Estimating the changing burden of disease attributable to high fasting plasma glucose in South Africa for 2000, 2006 and 2012

V Pillay-van Wyk,[1] PhD; **A Cois,**[1,2] PhD; **A P Kengne,**[3] MD, PhD; **R A Roomaney,**[1] MPH; **N Levitt,**[4] MD, FCP (SA); **E B Turawa,**[1] MSc; **N Abdelatif,**[5] MSc; **I Neethling,**[1,6] PhD; **O F Awotiwon,**[1] MBBS, MSc; **B Nojilana,**[1] PhD; **J D Joubert,**[1] MA, PhD; **R Pacella,**[6] PhD; **D Bradshaw,**[1,7] DPhil

[1] *Burden of Disease Research Unit, South African Medical Research Council, Cape Town, South Africa*
[2] *Division of Health Systems and Public Health, Department of Global Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*
[3] *Non-communicable Diseases Research Unit, South African Medical Research Council, Cape Town, South Africa*
[4] *Chronic Disease Initiative for Africa, Division of Endocrinology and Diabetic Medicine, Faculty of Health Sciences, University of Cape Town, South Africa*
[5] *Biostatistics Research Unit, South African Medical Research Council, Cape Town, South Africa*
[6] *Institute for Lifecourse Development, Faculty of Education, Health and Human Sciences, University of Greenwich, London, UK*
[7] *School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, South Africa*

Corresponding author: *V Pillay-van Wyk (victoria.pillay-vanwyk@mrc.ac.za)*

Background. Worldwide, higher-than-optimal fasting plasma glucose (FPG) is among the leading modifiable risk factors associated with all-cause mortality and disability-adjusted life years (DALYs) due to the direct sequelae of diabetes and the increased risk for cardiovascular and chronic kidney disease.
Objectives. To report deaths and DALYs of health outcomes attributable to high FPG by age and sex for South Africa (SA) for 2000, 2006 and 2012.
Methods. Comparative risk assessment methodology was used to estimate the burden attributable to high FPG. A meta-regression analysis was performed using data from national and small-area studies to estimate the population distribution of FPG and diabetes prevalence. Attributable fractions were calculated for selected health outcomes and applied to local burden estimates from the second South African National Burden of Disease Study (SANBD2). Age-standardised rates were calculated using World Health Organization world standard population weights.
Results. We estimated a 5% increase in mean FPG from 5.31 (95% confidence interval (CI) 5.18 - 5.43) mmol/L to 5.57 (95% CI 5.41 - 5.72) mmol/L and a 75% increase in diabetes prevalence from 7.3% (95% CI 6.7 - 8.3) to 12.8% (95% CI 11.9 - 14.0) between 2000 and 2012. The age-standardised attributable death rate increased from 153.7 (95% CI 126.9 - 192.7) per 100 000 population in 2000 to 203.5 (95% CI 172.2 - 240.8) per 100 000 population in 2012, i.e. a 32.4% increase. During the same period, age-standardised attributable DALY rates increased by 43.8%, from 3 000 (95% CI 2 564 - 3 602) per 100 000 population in 2000 to 4 312 (95% CI 3 798 - 4 916) per 100 000 population in 2012. In each year, females had similar attributable death rates to males but higher DALY rates. A notable exception was tuberculosis, with an age-standardised attributable death rate in males double that in females in 2000 (14.3 v. 7.0 per 100 000 population) and 2.2 times higher in 2012 (18.4 v. 8.5 per 100 000 population). Similarly, attributable DALY rates were higher in males, 1.7 times higher in 2000 (323 v. 186 per 100 000 population) and 1.6 times higher in 2012 (502 v. 321 per 100 000 population). Between 2000 and 2012, the age-standardised death rate for chronic kidney disease increased by 98.3% (from 11.7 to 23.1 per 100 000 population) and the DALY rate increased by 116.9% (from 266 to 578 per 100 000 population).
Conclusion. High FPG is emerging as a public health crisis, with an attributable burden doubling between 2000 and 2012. The consequences are costly in terms of quality of life, ability to earn an income, and the economic and emotional burden on individuals and their families. Urgent action is needed to curb the increase and reduce the burden associated with this risk factor. National data on FPG distribution are scant, and efforts are warranted to ensure adequate monitoring of the effectiveness of the interventions.

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The article in context

Evidence before this study. The first South African Comparative Risk Assessment Study (SACRA1) conducted for 2000 assessed the attributable burden from five health-related outcomes from diabetes and reported a diabetes prevalence of 5.5% among South Africans aged ≥30 years. An estimated 22 412 (95% confidence interval (CI) 20 755 - 24 872) deaths were attributable to diabetes, while a total of 258 028 DALYs (95% CI 236 856 - 290 849), representing 1.6% (95% CI 1.5 - 1.8) of the total DALYs in SA in 2000, were attributable to diabetes.
Added value of this study. Given the shift in focus from treating theoretically decided cut-off points for disease towards managing continuous distributions of risks for the control of non-communicable diseases (NCDs), our study used updated methodology to estimate the attributable burden from 19 health-related outcomes for the three time points 2000, 2006 and 2012 incorporating high fasting

plasma glucose (FPG)-related risk as both continuous (for 7 outcomes) and using a dichotomous approach (diabetes v. no diabetes) for 12 outcomes. A meta-regression model integrating multiple data sources was used to estimate the distribution of FPG in the population and the diabetes prevalence. We showed a 5% increase in mean FPG and a 75% increase in diabetes prevalence between 2000 and 2012, and a shocking 43.8% increase in attributable DALY rates over the study period. Our study reports a changing age pattern over time among females, with increasing proportions of the attributable deaths among women aged ≥80 years resulting from increases in cardiovascular and chronic kidney disease. There has been a concerning 98.3% increase in the age-standardised attributable DALY rates from chronic kidney disease for both males and females.

Implications of the available evidence. SA is not winning the battle against adverse health outcomes from high plasma glucose, which is often compounded by the challenges of high blood pressure. The disease burden is costly in terms of quality of life, ability to earn an income, and the physical, economic and emotional burden on the individual and their family (caregivers). A multipronged approach is needed to mitigate the impact of raised glucose levels and blood pressure. This approach should include mass screening and health promotion activities that promote lifestyle changes and close the gaps between screening and diagnosis, diagnosis and treatment, and treatment and control. The National Strategic Plan for the Prevention and Control of Non-communicable Diseases for SA (NSP for NCDs) has implemented a 90/60/50 plan to tackle the health burden from raised glucose levels and raised blood pressure. Monitoring and evaluation of the outcomes in this plan while making changes for maximum impact are critical to ensure its success.

Worldwide, higher-than-optimal FPG, including diabetes mellitus and pre-diabetes as its extreme form, is one of the leading modifiable risk factors associated with all-cause mortality and DALYs. This is due to the direct sequelae of diabetes, as well as the increased risk of cardiovascular disease (including myocardial infarction) and chronic kidney disease that is documented in non-diabetic individuals with elevated FPG.[1-3]

Diabetes is a fast-growing metabolic disorder affecting ~463 million people aged 20 - 79 years worldwide, with the majority living in low- to middle-income countries.[4] The global prevalence of diabetes in 2019 was 9.3%, and one in two people living with diabetes is undiagnosed.[5] It is projected that by 2030, ~578 million adults will be living with diabetes, and this will probably rise to 700 million by 2045, with 374 million adults experiencing impaired glucose tolerance.[4] The increasing prevalence of diabetes worldwide is driven by the complex interplay of demographic, environmental, socioeconomic, lifestyle and genetic factors.[6] Globally, 50.1% of persons aged 20 - 79 years with diabetes are undiagnosed, with the proportion in Africa being 59.7%. About 77% of deaths due to diabetes occurred in people aged <60 years.

The prevalence of diabetes is increasing rapidly over time in SA, and ~4.5 million of the population have diabetes, of whom >2 million are undiagnosed.[4] SACRA1, conducted for 2000, assessed the attributable burden from 17 risk factors[7] and reported a diabetes prevalence of 5.5% among South Africans aged ≥30 years, with an expected increased prevalence with age. Similarly, ~22 412 (95% CI 20 755 - 24 872) or 4.3% (95% uncertainty interval (UI) 4.0 - 4.8) of all deaths in SA in 2000 were attributable to diabetes, while 258 028 DALYs (95% CI 236 856 - 290 849), representing 1.6% (95% CI 1.5 - 1.8) of all DALYs, were due to diabetes (including the direct burden from diabetes, as well as cardiovascular disease and chronic kidney disease attributable to diabetes as a risk factor).[8]

Although the SA government has developed guidelines on screening programmes for early diagnosis and management of diabetes,[9] the rapidly increasing prevalence[10,11] stresses the need to regularly update the burden of disease due to this risk factor in the country, in order to refine health policy and programmes. This article reports the estimated number of deaths and DALYs of 19 health outcomes[12] attributable to higher-than-optimal plasma glucose, with or without diabetes (hereafter referred to as 'high fasting plasma glucose' or high FPG), by age and sex for SA for 2000, 2006 and 2012. The year 2006 was included because mortality in SA peaked in that year as a result of trends in HIV/AIDS.

