25.3) and by 55% for males (from 15.0 to 23.1). In contrast, the death ASR for cardiovascular disease decreased by 13% for females (from 179.5 to 155.5), but showed little change for males (113.9 and 109.2).

Table 2. Estimated mean (SD) body mass index (kg/m^2) for ≥ 20 -year-olds by age group and sex in South Africa for 2000, 2006 and 2012

	20	00	20	06	20	12
Age group	Males,	Females,	Males,	Females,	Males,	Females,
(years)	mean (SD)					
20 - 24	22.1 (3.9)	24.6 (5.1)	22.1 (3.9)	25.0 (5.5)	22.1 (3.8)	25.5 (5.9)
25 - 29	23.2 (4.4)	26.2 (5.5)	23.2 (4.3)	26.9 (5.9)	23.2 (4.2)	27.6 (6.3)
30 - 34	23.8 (4.4)	27.6 (6.2)	23.8 (4.3)	28.2 (6.3)	23.9 (4.2)	28.9 (6.5)
35 - 39	24.1 (4.9)	28.9 (6.7)	24.3 (4.5)	29.4 (6.8)	24.5 (4.2)	29.8 (7.0)
40 - 44	24.8 (5.3)	29.2 (6.6)	24.7 (4.9)	29.7 (6.9)	24.7 (4.5)	30.2 (7.2)
45 - 49	25.0 (5.6)	29.5 (7.3)	25.1 (5.2)	30.0 (7.4)	25.1 (4.9)	30.6 (7.6)
50 - 54	25.6 (5.6)	29.5 (7.1)	25.6 (5.7)	30.4 (7.6)	25.6 (5.8)	30.8 (7.9)
55 - 59	25.1 (5.0)	29.5 (7.6)	25.6 (5.1)	30.3 (7.6)	26.1 (5.3)	31.1 (8.1)
60 - 64	24.5 (5.1)	29.5 (7.6)	25.1 (5.1)	30.0 (7.8)	25.6 (5.2)	30.5 (8.1)
65 - 69	24.8 (5.0)	29.1 (7.6)	25.4 (5.2)	29.8 (7.6)	25.9 (5.4)	30.5 (7.6)
70 - 74	24.6 (5.8)	27.4 (6.8)	25.2 (5.9)	28.2 (7.1)	25.7 (6.0)	29.0 (7.4)
75 - 79	24.9 (6.4)	27.7 (8.0)	25.3 (5.9)	28.1 (7.9)	25.7 (5.3)	28.5 (7.9)
≥80	22.4 (4.5)	26.8 (8.3)	23.2 (4.5)	27.2 (8.1)	24.0 (4.4)	27.6 (7.8)
Total ≥20	23.9 (4.9)	27.7 (6.7)	24.4 (5.0)	28.8 (7.2)	24.7 (5.0)	29.4 (7.5)

The contribution of the disease outcomes to the DALYs attributable to high BMI are shown by sex for 2000 and 2012 in Fig. 4. This also highlights the growing contribution of diabetes and chronic kidney disease to the attributable burden for both males and females, and the decreasing, although still very large, contribution of cardiovascular disease.

Discussion

This study found an increase in the mean BMI of 4% for males and 6% for females between 2000 and 2012. In 2000, 32.3% of adult women aged ≥ 20 years were obese, and this increased steadily to 38.9% in 2012, with a noticeable increase in the proportion of adult women categorised in the higher grades of obesity, associated with a markedly increased risk of mortality.^[9] The study found a 6.2% increase in the ASRs for male deaths and a 6.6% increase for male DALYs. However, the ASRs for female deaths decreased by 3.9% and female DALYs increased by 7.8%. The paradoxical result is due to the complex shifts in the disease burden and risk factor profile that have occurred in SA during this period, and is related to the observed decrease in cardiovascular disease (which has a high fatal/non-fatal ratio) and increases in diabetes and chronic kidney disease.^[18]

By 2012, high BMI accounted for 11.1% (95% UI 8.8 - 12.8) of total deaths and 6.9% (95% UI 5.6 - 7.8) of total DALYs, placing it among the leading risk factors. This followed a dip in the attributable burden proportion in 2006, due to HIV/AIDS accounting for a considerably higher proportion of deaths and DALYs in that year. The strong gender differences in the prevalence of overweight and obesity are reflected in the attributable burden, with 15.4% (95% UI 12.8 - 17.0) of