Methods

Comparative risk assessment methodology developed by the World Health Organization (WHO)[13] and Global Burden of Diseases, Injuries, and Risk Factors (GBD) studies[14] was used to estimate the attributable burden from high FPG by considering conditions consequential to exposure to diabetes and those consequential to exposure to high FPG. The attributable fraction was calculated for selected health outcomes and applied to local estimates of the burden of disease from the second South African National Burden of Disease Study (SANBD2) for the respective years.[15]

Estimation of exposure

Prevalence of diabetes

According to the American Diabetes Association and WHO diagnostic criteria, we define diabetes as FPG >7.0 mmol/L and/or currently taking diabetes medication. Alternative diagnostic criteria are a 2-hour plasma glucose level >11.1 mmol/L after an oral glucose tolerance test (OGTT), or glycated haemoglobin (HbA1c) >6.5%.[16,17]

Results from seven studies identified in a recent systematic review[10] were used to model the prevalence of diabetes between 2000 and 2012 in SA. Estimates from studies published before and after the review period (1997 - 2018) were also included because of the paucity of the available data and the need to ensure 'anchor' points for the trend estimates in some subpopulations. Table 1 summarises the key characteristics of the considered studies, which included two national surveys and a set of local studies among specific population groups. Studies identified by the systematic review but not included in the meta-regression model described below are listed in Table S1 in the appendix (https://www.samedical.org/file/1846) with the reason for exclusion.

For the two national surveys,[18,19] age-, sex- and population group-specific estimates of diabetes prevalence were directly calculated from individual-level data, with standard methods. Estimates from the local studies were recovered from the published articles or provided by the authors. When the age categories did not match those used in this analysis, the estimates were linearly interpolated to approximate the prevalence in the relevant categories. When not directly provided, CIs were calculated with the normal approximation for prevalence

Table 1. Characteristics and reported prevalence of data sources used for the estimation of the prevalence of diabetes in the South African adult population[10]

Source	Year*	Population group	Age range (years)	Sample size, *N*†	Diagnostic test	Prevalence, % (95% CI)
National surveys						
SANHANES-1, 2014[18]	2012	All	>15	4 750	HbA1c	14.7 (11.8 - 18.3)
SADHS, 2019[19]	2016	All	>15	6 122	HbA1c	14.9 (13.6 - 16.3)
Local studies						
Omar *et al.*, 1993[20]	1992	Urban black African	>15	479	OGTT	5.3
Levitt *et al.*, 1993[21]	1990	Urban black African	>30	729	OGTT	7.0 (4.9 - 9.1)
Omar *et al.*, 1994[22]	1992	Asian	>15	2 479	OGTT	6.9
Mollentze *et al.*, 1995[23]	1990	Urban and non-urban black African	>25	758 (rural) 853 (urban)	OGTT	4.8 (rural) 6.0 (urban)
Levitt *et al.*, 1999[24]	1996	Urban black African	>15	974	OGTT	10.8 (8.2 - 13.5)
Bradshaw *et al.*, 2007[8]‡	2000	All	>30	Pooled data	FPG/OGTT	5.5
Motala *et al.*, 2008[25]	1999 - 2000	Non-urban black African	>15	999	FPG/OGTT	5.4 (4.0 - 7.2)
Peer *et al.*, 2012[26]	2008 - 2009	Urban black African	>25	1 099	OGTT	12.1 (10.2 - 14.0)
Hird *et al.*, 2016[27]	2013 - 2014	Urban black African	>18	1 190	FPG/OGTT	16.5 (14.1 - 19.0)
Zemlin *et al.*, 2019[28]§	2015	Coloured	>25	1 409	OGTT	19.3 (17.3 - 21.4)

CI = confidence interval; SANHANES-1 = South African National Health and Nutrition Examination Survey; SADHS = South Africa Demographic and Health Survey; HbA1c = glycated haemoglobin; OGTT = oral glucose tolerance test, FPG = fasting plasma glucose.
*Year(s) of data collection/reference for the estimates.
†Total sample with valid measurements.
‡No direct data collection (estimates from local studies) – studies used in the first South African Comparative Risk Assessment Study.[7]
§Not included in Pheiffer *et al.*[11]

>10% and samples >50 and with the Bayesian method described by Gelman *et al.*[29] in the other cases.

A fixed-effect linear meta-regression model was fitted to the available data, with: (*i*) prevalence of diabetes as the outcome; (*ii*) year of data collection and interactions between age group, sex and population group (urban black African, rural black African, white, coloured and Asian/Indian) as independent variables; and (*iii*) type of test used for diabetes diagnosis (OGTT, FPG or HbA1c) as a confounder. When data collection spread across 2 years, the midpoint was used. The arcsine square root transformation was applied to the outcome variable to stabilise the variance for small proportions and to avoid unrealistic estimates outside the interval 0 - 1. This transformation was preferred to the logistic transformation because of the presence, in the input data, of zero estimates and small sample size for some subgroups where the logistic transformation is known to perform poorly.[30] The following model was fitted to the data using a maximum likelihood estimator:

$$t_i = \text{asin}(\sqrt{p}) = \beta_0 + \beta_1 \cdot Test\_FPG_i + \beta_2 \cdot Test\_HbA1c_i + \beta_3 \cdot Year_i + \beta_4 \cdot Group\_2_i + \cdots \beta_{52} \cdot Group\_50_i + \beta_{53} \cdot Year_i \cdot Group_{2i} + \cdots \beta_{101} \cdot Year_i \cdot Group_{50i} + \varepsilon_i$$

where $Test\_FPG_i$ and $Test\_HbA1c_i$ are the dummy variables identifying the test used for assessing diabetes prevalence for the *ith* data point (using OGTT as a reference); $Group_{\_2i}$ to $Group_{\_50i}$ are dummy variables identifying the sex*population group*age group combinations for the *ith* data point; and $Year_i$ is the year of reference for the *ith* data point (continuous variable).

For the estimation, a normal distribution of the error term ε_i was assumed, and each observation was weighted by the inverse variance of each (transformed) data point.

The fitted model was used to predict the transformed prevalence for each age, sex and population group by year (and their standard deviation), which were back-transformed in the original scale. The variables *Test_FPG* and *Test_HbA1c* were both set to 0 so that the prediction represents the prevalence of diabetes that would have been observed if the diagnosis was carried out with the OGTT method. National predicted prevalence estimates (by age and sex) were calculated as weighted averages of the estimates in each population group, with weights given by the population size in the group.[31] Urban/rural proportions were sourced from the World Bank estimates for the whole population of SA and assumed approximately valid also for the black population group. CIs for the national estimates were calculated by simulation, by randomly drawing 10 000 samples from the distribution of the group-specific estimates of prevalence, calculating their weighted average and considering the 2.5th and 97.5th percentiles of the distribution of the weighted average across the samples as the lower and upper bounds of the 95% CI.

Fasting plasma glucose

Owing to the dearth of population data on FPG, we adopted an indirect approach to estimate the continuous exposure of interest, i.e. we first estimated the age- and sex-specific prevalence of diabetes in the population, and then used these values to infer the parameters of the underlying distribution of FPG, outlined below.

Within each age and sex group and year, we assumed a log-normal distribution of FPG and, according to the diagnostic criteria, that the proportion of subjects with FPG ≥7 mmol/L was equal to the prevalence of diabetes.[12] For each group, we estimated the mean FPG by using the crosswalk equation described by Danaei *et al.*:[32]

$$mean\ FPG = 4.83 + 7.47 \cdot p + 0.0046 \cdot age - 0.095 \cdot sex - 0.061 \cdot age \cdot p + 0.60 \cdot sex \cdot p$$

where p is the prevalence of diabetes; *sex* is coded 0 for males and 1 for females; and *age* is the midpoint of the age range of each group.

We calculated the two log-normal parameters (μ_l and σ_l) of the FPG distribution by numerical optimisation, such that the distribution had a mean equal to *meanFPG* and the cumulative distribution for FPG ≥7 mmol/L was equal to the estimated prevalence of diabetes. We estimated the standard deviation of μ_l and σ_l by simulation, sampling randomly from the distribution of the estimated prevalence and from the distribution of the regression coefficients in the cross-

walk equation. Calculations were done with R statistical software, version 3.6.1 (R Foundation for Statistical Computing, Austria) and Stata version 14 (StataCorp., USA).

Health-related outcomes and relative risks

Seven disease outcomes due to high FPG as a continuous risk (Table 2A) and 12 due to the presence of diabetes (categorical risk) (Table 2B) were considered. The latter also includes diabetes mellitus as an outcome that is 100% attributable to high FPG. For each risk-outcome pair, relative risks (RRs) were sourced from GBD 2017.[12]

Burden estimates

SANBD2 provided estimates of deaths and years of life lost (YLLs) for the disease outcomes for 2000, 2006 and 2012.[15] Estimates of DALYs were derived using the ratio of the years lived with disability (YLDs) to YLLs estimated in the GBD study for SA[12] and applied to the local estimates of YLLs.

Population attributable burden

A set of customised Excel 365 spreadsheets (Microsoft Corp., USA) were used to calculate, for each of the health outcomes listed in Table 2A, the potential impact fraction (PIF) for high FPG as a continuous exposure and the population attributable fraction (PAF) for the presence of diabetes for the outcomes in Table 2B.

The PIF is the proportion by which an outcome would be reduced in a given population if the exposure to the risk factor (high FPG) were reduced to the counterfactual theoretical minimum exposure level (TMREL). Following GBD 2017 methodology described in the appendix (https://www.samedical.org/file/1846), the TMREL is assumed to follow a uniform distribution between 4.5 and 5.4 mmol/L.[12]

For a cause *o*, age group *a*, sex *s* and year y, the PIF is calculated as:

$$PIF = \frac{\int_{x=0.9}^{25} RR_{oas}(x) \cdot P_{asy}(x) \cdot dx - \int_{x=0.9}^{25} RR_{oas}(x) \cdot P_{TMREL}(x) \cdot dx}{\int_{x=0.9}^{25} RR_{oas}(x) \cdot P_{asy}(x) \cdot dx}$$

where $RR_{oas}(x)$ = RR for health outcome *o*, age group *a* and sex *s* as a function of the FPG level *x*, as reported in Table 2; $P_{asy}(x)$ = distribution of FPG in age group *a*, sex *s* and year *y*, defined by the corresponding log-normal parameters μ_l and σ_l; and $P_{TMREL}(x)$ = counterfactual theoretical minimum distribution of FPG, assumed to be the same across all age groups, sexes and years.

The *IntLognormalperunitRR* function in the EpigearXL Excel add-on was used for the calculation of the integrals in the PIF expression.

Similarly, the population attributable burden for diabetes was estimated as a special case of the PIF for a binary exposure:

$$PAF = \frac{RR_{oas} \cdot P_{asy} - 1}{RR_{oas} \cdot P_{asy}}$$

where RR_{oas} = RR for health outcome *o*, age group *a* and sex *s* for diabetic v. non-diabetic subjects, as reported in Table 2; and P_{asy} = prevalence of diabetes in age group *a*, sex *s* and year *y*.

We estimated the burden attributable to high FPG by multiplying the burden metric (deaths, YLLs, YLDs and DALYs) sourced from SANBD2[15] by the PIF/PAF for the risk-outcome pair for each age, sex, and year 2000, 2006 and 2012. We then calculated the overall attributable burden as the sum across all outcomes. Age-standardised attributable death and DALY rates were calculated using population estimates from Dorrington[31] and WHO world standard population weights.[33]

Uncertainty analysis

Monte Carlo simulation-modelling techniques were used to present uncertainty ranges around point estimates reflecting the uncertainty in the exposure estimates and in the RR functions. Ersatz software version 1.35 was used, which allows multiple recalculations of a spreadsheet (set to 2 000 draws) with different values selected from distributions defined for the input variables. A normal distribution was specified for the mean of the population distribution of FPG using the *ErNormal* function, and a beta distribution was specified for the prevalence of diabetes using the *ErBeta* function. The uncertainty in the RRs in Table 2 was modelled with the *ErRelativeRisk* function, which assumes that the natural logarithm of RR is normally distributed with mean log(RR).[34] The 2.5th and 97.5th percentiles of the distribution of the replicated calculation were used as the lower and upper uncertainty bounds of the estimates.

Results

Figs S1 and S2 in the appendix (https://www.samedical.org/file/1846) show the estimated age- and sex-specific trends in the prevalence of diabetes and mean FPG from the meta-regression model. Tables S2 and S3 in the appendix show the estimated prevalence of diabetes and the parameters of the FPG distribution in 2000, 2006 and 2012. Between 2000 and 2012, the estimates show a 5% increase in mean FPG from 5.31 (standard error (SE) 0.06) mmol/L to 5.57 (SE 0.08) mmol/L and a 75% increase in diabetes prevalence from 7.3% (95% CI 6.7 - 8.3) to 12.8% (95% CI 11.9 - 14.0). A similar increase was observed with increasing age. A similar pattern was observed for females and males. Over the age of 35 years, females had higher mean FPG and diabetes prevalence than males (Fig. 1).

Age-standardised attributable death rates in persons increased by 32.4% from 153.7 per 100 000 population (95% CI 126.9 - 192.7) in 2000 to 203.5 per 100 000 population (95% CI 172.2 - 240.8) in 2012. The age-standardised attributable DALY rate was 3 000 per 100 000 population (95% CI 2 564 - 3 602) in 2000 and 4 312 per 100 000 population (95% CI 3 798 - 4 916) in 2012, i.e. a 43.8% increase (Table S4 in the appendix: https://www.samedical.org/file/1846). Females and males showed similar age-standardised death rates. Females had a 1.1 times higher attributable DALY rate than males for each year (Table S4 in the appendix). Female attributable death and DALY rates increased by 28.4% and 45.3%, respectively, between 2000 and 2012, while rates in males increased by 38.3% and 42.0%, respectively (Table S4 in the appendix).

The contribution of high FPG to total deaths in SA increased over the period investigated (Table 3). High FPG contributed to 5.2%, 5.3% and 8.1% of total person deaths for the years 2000, 2006 and 2012, respectively. A similar pattern of increase was observed for DALYs; 2.8% in 2000, 2.9% in 2006 and 4.7% in 2012 (Table 3).

The top 10 causes of deaths attributable to high FPG were the same in 2000 and 2012. Diabetes and cardiovascular disease (ischaemic heart disease, haemorrhagic stroke, ischaemic stroke and peripheral vascular disease) were the most signifcant outcomes of high FPG, followed by chronic kidney disease and tuberculosis (Fig. 3A). The age-standardised death rate for chronic kidney disease increased by 98.3% between 2000 and 2012 (11.7 v. 23.1 per 100 000 population) (Table S4 in the appendix: https://www.samedical.org/file/1846), and the age-standardised DALY rate for chronic kidney disease increased by 116.9% between 2000 and 2012 (266.3 v. 577.6 per 100 000 population). A similar pattern in deaths and DALYs was observed by sex (Figs 3A and B) except for tuberculosis, where males had more deaths and DALYs than females. Age-standardised attributable death rates for tuberculosis for males were 2 times higher than for females in 2000 (14.3 v. 7.0 per 100 000 population)

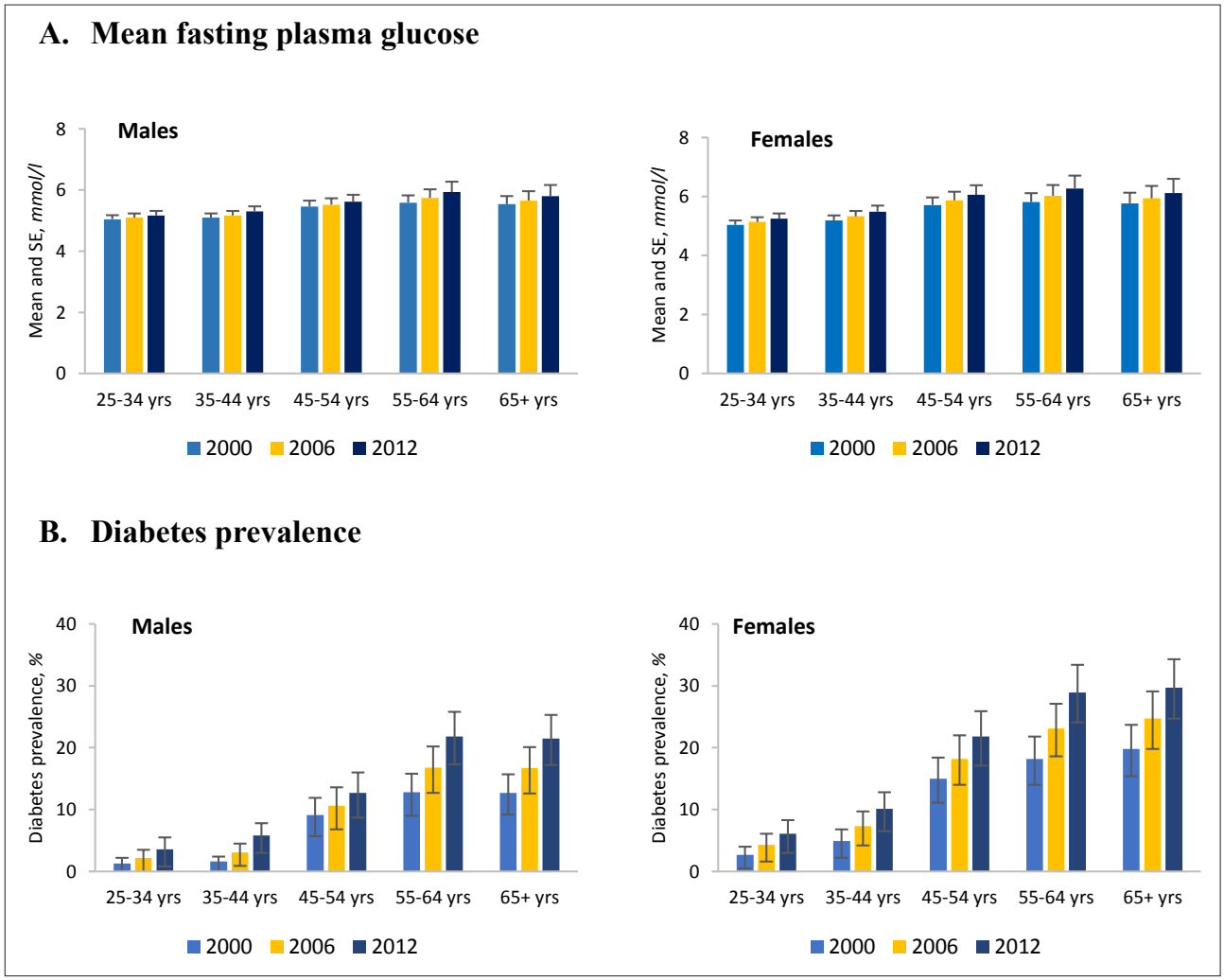

Fig. 1. Mean high fasting plasma glucose (A) and diabetes prevalence (B) by sex and year in South Africa for 2000, 2006 and 2012.