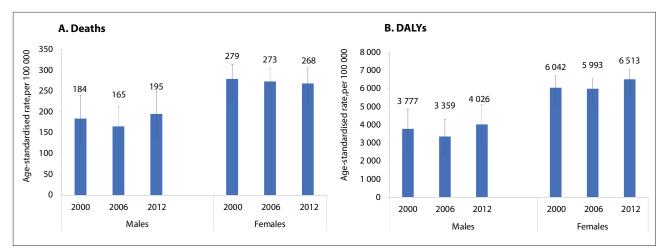


Fig. 2. High body mass index-attributable age-standardised death (A) and DALY (B) rates by sex in South Africa for 2000, 2006 and 2012. (DALY = disability-adjusted life year.)

Disease outcome*AF, %2000Hypertensive heart diseaseHypertensive heart disease47.3Haemorrhagic stroke36.736.536.736.736.736.736.736.736.736.736.736.736.736.736.736.737.836.737.836.737.836.737.8 <trr>36.7<trr>37.8<th>Deaths, n</th><th></th><th></th><th>Females</th><th>S</th><th></th><th>Persons</th><th>us</th></trr></trr>	Deaths, n			Females	S		Persons	us
rtensive heart disease 47.3 horrhagic stroke 36.7 M (excluding CKD) 55.1 emic heart disease 20.5 ma		DALYs, n	$AF,^{\dagger}\%$	Deaths, n	DALYs, n	AF_{7}^{\dagger} %	Deaths, n	DALYs, n
47.3 36.7 55.1 22.4 20.5								
36.7 55.1 22.4 20.5	2 877	52 781	71.8	7 559	128 401	62.8	10436	181 181
55.1 22.4 20.5 22.8	3 087	62 475	48.8	5 817	120 093	43.8	8 904	182 568
22.4 20.5 22.8	2 479	64 435	74.6	5 358	132 627	67.1	7 837	197 062
20.5	2 844	56 331	34.8	4 061	79 097	28.3	6 904	135 427
22.8	1 259	23 469	28.2	2 816	51 810	25.3	4 076	75 279
0.11	877	22 751	41.4	1 467	38 279	31.7	2 345	61 030
CKD due to hypertension 35.4 7	762	17 810	58.5	1 250	29 404	47.0	2 012	47 214
Oesophageal cancer 22.8 7	759	13 411	38.5	804	15 138	28.9	1 563	28 549
CKD due to unspecified causes 33.1 3	342	7 856	50.9	525	13 459	42.0	867	21 316
Liver cancer 16.9 2	269	5 075	20.8	198	3 753	18.4	467	8 828
Alzheimer's and other dementias 11.1 7	75	2 552	22.8	248	5 458	18.3	323	8 010
			58.4	302	6 401	58.4	302	6 401
CKD due to glomerulonephritis 27.6	126	5 923	42.4	159	9 304	34.3	285	15 227
Gallbladder and biliary tract disease 24.6	48	958	63.7	177	3 753	47.5	225	4711
CKD due to T2DM 40.1	67	1 647	64.4	157	3 888	54.6	223	5 535
Colorectal cancer 10.5	124	2 208	7.1	89	1 589	8.8	212	3 797
Breast cancer -			8.2	209	4 040	8.0	209	4 040
Atrial fibrillation and flutter 17.4 3	38	3 026	35.4	125	5 829	28.5	162	8 855
Pancreas cancer 4.5 3	30	546	11.4	73	1 296	7.9	103	1 842
Leukaemia 5.0 2	24	488	15.3	56	1 189	9.5	79	1 677
Kidney cancer 14.2 2	26	471	35.6	48	1 045	23.3	74	1 515
Non-Hodgkin's lymphoma 5.3 2	28	643	8.1	33	742	6.5	61	1 385
Multiple myeloma 5.7 1	13	253	11.6	26	501	8.6	39	753
Gallbladder and biliary tract cancers 9.8 7		134	36.1	30	526	23.7	37	660
Ovarian cancer 0.0 0	0	0	4.9	26	549	4.9	26	549
Osteoarthritis of hip and knee 6.0 6	9	1 707	12.4	19	7 222	9.8	26	8 929
Thyroid cancer 13.9 4	4	81	16.6	11	245	15.7	15	326
Low back pain 5.4 2	2	14 648	11.5	3	29 197	8.0	6	43 846
Cataracts 6.1 0	0	158	12.4	0	787	10.6	0	945
Gout 33.8 C	0	112	50.4	0	96	39.8	0	207
Total attributable burden	16 173	361 948	ı	31 643	695 717	ı	47 816	1 057 665
(95% UI) (((11 271 - 20 890)	(253 528 - 464 269)		(25 875 - 35 750)	(582 424 - 773 027)		(37 474 - 56 084)	(839 392 - 1 230 269)
% of total burden - 6	6.1	3.7	ı	13.3	6.6	ı	9.5	5.3
(95% UI) (((4.2 - 7.8)	(2.6 - 4.8)		(10.9 - 15.0)	(5.6 - 7.4)		(7.4 - 11.1)	(4.2 - 6.1)