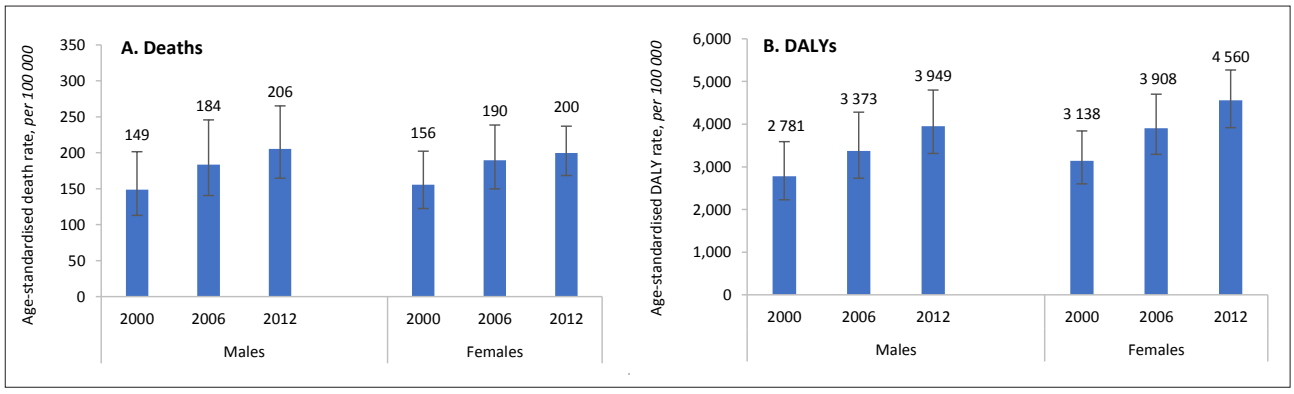

Fig. 2. High fasting plasma glucose age-standardised (A) attributable death and (B) attributable DALY rates per 100 000 population in South Africa for 2000, 2006 and 2012.

and 2.2 times higher than for females for 2012 (18.4 v. 8.5 per 100 000 population), as shown in Table S4 in the appendix (https://www.samedical.org/file/1846).

The age distribution of deaths attributable to high FPG for the three time periods for males and females is shown in Fig. 4. In each period, female deaths peaked in the 70 - 79-year-olds (except in 2012, where they peaked in the ≥80 years age group), while male deaths peaked in the 45 - 49-year-olds. Diabetes was the biggest contributor to deaths at all ages for females and males. Most cardiovascular deaths occurred in those aged >45 years. In general, the number of deaths in <45-year-olds, an age group where these conditions are expected to be less prevalent, has increased over time. For females, the proportion of the female attributable deaths in the ≥80 years age group increased from 22.1% in 2000 to 27.0% in 2012. In contrast, the proportion of male attributable deaths in the ≥80 years age group increased from 12.6% to 14.6%, respectively.

Discussion

Our study is an update of SACRA1,[8] with some fundamental

Table 2A. RRs for outcomes associated with high FPG as a continuous variable

					RR (per unit increase of FPG)							
					Male				Female			
Exposure	Outcome	ICD-10 code	Risk attribution method	Age group (years)	RR	LL	UL	SE	RR	LL	UL	SE
High fasting plasma glucose	Ischaemic heart disease	I20 - I25	PIF	25 - 29	1.47	1.15	2.10	0.15	1.47	1.15	2.20	0.15
				30 - 34	1.37	1.15	1.74	0.11	1.37	1.15	1.74	0.11
				35 - 39	1.27	1.13	1.45	0.06	1.27	1.13	1.45	0.06
				40 - 44	1.22	1.09	1.37	0.06	1.22	1.09	1.37	0.06
				45 - 49	1.21	1.11	1.33	0.05	1.21	1.11	1.33	0.05
				50 - 54	1.20	1.12	1.30	0.04	1.20	1.12	1.30	0.04
				55 - 59	1.19	1.12	1.27	0.03	1.19	1.11	1.27	0.03
				60 - 64	1.18	1.11	1.27	0.03	1.18	1.11	1.27	0.03
				65 - 69	1.17	1.08	1.27	0.04	1.17	1.08	1.27	0.04
				70 - 74	1.17	1.08	1.27	0.04	1.17	1.08	1.27	0.04
				75 - 79	1.17	1.10	1.26	0.04	1.17	1.10	1.26	0.04
				80 - 84	1.17	1.07	1.32	0.05	1.17	1.07	1.32	0.05
	Ischaemic stroke	G45 - G46.8, I63 - I63.9, I65 - I66.9, I67.2 - I67.8, I69.3 - I69.4	PIF	25 - 29	1.53	1.11	2.23	0.18	1.53	1.11	2.23	0.18
				30 - 34	1.40	1.10	1.85	0.13	1.40	1.10	1.85	0.13
				35 - 39	1.28	1.08	1.56	0.09	1.28	1.08	1.56	0.09
				40 - 44	1.21	1.04	1.44	0.08	1.21	1.04	1.44	0.08
				45 - 49	1.20	1.08	1.38	0.06	1.20	1.08	1.38	0.06
				50 - 54	1.20	1.10	1.33	0.05	1.20	1.10	1.33	0.05
				55 - 59	1.19	1.08	1.30	0.05	1.19	1.08	1.30	0.05
				60 - 64	1.19	1.10	1.30	0.04	1.19	1.10	1.30	0.04
				65 - 69	1.18	1.07	1.31	0.05	1.18	1.07	1.31	0.05
				70 - 74	1.17	1.06	1.31	0.05	1.17	1.06	1.31	0.05
				75 - 79	1.16	1.08	1.30	0.05	1.16	1.08	1.30	0.05
				80 - 84	1.13	1.06	1.33	0.06	1.13	1.06	1.33	0.06
	Haemorrhagic stroke	I60 - I62, I62.1 - I62.9, I67.0 - I67.1, I68.1 - I68.2, I69.0 - I69.2	PIF	25 - 29	1.51	1.11	2.22	0.18	1.51	1.11	2.22	0.18
				30 - 34	1.38	1.11	1.84	0.13	1.38	1.11	1.84	0.13
				35 - 39	1.26	1.09	1.49	0.08	1.26	1.09	1.49	0.08
				40 - 44	1.20	1.05	1.37	0.07	1.20	1.05	1.37	0.07
				45 - 49	1.19	1.08	1.33	0.05	1.19	1.08	1.33	0.05
				50 - 54	1.19	1.11	1.30	0.04	1.19	1.11	1.30	0.04
				55 - 59	1.19	1.11	1.26	0.03	1.19	1.11	1.26	0.03
				60 - 64	1.19	1.11	1.25	0.03	1.19	1.11	1.25	0.03
				65 - 69	1.18	1.10	1.26	0.04	1.18	1.10	1.26	0.04
				70 - 74	1.18	1.09	1.26	0.04	1.18	1.09	1.26	0.04
				75 - 79	1.16	1.09	1.23	0.03	1.16	1.09	1.23	0.03
				80 - 84	1.12	1.06	1.25	0.04	1.12	1.06	1.25	0.04
	Peripheral vascular disease	I73	PIF	25 - 29	8.26	6.04	9.30	0.11	8.26	6.04	9.30	0.10
				30 - 34	6.65	5.38	7.45	0.08	6.65	5.38	7.45	0.10
				35 - 39	5.04	4.44	5.67	0.06	5.04	4.44	5.67	0.10
				40 - 44	4.14	3.56	4.76	0.07	4.14	3.56	4.76	0.10
				45 - 49	3.95	3.45	4.50	0.07	3.95	3.45	4.50	0.10
				50 - 54	3.76	3.35	4.23	0.06	3.76	3.35	4.23	0.10
				55 - 59	3.57	3.21	3.97	0.05	3.57	3.21	3.97	0.10
				60 - 64	3.37	3.08	3.71	0.05	3.37	3.08	3.71	0
				65 - 69	3.18	2.92	3.47	0.04	3.18	2.92	3.47	0
				70 - 74	2.99	2.76	3.25	0.04	2.99	2.76	3.3	0
				75 - 79	2.80	2.56	3.05	0.04	2.80	2.56	3.05	0
				80 - 84	2.32	1.98	2.67	0.08	2.32	1.98	2.67	0.10
	CKD due to hypertension	I12 - I13	PIF	All	1.39	1.27	1.51	0.04	1.39	1.27	1.51	0.04
	CKD due to glomerulonephritis	N03 - N06	PIF	All	1.39	1.27	1.51	0.04	1.39	1.27	1.51	0.04
	CKD due to other causes and unspecified causes	N02, N07 - N08, N18	PIF	All	1.39	1.27	1.51	0.04	1.39	1.27	1.51	0.04

RR = relative risk; FPG = fasting plasma glucose; LL = lower confidence limit; UL = upper confidence limit; SE = standard error; CKD = chronic kidney disease; PIF = potential impact fraction.

Table 2B. RRs for outcomes associated with diabetes (categorical risk)

Exposure	Outcome	ICD-10 code	Risk attribution method	Age group (years)	RR (diabetes v. no diabetes) Male RR	LL	UL	SE	Female RR	LL	UL	SE
Diabetes	Tuberculosis	A15 - A19, B90, U51, U52	PAF	25 - 29	2.73	1.97	3.60	0.15	2.73	1.97	3.60	0.15
				30 - 34	2.80	2.06	3.66	0.15	2.80	2.06	3.70	0.15
				35 - 39	2.87	2.05	3.70	0.15	2.87	2.05	3.70	0.15
				40 - 44	2.80	1.97	3.63	0.16	2.80	1.97	3.60	0.16
				45 - 49	2.58	1.91	3.27	0.14	2.58	1.91	3.30	0.14
				50 - 54	2.36	1.82	2.94	0.12	2.36	1.82	2.90	0.12
				55 - 59	2.15	1.69	2.67	0.12	2.15	1.69	2.70	0.12
				60 - 64	1.93	1.49	2.44	0.13	1.93	1.49	2.40	0.13
				65 - 69	1.71	1.23	2.32	0.16	1.71	1.23	2.30	0.16
				70 - 74	1.60	1.13	2.24	0.18	1.60	1.13	2.24	0.18
				75 - 79	1.59	1.18	2.12	0.15	1.59	1.18	2.12	0.15
				80 - 84	1.56	1.18	2.17	0.16	1.56	1.18	2.17	0.16
	Colorectal cancer	C18 - C21	PAF	All	1.53	1.08	2.30	0.19	1.53	1.09	2.32	0.19
	Liver cancer	C22	PAF	All	1.52	1.09	2.30	0.19	1.51	1.08	2.29	0.19
	Lung cancer	C33 - C34	PAF	All	1.52	1.08	2.31	0.19	1.51	1.09	2.30	0.19
	Pancreatic cancer	C25	PAF	All	1.52	1.09	2.31	0.19	1.52	1.08	2.31	0.20
	Breast cancer	C50	PAF	All	1.51	1.09	2.21	0.18	1.51	1.09	2.21	0.18
	Ovarian cancer	C56	PAF	All	-	-	-	-	1.52	1.09	2.32	0.19
	Bladder cancer	C67	PAF	All	1.51	1.08	2.26	0.19	1.51	1.08	2.25	0.19
	Alzheimer's disease and other dementias	F00 - F03, G30 - G31	PAF	All	1.52	1.08	2.30	0.19	1.52	1.08	2.30	0.19
	Glaucoma	H36, H40, H42	PAF	All	1.52	1.10	2.33	0.19	1.52	1.08	2.33	0.20
	Cataracts	H25 - H26	PAF	All	1.52	1.09	2.26	0.19	1.52	1.09	2.29	0.19
	Diabetes mellitus	E10 - E14	100% attributable to high FPG									

RR = relative risk; LL = lower confidence limit; UL = upper confidence limit; SE = standard error; PAF = population attributable fraction; FPG = fasting plasma glucose.

differences between the studies: (*i*) the current study has estimated the attributable burden from higher-than-optimal glucose levels, which includes diabetes and non-diabetic hyperglycaemia, while SACRA1 estimated the burden attributable to diabetes only; (*ii*) the present study has estimated the attributable burden for 19 health-related outcomes, while SACRA1 used 5 health-related outcomes; (*iii*) the present study has estimated the attributable burden for individuals aged ≥25 years, while SACRA1 estimated the burden for individuals aged ≥30 years; and (*iv*) the present study includes estimates for 2000, 2006 and 2012. SACRA1 estimated that 4.3% of deaths from all causes and 1.6% of DALYs from all causes were attributable to diabetes, while the current study estimates that 5.2% of deaths and 2.8% of DALYs for all causes for 2000 were attributable to high FPG. The similar attribution for deaths and difference in DALYs is difficult to interpret, as the studies were methodologically different. However, it could be postulated that the additional conditions considered in the present study compared with SACRA1 had more non-fatal burden, hence the almost 1.6 times more DALYs reported for the year 2000 in the present study.

We found that mean FPG (5% increase) and diabetes prevalence (75% increase) have been increasing over time. The increasing diabetes prevalence over time is consistent (although with different magnitude) with findings of the African Working Group of the NCD Risk Factor Collaboration (NCD-RisC), which reported an increasing trend in diabetes prevalence across Africa between 1980 and 2014[35] and showed that diabetes prevalence in SA was estimated to have increased from 4.8% to 9.7% in men and from 7.7% to 12.6% in women between 1980 and 2014.[35] In the global trends study by Danaei *et al.*,[32] which accounted for four SA studies published between 1993 and 2008, the estimated mean FPG for SA increased by ~1.8% between 2000 and 2008, translating into a 15.5% (in men) and 12.5% (in women) increase in diabetes prevalence over the same period.

Mean FPG and diabetes prevalence were higher in females than males across the study period. This pattern has been reported previously.[36,37] Variable patterns of sex difference in diabetes prevalence have been reported in recent studies across Africa, with rates being mostly similar or higher in males in settings with low diabetes prevalence, and higher in females in settings with high diabetes prevalence.[35,36] A detailed elaboration of mechanisms suggested to explain the sex difference in diabetes estimates across populations and settings is available elsewhere.[38] Obesity is considered to be the single biggest risk factor for high FPG rates worldwide,[39-41] including SA.[42] Obesity in SA is disproportionally more common in females than males,[19] accounting at least in part for some of the observed sex differences in high FPG estimates. In the NCD-RisC African study, absolute change in body mass index over time was moderately associated with relative change in diabetes prevalence in women (r=0.76), while a weak association (r=0.34) was observed in males.[35]

Our study shows a 32.4% increase in the attributable death rate and a 43.8% increase in the attributable DALY rate from high FPG between 2000 and 2012. A 29% increase in diabetes mortality between 1997 and 2012 was reported in SANBD2.[15]

While age-standardised death rates were similar for males and females across all years, age-standardised DALY rates were 10% higher among females. This higher DALY rate is compounded by females living to older ages[43] and results in a more substantial morbidity burden in older age females compared with males.

The disproportionate increase in deaths from high FPG from cardiovascular disease and chronic kidney disease in females aged ≥80 years is striking and could partly be due to the changing age distribution of deaths among females. The different peaks for deaths attributable to high FPG, in females at 70 - 79 years and in males at 45 - 59 years, reflects that males are challenged with poor health-seeking behaviour combined with the unmet need for care, resulting in late detection of high FPG.[44] The finding that males had a higher tuberculosis burden than females has been observed in GBD studies[12,45] and a WHO report (2018)[46] and could also be related to males' health-seeking behaviour and access to care.

The 137.1% increase in death rates and the 165.6% increase in DALY rates for chronic kidney disease, particularly chronic kidney disease due to hypertension, between 2000 and 2012 is concerning. The South African Renal Registry[47] reports that hypertensive renal disease was the most commonly reported type of chronic kidney disease for the country in 2017. Raised glucose levels together with raised blood pressure are placing a severe health burden on South Africans and the health system. According to the South Africa Demographic and Health Survey 2016,[19] 46% of women and 44% of men in SA had hypertension, with indications that figures had nearly doubled in less than 20 years. Furthermore, >80% of those with hypertension were untreated and/or had uncontrolled hypertension.[19] Increasingly, hypertension is being recognised as a common comorbidity that occurs with diabetes across Africa.[48]

The development of subclinical dysglycaemia and progression to overt diabetes can be postponed through lifestyle interventions, although locally appropriate evidence to support the implementation of such approaches in SA and Africa at large are lacking.[49,50] Furthermore, once diabetes develops, early diagnosis and appropriate interventions targeting the optimisation of glycaemia and the overall cardiovascular risk profile can prevent progression to the stage of complications and disabilities.[49] Stokes *et al.*[51] reported from the 2012 South African National Health and Nutrition Examination Survey (SANHANES-1)[18] that 'Among individuals with diabetes, a total of 45.4% were unscreened, 14.7% were screened but undiagnosed, 2.3% were diagnosed but untreated, 18.1% were treated but uncontrolled, and 19.4% were treated and controlled', suggesting that 80.6% of the diabetic population in SA had unmet need for care. SANHANES-1 probably underestimates the true magnitude of the detection, treatment and control of diabetes in SA, considering that diabetes diagnosis in SANHANES-1 was based on HbA1c, which has been shown to perform less well than OGTT for diabetes diagnosis in South Africans.[52] Nevertheless, our findings together with SANHANES-1[18,51] reflect that there is a huge problem in SA in the management and care of individuals exposed to high FPG. The root cause for this needs to be identified and addressed, and could range from limited population-wide health promotion to prevent the uptake and augmentation of risk to lack of screening among those at high risk of hyperglycaemia resulting in delayed diagnosis, and non-optimal management and ongoing monitoring of those eventually diagnosed with diabetes. The association between diabetes and other risks such as obesity, low physical activity, poor diet, smoking and alcohol use has been reported previously,[6] and a more holistic approach is therefore needed to reduce the burden from high FPG.