Disease outcome* A 2006 44 Hypertensive heart disease 44								rersons	
rtensive heart disease	AF,† %	Deaths, n	DALYs, n	AF,* %	Deaths, n	DALYs, n	AF_{2}^{\dagger} %	Deaths, n	DALYs, n
	48.2	3 008	52 845	72.8	8 889	147 842	64.5	11 897	200 686
T2DM excluding CKD 56	56.0	3 472	87 503	76.0	7 593	193 521	68.4	11 066	281 024
Haemorrhagic stroke 36	36.7	3 331	72 454	50.4	6 707	148 090	44.8	10 038	220 544
Ischaemic heart disease 23	23.3	3 448	67 757	36.7	4 827	95 455	29.6	8 275	163 212
Ischaemic stroke 2.	21.0	1 424	26 066	29.3	3 375	62 394	26.2	4 800	88 460
CKD due to hypertension 35	37.7	1 106	25 556	61.2	1 973	47 068	50.0	3 079	72 624
	24.1	1 059	27 609	43.3	1 948	54 570	33.8	3 007	82 179
Oesophageal cancer 24	24.5	667	11 565	40.4	731	12 817	30.8	1 398	24 381
ified causes	33.9	456	11 025	50.9	598	17 160	41.8	1 054	28 185
Liver cancer 13	17.7	241	4 569	22.1	192	3 626	19.4	433	8 194
Altzheimer's and other dementias	12.3	94	2 399	23.9	335	9 315	19.8	429	11 714
- Uterine cancer		1		60.7	408	8 191	60.7	408	8 191
CKD due to glomerulonephritis 29	29.7	176	9 062	44.3	222	15 257	36.4	398	24 319
ease	26.7	80	1 728	66.4	286	7 674	50.2	365	9 402
Colorectal cancer 1	11.4	168	2 924	7.7	117	2 142	9.5	285	5 066
- Breast cancer		1	1	8.8	275	5 435	8.6	275	5 435
CKD due to T2DM 4.	41.8	72	1 593	65.4	175	4 202	56.2	247	5 795
Atrial fibrillation and flutter	19.0	44	2 187	37.2	146	4 689	30.5	190	6 876
Pancreas cancer 4.	4.9	36	619	12.0	96	1 634	8.6	132	2 253
Leukaemia 5.	5.4	26	504	16.3	71	1 469	10.6	97	1 973
Kidney cancer 11	15.4	36	667	37.0	53	1 022	23.6	89	1 689
Non-Hodgkin's lymphoma 5.	5.6	38	852	8.7	45	1 149	6.9	83	2 001
Gallbladder and biliary tract cancers 10	10.2	7	122	38.7	50	784	29.0	56	906
Multiple myeloma 6.	6.1	16	284	12.5	34	674	9.4	50	958
- Ovarian cancer		1	1	5.1	38	771	5.1	38	771
Thyroid cancer 14	14.0	6	116	17.6	14	332	16.4	20	448
Osteoarthitis of the hip and knee 6.	6.8	4	2 039	13.5	15	9 066	11.1	19	11 105
Low back pain 6.	6.2	5	16 682	11.8	11	37 627	9.2	16	54 308
Cataracts 6.	6.7	0	176	13.1	0	878	11.3	1	1 054
Gout 31	35.0	0	252	53.1	0	171	40.6	1	423
- Total attributable burden		19 020	429 152	ı	39 222	895 023	1	58 242	1 324 174
(95% UI)		(13 213 - 24 399)	(298 174 - 547 912)		(32 480 - 43 613)	(759 431 - 979 244)		(46 144 - 43 613)	(1 062 592 - 1 523 766)
% of total burden		5.5	3.5	ı	11.7	6.9	ı	8.6	5.3
(95% UI)		(3.9 - 7.1)	(2.4 - 4.5)		(9.7 - 13.1)	(5.9 - 7.6)		(6.8 - 10.0)	(4.2 - 6.0)