Our study shows that DALYs attributable to higher-than-optimal plasma glucose levels have increased by 56% over a 12-year period, signalling an urgent need to curb the trend. Since 2009, the government's focus on NCDs has expanded with the adoption of a National Plan for NCDs in 2012 and policies to address unhealthy diets/nutrition and physical inactivity.[53] The subsequent NSP for NCDs[54] has emphasised the early identification and effective management and control of NCDs. A 90/60/50 target has been set, whereby 90% of people with raised plasma glucose should know that they have raised plasma glucose, 60% of those with raised plasma glucose should receive intervention, and 50% of those receiving interventions should be controlled. However, these supportive plans have not achieved the desired impact owing to barriers and challenges to their implementation, including lack of funding to support effective policy implementation and co-ordination, lack of multisectoral action in the implementation process, and lack of panel data to measure the impact of population-level interventions.[55] Programmes targeting risk factors for NCDs, including unhealthy diets and physical inactivity, have also been developed in SA. Such programmes include National Recreation Day,[56] the Big Walk Campaign,[57] the Move for Health Day,[58] the National School Nutrition Programme,[59] Western Cape on Wellness (WoW)[60] and Healthy Food – Discovery Health.[61] Most of these programmes are not implemented nationwide, however, and their development is not always evidence based.

The limited national data on FPG and the prevalence of diabetes in South Africans[11] meant that we had to model estimates from the few available national surveys and some small-area studies that used different methods to identify individuals with high FPG and diabetes (Table 1, and Table S1 in the appendix: https://www.samedical.org/file/1846). The model allowed for differences by population group, with urban and rural categories for black Africans to allow for changes in urbanisation in this group during the study time period; other population groups had high urban proportions throughout the period. Population-based surveys using the same accurate diagnostic methods to determine exposure to high FPG and identify people living with diabetes would provide empirical estimates for the analysis done in this study. Nonetheless, the current study is based on more data points than previous efforts to estimate diabetes prevalence trends for SA.[32] While it would be ideal to have more recent data for this study, the trends between 2000 and 2012 point to hugely troubling health trends, which undoubtedly remain a matter of concern. The COVID-19 pandemic has confirmed the dynamic nature of the spectrum of health outcomes of higher-than-optimal plasma glucose by demonstrating that once infected with SARS-CoV-2, people with uncontrolled diabetes were at higher risk of developing the severe form of COVID-19 and dying from the disease than people without diabetes or with controlled diabetes.[62,63] Future efforts to estimate the health outcomes of diabetes should integrate this emerging condition, and perhaps integrate the impact of the growing comorbid dysglycaemia in people living with HIV infection.[64-67]

Conclusion

High FPG is racing towards being a public health crisis with an attributable burden doubling between 2000 and 2012, exacerbated by high levels of hypertension. The burden of exposure to higher-than-optimal plasma glucose is costly in terms of quality of life, ability to earn an income, and the physical, economic and emotional burden on the affected individuals, their households and society. The NSP for NCDs reports that the cost of all diabetes cases by 2030 will be ~ZAR35 billion (USD2.5 billion).[54,68] Monitoring and evaluating the impact of the 90/60/50 plan, while making necessary changes to

Table 3. (continued) Burden attributed to high fasting plasma glucose in males, females and persons in South Africa for 2000, 2006 and 2012

	Males			Females			Persons		
Disease outcome*	**AF, %†**	**Deaths, *n***	**DALYs, *n***	**AF, %†**	**Deaths, *n***	**DALYs, *n***	**AF, %†**	**Deaths, *n***	**DALYs, *n***
Pancreatic cancer	7.1	52	824	10.6	85	1 328	8.9	138	2 152
Ovarian cancer	0	-	-	9.9	72	1 294	9.9	72	1 294
Bladder cancer	7.3	30	423	10.2	19	298	8.2	49	721
Dementia	7.5	58	1 052	11.0	153	3 638	9.7	211	4 690
Peripheral vascular disease	23.8	98	1 609	29.7	80	1 294	26.1	178	2 903
Glaucoma	0	-	105	0	-	368	0	-	473
Cataracts	0	-	196	0	-	732	0	-	928
Total attributable burden	-	**14 385**	**297 624**	-	**21 280**	**444 407**	-	**35 666**	**742 031**
(95% UI)		(11 284 - 18 793)	(244 979 - 375 288)		(16 796 - 26 861)	(375 465 - 533 506)		(29 729 - 43 673)	(642 776 - 877 444)
% of total burden	-	**4.2**	**2.4**	-	**6.4**	**3.4**	-	**5.3**	**2.9**
(95% UI)		(3.3 - 5.5)	(2.0 - 3.1)		(5.0 - 8.0)	(2.9-4.1)		(4.4 - 6.5)	(2.5 - 3.5)
2012									
Diabetes	100	7 315	173 824	100	11 299	303 452	100	18 614	477 275
Ischaemic heart disease	18.2	2 406	41 217	25.9	3 011	47 785	21.8	5 417	89 002
Haemorrhagic stroke	17.2	1 473	25 202	22.9	2 858	47 484	20.6	4 331	72 686
Ischaemic stroke	17.8	1 206	17 703	24.1	2 797	39 286	21.8	4 002	56 989
Tuberculosis	12.8	1 845	55 479	17.1	1 119	43 032	14.1	2 964	98 512
CKD due to hypertension	35.4	1 344	29 036	51.7	2 056	47 353	43.8	3 400	76 390
CKD due to glomerulonephritis	30.3	148	10 040	40.5	137	14 022	34.5	285	24 062
CKD due to other causes	33.8	511	12 396	47.1	652	18 011	40.1	1 163	30 407
Lung cancer	9.0	404	6 427	12.3	255	4 239	10.1	659	10 667
Breast cancer	8.2	6	101	11.2	436	8 758	11.2	442	8 860
Colorectal cancer	8.9	166	2 619	12.2	197	3 270	10.4	363	5 888
Liver cancer	8.1	115	1 883	11.5	96	1 639	9.4	211	3 522
Pancreatic cancer	9.0	78	1 175	12.6	114	1 771	10.8	191	2 946
Ovarian cancer	0	-	-	11.9	103	1 850	11.9	103	1 850
Bladder cancer	9.3	47	666	11.5	26	466	10.0	73	1 131
Dementia	9.7	80	1 413	13.2	187	4 073	12.0	267	5 485
Peripheral vascular disease	28.1	114	1 782	33.9	103	1 793	30.6	217	3 575
Glaucoma	0	-	138	0	-	534	0	-	672
Cataracts	0	-	252	0	-	991	0	-	1 242
Total attributable burden	-	**17 257**	**381 354**	-	**25 445**	**589 809**	-	**42 702**	**971 163**
(95% UI)	-	(14 062 - 21 669)	(322 584 - 456 886)	-	(20 524 - 31 227)	(506 883 - 681 109)	-	(36 486 - 50 307)	(85 9191 - 1 101 534)
% of total burden	-	**6.2**	**3.8**	-	**10.1**	**5.6**	-	**8.1**	**4.7**
(95% UI)	-	(5.1 - 7.8)	(3.2 - 4.5)	-	(8.1 - 12.4)	(4.8 - 6.5)	-	(6.9 - 9.5)	(4.2 - 5.4)

AF = attributable fraction based on the numbers of attributable deaths; DALY = disability-adjusted life year; CKD = chronic kidney disease; UI = uncertainly interval.
*Disease outcomes ranked according to person deaths for each year.
†AF reported for deaths.

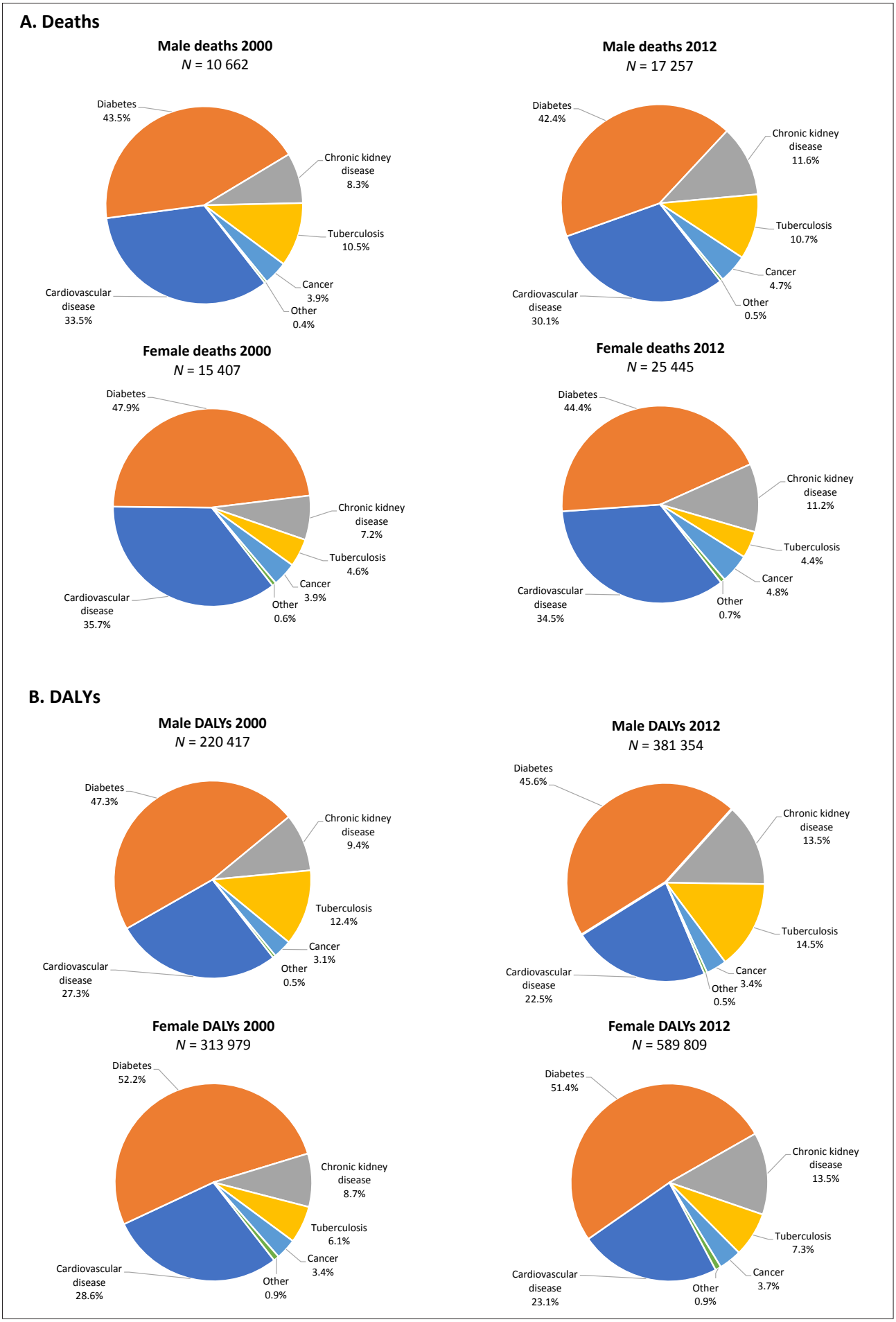

Fig 3. Distribution of (A) deaths and (B) DALYs attributable to high fasting plasma glucose by disease outcome by sex in South Africa for 2000 and 2012.

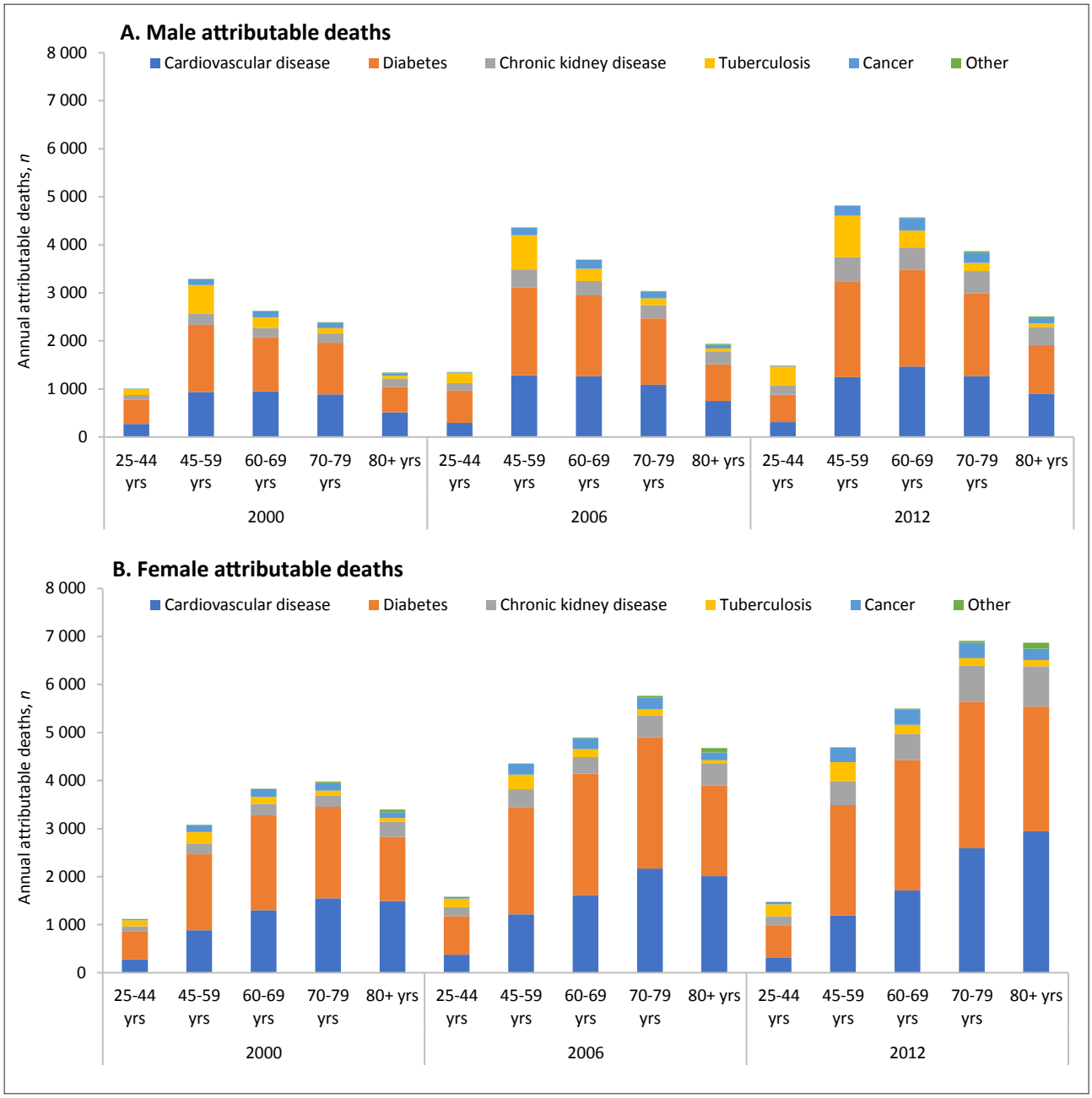

Fig 4. Distribution of (A) male and (B) female attributable deaths by age group and disease outcomes by sex in South Africa for 2000, 2006 and 2012.

improve impact, is critical to ensuring that SA mitigates the health consequences of high plasma glucose. Urgent action is needed to curb the increase and reduce the burden associated with this risk factor, and should be supported with national data to monitor the effectiveness of the interventions.

Disclaimer. The population group classification used in this article is based on self-reporting according to apartheid-era groups defined by the Population Registration Act of 1950, i.e. black African, coloured, Indian/Asian and white. This classification is used because it has important correlates with lifestyle, culture and socioeconomic conditions that impact on health and health-related behaviours. The authors do not subscribe to this classification for any other purpose.

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

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Conflicts of interest. None.