		Males	S		Females	es		Persons	15
Disease outcome*	AF, [†] %	Deaths, n	DALYs, n	$AF,^{\dagger}\%$	Deaths, n	DALYs, n	AF, %	Deaths, n	DALYs, n
2012									
T2DM excluding CKD	56.5	4 040	108 693	75.4	8 342	256 268	68.0	12 382	364 961
Hypertensive heart disease	49.9	3 244	54 346	73.2	8 902	145 136	65.1	12 146	199 482
Haemorrhagic stroke	36.2	3 122	64 423	48.0	6 019	127 976	43.2	9 141	192 399
Ischaemic heart disease	24.3	3 219	63 216	36.6	4 280	84 781	30.1	7 499	147 997
Ischaemic stroke	21.6	1 466	26 077	28.0	3 252	59 645	25.6	4 718	85 722
CKD due to hypertension	40.1	1 529	36 205	63.0	2 515	71 232	51.8	4 044	107 438
Asthma	25.3	779	21 129	45.3	1 347	40 459	35.1	2 126	61 587
Oesophageal cancer	25.9	650	10 903	42.2	706	12 289	32.4	1 356	23 192
CKD due to unspecified causes	36.1	554	14 680	54.6	777	26 047	45.0	1 331	40 727
Liver cancer	18.8	268	4 947	23.3	196	3 821	20.5	464	8 768
Alzheimer's and other dementias	13.4	110	2 368	24.7	350	8 404	20.6	460	10 772
Uterine cancer		1		62.7	404	8 191	62.7	404	8 191
Breast cancer	ı	1		9.8	381	7 374	9.6	381	7 374
Gallbladder and biliary tract disease	28.3	77	1 863	68.4	302	8 132	53.2	379	9 995
Colorectal cancer	12.1	226	3 933	8.2	131	2 469	10.3	358	6 402
CKD due to glomerulonephritis	31.8	163	12 227	47.5	174	22 727	38.4	337	34 954
CKD due to T2DM	42.7	86	2 148	66.3	195	6 128	56.7	282	8 276
Atrial fibrillation and flutter	20.6	57	3 594	38.6	171	6 293	31.7	228	9 887
Pancreas cancer	5.2	45	733	12.7	114	1 945	9.0	159	2 678
Leukaemia	5.8	32	583	17.2	83	1 725	11.1	114	2 308
Kidney cancer	16.8	46	794	38.9	60	1 159	24.8	107	1 953
Non-Hodgkin's lymphoma	5.8	45	1 043	9.4	63	1 618	7.4	108	2 661
Gallbladder and biliary tract cancers	11.1	6	147	41.8	57	1 070	30.6	66	1 218
Multiple myeloma	6.6	18	324	13.1	42	844	10.1	60	1 169
Ovarian cancer	ı	ı	ı	5.4	48	958	5.4	48	958
Osteoarthitis of the hip and knee	7.4	5	2 547	14.1	22	11 584	12.0	27	14 131
Thyroid cancer	15.6	4	72	18.5	21	476	18.0	25	548
Low back pain	6.9	2	19 783	13.4	5	45 896	10.9	7	65 679
Cataracts	7.3	0	193	13.8	0	1 056	12.2	0	1 248
Gout	35.3	0	188	55.5	0	175	42.8	0	363
Total attributable burden	ı	19 797	457 157	ı	38 960	965 881	ı	58 757	1 423 038
(95% UI)		(13 941 - 25 119)	(319 942 - 580 349)		(32 333 - 43 041)	(829 368 - 1 042 859)		(46 740 - 67 590)	(1 154 800 - 1 614 572)
% of total burden	ı	7.2	4.5	ı	15.4	9.2	ı	11.1	6.9
(05% 111)		(5.0 - 9.1)	(3.2 - 5.7)		(12.8 - 17.0)	(7.9 - 10.0)		(8.8 - 12.8)	(5.6 - 7.8)

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			Males				Females	
				Change				Change
Disease outcome	2000	2006	2012	2000 - 2012, %	2000	2006	2012	2000 - 2012, %
Cardiovascular disease	113.9	97.2	109.2	-4.2	179.5	97.2	155.4	-13.4
Hypertensive heart disease	34.1	27.7	34.6	1.5	66.3	88.8	61.0	-8.1
Ischaemic heart disease	32.4	29.9	31.2	-3.6	35.8	44.7	29.3	-18.3
Ischaemic stroke	14.8	12.7	14.7	-0.9	25.3	31.9	22.7	-10.4
Haemorrhagic stroke	32.1	26.4	28.0	-12.8	51.0	56.0	41.4	-18.9
T2DM	27.8	29.7	39.0	40.3	47.8	53.3	57.8	20.9
Chronic kidney disease	15.0	15.9	23.1	54.7	18.5	20.6	25.3	36.8
Asthma	10.1	9.2	7.9	-22.0	12.5	12.9	9.0	-28.1
Cancer	15.2	11.1	13.5	-10.7	17.0	15.0	16.0	-6.0
Other	1.7	1.8	2.2	33.7	3.8	1.8	4.6	19.3
Total attributable deaths	184	165	195	6.2	279	273	268	-3.9
Total attributable DALYs	3 777	3 359	4 0 2 6	6.6	6 042	5 993	6 513	7.8

Table 4. High body mass index-attributable deaths rates (ASR per 100 000) for selected disease outcomes and total death rates and DALY rates by sex

ASR = age-standardised rate; T2DM = type 2 diabetes mellitus; DALY = disability-adjusted life year.

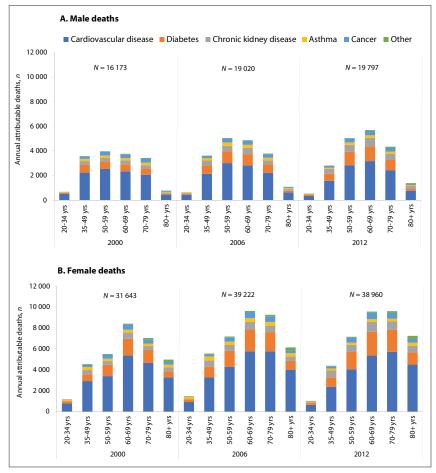


Fig. 3. Number of deaths attributable to high body mass index in adults by age group and disease outcome for males (A) and females (B) in South Africa for 2000, 2006 and 2012.

all female deaths and 7.2% (95% UI 5.0 - 9.1) of all male deaths being attributable to high BMI, with similar sex differences for DALYs.

Our updated estimate of the burden attributable to high BMI for the year 2000 has been revised upwards since SACRA1, largely as a result of more conditions being considered as associated with high BMI. While SACRA1 made use of the best available RR estimates at the time, owing to data limitations these were often based on single studies for each health outcome. However, since SACRA1, a much stronger evidence base has been identified in the annual GBD updates through concerted effort to incorporate new data and improved methods to enhance the precision and accuracy of estimation. In addition, the strict criteria based on the World Cancer Research Fund criteria to judge evidence have been applied. We acknowledge a recent observational study in a rural setting in SA with a high rate of HIV infection, which found that being overweight and obese reduced mortality compared with the individuals of normal weight in the study.^[41] As this finding needs to be corroborated and the mechanism/s identified, it is not yet possible to assess whether or not our estimates may be an overestimation of the burden attributable to high BMI.

The PAFs and proportions of total deaths attributable to high BMI in our study are similar to those estimated for SA by GBD 2019 for the respective years. However, the male PAFs tended to be lower in our study and the female PAFs tended to be higher, suggesting slight differences in the exposure estimates. The estimated trends in average BMI were similar to those reported by global studies,[2,42,43] with the exception of the early estimates by Stevens et al.,^[44] who projected a rapid increase in BMI in SA males, markedly reducing the gender differential characteristic of the SA population. We found that the differential did not change much during this period, with the prevalence of overweight and obesity in 2000 being 62.2% in females relative to 36.8% in males (ratio of 1.6:1), increasing for both females and males to 67.8% and 38.2%, respectively (ratio of 1.7:1), in 2012.

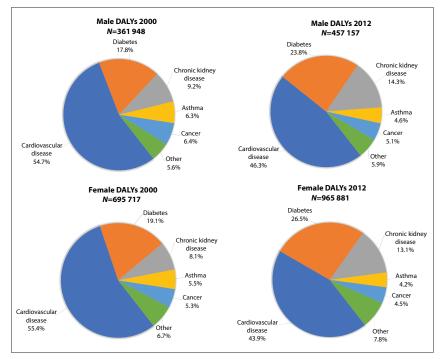


Fig. 4. DALYs attributable to high body mass index in \geq 20-year-olds by sex in South Africa for 2000 and 2012. (DALY = disability-adjusted life year.)

Our study does not consider the joint effects of a combination of risk factors, such as physical inactivity and high blood pressure, that share a common causal pathway in the development of cardiovascular disease and T2DM. Such an analysis would assist in identifying which risk factors have the larger impacts on these health outcomes. In addition, SA does not have a regular series of health surveys that measure heights and weights using standardised field methodologies. However, national datasets have been carefully evaluated so that the data could be pooled to develop a consistent set of estimates of the trend in BMI. While it would be ideal to have more recent data for such a study, the trends between 2000 and 2012 point to hugely troubling health trends, which undoubtedly remain a matter of concern. A further limitation of the study is that we provide a national perspective without investigating subnational differentials.

Conclusion

SA adopted a National Strategic Plan for the Prevention and Control of Noncommunicable Diseases^[45] in 2012, including setting an ambitious target to reduce obesity by 10% by 2020. The findings of the present study highlight the increasing mean BMI levels, resulting in a sizeable burden of disease by 2012, and the findings of the 2016 SADHS make it clear that the country is far from being on target to reduce obesity.

The Lancet Commission on Obesity has called for a reframing of the global challenge of obesity, focusing on the underlying systems such as food systems, urban systems and economic systems.[46] These complex adaptive systems are fundamentally designed to improve people's lives, yet create obesogenic environments and coexist with poverty. Increasingly, the role of global interests in food production and marketing is being recognised,[47] and Kleinert and Horton[48] emphasise that changing societal approaches to food, beverages and physical activity is one of the most important challenges that must be tackled to halt and reverse the obesity pandemic. Members of the Commission call for action to address the syndemic of undernutrition, obesity and climate change and 'join up the silos of thinking and action to create platforms to work collaboratively on common systemic drivers and double-duty or triple-duty actions?^[49]

Obesity guidelines^[50] released by the SA government in 2015 go some way to adopting such an approach, and provide the country with a comprehensive strategy including establishment of a high-level intersectoral committee. The strategy also outlines the need for population-wide initiatives to increase physical activity and reduce childhood obesity, and calls for research to provide sound scientific evidence to support policies and programmes. Such research should also address the wealth disparities associated with obesity and poor health outcomes,^[51] as well as estimating the RR in the SA setting. The SA government has taken bold steps by introducing taxation on sugar-sweetened beverages,^[52] but much of the strategy outlined in the strategy remains to be implemented.

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Author contributions. Conceived and designed the study: JDJ, RP. Analysed the data: NA, AC, VPvW. Prepared data for analysis: AC. Interrogated and interpreted results: all. Drafted manuscript: DB, NA, AC, JDJ, VPvW. Critical review of manuscript for important intellectual content: all. Senior authors: DB, VPvW, RP. Agreed to final version: all.

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Conflicts of interest. None.

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