1. Peykari N, Saeedi MS, Djalalinia S, et al. High fasting plasma glucose mortality effect: A comparative risk assessment in 25 - 64 years old Iranian population. Int J Prev Med 2016;7:75. https://doi.org/10.4103/2008-7802.182732
2. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990 - 2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380(9859):2224-2260. https://doi.org/10.1016/S0140-6736(12)61766-8
3. Jin C, Chen S, Vaidya A, et al. Longitudinal change in fasting blood glucose and myocardial infarction risk in a population without diabetes. Diabetes Care 2017;40(11):1565-1572. https://doi.org/10.2337/dc17-0610
4. International Diabetes Federation. IDF Diabetes Atlas 9th edition. 2019. https://www.diabetesatlas.org/en/resources/ (accessed 14 December 2020).
5. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas. Diabetes Res Clin Pract 2019;157:107843. https://doi.org/10.1016/j.diabres.2019.107843
6. Moradi-Lakeh M, Forouzanfar MH, El Bcheraoui C, et al. High fasting plasma glucose, diabetes, and its risk factors in the eastern Mediterranean region, 1990 - 2013: Findings from the Global Burden of Disease Study 2013. Diabetes Care 2017;40(1):22-29. https://doi.org/10.2337/dc16-1075
7. Norman R, Bradshaw D, Schneider M, et al. A comparative risk assessment for South Africa in 2000: Towards promoting health and preventing disease. S Afr Med J 2007;97(8):637-641.
8. Bradshaw D, Norman R, Pieterse D, et al. Estimating the burden of disease attributable to diabetes in South Africa in 2000. S Afr Med J 2007;97(8 Pt 2):700-706.
9. National Department of Health, South Africa. Management of type 2 diabetes in adults at primary care level. 2014. https://www.knowledgehub.org.za/system/files/elibdownloads/2019-07/Management%2520of%2520ype%25202%2520Diabetes%2520%25202014.pdf (accessed 14 December 2021).
10. Pheiffer C. The prevalence of type 2 diabetes in South Africa: A systematic review. MPH thesis. Cape Town: University of Cape Town, 2020. http://hdl.handle.net/11427/32479 (accessed 15 December 2021).
11. Pheiffer C, Pillay-van Wyk V, Turawa E, et al. Prevalence of type 2 diabetes in South Africa: A systematic review and meta-analysis. Int J Environ Res Public Health 2021;18(11):5868. https://doi.org/10.3390/ijerph18115868
12. GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990 - 2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392(10159):1923-1994. https://doi.org/10.1016/s0140-6736(18)32225-6
13. World Health Organization. Reducing risk, promoting healthy life. Geneva: WHO, 2002. http://www.who.int/whr/2002/en/summary_riskfactors_chp4.pdf (accessed 15 December 2020).
14. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet 1997;349(9063):1436-1442. https://doi.org/10.1016/S0140-6736(96)07495-8
15. Pillay-van Wyk V, Msemburi W, Laubscher R, et al. Mortality trends and differentials in South Africa from 1997 to 2012: Second National Burden of Disease Study. Lancet Glob Health 2016;4(9):e642-e653. https://doi.org/10.1016/S2214-109X(16)30113-9
16. World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications: Report of a WHO consultation. Part 1: Diagnosis and classification of diabetes mellitus. Geneva: WHO, 1999. https://apps.who.int/iris/handle/10665/66040 (accessed 14 December 2020).
17. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009;32(7):1327-1334. https://doi.org/10.2337/dc09-9033
18. Shisana O, Labadarios D, Rehle T, et al. The South African National Health and Nutrition Examination Survey, 2012: SANHANES-1: The health and nutritional status of the nation. 2014. http://repository.hsrc.ac.za/handle/20.500.11910/2864 (accessed 22 December 2020).
19. National Department of Health, Statistics South Africa, South African Medical Research Council and ICF. South Africa Demographic and Health Survey 2016. Pretoria: NDoH, 2019. http://dhsprogram.com/pubs/pdf/FR337/FR337.pdf (accessed 21 December 2020).
20. Omar MAK, Seedat M, Motala A, et al. The prevalence of diabetes mellitus and impaired glucose tolerance in a group of urban South African blacks. S Afr Med J 1993;83(9):641-643.
21. Levitt NS, Katzenellenbogen JM, Bradshaw D, et al. The prevalence and identification of risk factors for NIDDM in urban Africans in Cape Town, South Africa. Diabetes Care 1993;16(4):601-607. https://doi.org/10.2337/diacare.16.4.601
22. Omar MA, Seedat MA, Dyer RB, et al. South African Indians show a high prevalence of NIDDM and bimodality in plasma glucose distribution patterns. Diabetes Care 1994;17(1):70-73. https://doi.org/10.2337/diacare.17.1.70
23. Mollentze W, Moore A, Steyn A, et al. Coronary heart disease risk factors in a rural and urban Orange Free State black population. S Afr Med J 1995;85(2):90-96.
24. Levitt NS, Steyn K, Lambert EV, et al. Modifiable risk factors for type 2 diabetes mellitus in a peri-urban community in South Africa. Diabet Med 1999;16(11):946-950. https://doi.org/10.1046/j.1464-5491.1999.00185.x
25. Motala AA, Esterhuizen T, Gouws E, et al. Diabetes and other disorders of glycemia in a rural South African community: Prevalence and associated risk factors. Diabetes Care 2008;31(9):1783-1788. https://doi.org/10.2337/dc08-0212
26. Peer N, Steyn K, Lombard C, et al. Rising diabetes prevalence among urban-dwelling black South Africans. PLoS ONE 2012;7(9):e43336. https://doi.org/10.1371/journal.pone.0043336
27. Hird TR, Pirie FJ, Esterhuizen TM, et al. Burden of diabetes and first evidence for the utility of HbA1c for diagnosis and detection of diabetes in urban black South Africans: The Durban Diabetes Study. PLoS ONE 2016;11(8):e0161966. https://doi.org/10.1371/journal.pone.0161966
28. Zemlin AE, Barkhuizen M, Kengne AP, et al. Performance of glycated albumin for type 2 diabetes and prediabetes diagnosis in a South African population. Clin Chim Acta 2019;488:122-128. https://doi.org/10.1016/j.cca.2018.11.005
29. Gelman A, Carlin JB, Stern HS, et al. Bayesian Data Analysis. 2nd ed. London: Chapman & Hall, 2004.
30. Holland S. Transformations of proportions and percentages. http://strata.uga.edu/8370/rtips/proportions.html (accessed 14 December 2020).
31. Dorrington R. Alternative South African mid-year estimates, 2013. Cape Town: Centre for Actuarial Research, University of Cape Town, 2013. http://www.care.uct.ac.za/sites/default/files/image_tool/images/561/Downloads/Mono11.pdf (accessed 22 December 2020).
32. Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: Systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet 2011;378(9785):31-40. https://doi.org/10.1016/s0140-6736(11)60679-x
33. Ahmad OB, Boschi-Pinto C, Lopez AD, et al. Age standardisation of rates: A new WHO standard. Geneva: World Health Organization, 2001. https://www.researchgate.net/publication/284696312_Age_Standardization_of_Rates_A_New_WHO_Standard (accessed 20 December 2020).
34. Barendregt JJ. The effect size in uncertainty analysis. Value Health 2010;13(4):388-391. https://doi.org/10.1111/j.1524-4733.2009.00686.x
35. NCD Risk Factor Collaboration – Africa Working Group. Trends in obesity and diabetes across Africa from 1980 to 2014: An analysis of pooled population-based studies. Int J Epidemiol 2017;46(5):1421-1432. https://doi.org/10.1093/ije/dyx078
36. Hilawe EH, Yatsuya H, Kawaguchi L, et al. Differences by sex in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa: A systematic review and meta-analysis. Bull World Health Organ 2013;91(9):671-682D. https://doi.org/10.2471/BLT.12.113415
37. Kautzky-Willer A, Harreiter J, Pacini G. Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. Endocr Rev 2016;37(3):278-316. https://doi.org/10.1210/er.2015-1137
38. Goedecke JH, Mtintsilana A, Dlamini SN, et al. Type 2 diabetes mellitus in African women. Diabetes Res Clin Pract 2017;123:87-96. https://doi.org/10.1016/j.diabres.2016.11.017
39. Belkina AC, Denis GV. Obesity genes and insulin resistance. Curr Opin Endocrinol Diabetes Obes 2010;17(5):472-477. https://doi.org/10.1097/MED.0b013e32833c5c48
40. Wu Y, Ding Y, Tanaka Y, et al. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci 2014;11(11):1185-200. https://doi.org/10.7150/ijms.10001
41. Sanada H, Yokokawa H, Yoneda M, et al. High body mass index is an important risk factor for the development of type 2 diabetes. Intern Med 2012;51(14):1821-1826. https://doi.org/10.2169/internalmedicine.51.7410
42. Cois A, Day C. Obesity trends and risk factors in the South African adult population. BMC Obes 2015;2:42. https://doi.org/10.1186/s40608-015-0072-2
43. Dorrington R, Bradshaw D, Laubscher R, et al. Rapid mortality surveillance report 2012. Cape Town: South African Medical Research Council, 2014. www.mrc.ac.za/bod/reports.htm (accessed 22 December 2020)
44. Galdas PM, Cheater F, Marshall P. Men and health help-seeking behaviour: Literature review. J Adv Nurs 2005;49(6):616-623. https://doi.org/10.1111/j.1365-2648.2004.03331.x
45. Kyu HH, Maddison ER, Henry NJ, et al. The global burden of tuberculosis: Results from the Global Burden of Disease Study 2015. Lancet Infect Dis 2018;18(3):261-284. https://doi.org/10.1016/S1473-3099(17)30703-X
46. World Health Organization. Global tuberculosis report. Geneva: WHO, 2018. https://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf (accessed 12 December 2020).
47. Davids MR, Jardine T, Marais N, et al. South African Renal Registry Annual Report 2017. Afr J Nephrol 2019;22(1):60-71. https://doi.org/10.21804/22-1-3810
48. Ekoru K, Doumatey A, Bentley AR, et al. Type 2 diabetes complications and comorbidity in Sub-Saharan Africans. EClinicalMedicine 2019;16:30-41. https://doi.org/10.1016/j.eclinm.2019.09.001
49. Atun R, Davies JI, Gale EAM, et al. Diabetes in sub-Saharan Africa: From clinical care to health policy. Lancet Diabetes Endocrinol 2017;5(8):622-667. https://doi.org/10.1016/S2213-8587(17)30181-X
50. Hill J, Lavigne Delville C, Auorousseau AM, et al. Development of a tool to increase physical activity among people at risk for diabetes in low-resourced communities in Cape Town. Int J Environ Res Public Health 2020;17(3):865. https://doi.org/10.3390/ijerph17030865
51. Stokes A, Berry KM, Mchiza Z, et al. Prevalence and unmet need for diabetes care across the care continuum in a national sample of South African adults: Evidence from the SANHANES-1, 2011 - 2012. PloS ONE 2017;12(10):e0184264. https://doi.org/10.1371/journal.pone.0184264
52. Kengne AP, Erasmus RT, Levitt NS, et al. Alternative indices of glucose homeostasis as biochemical diagnostic tests for abnormal glucose tolerance in an African setting. Prim Care Diab 2017;11(2):119-131. https://doi.org/10.1016/j.pcd.2017.01.004
53. Ndinda C, Ndhlovu TP, Juma P, et al. The evolution of non-communicable diseases policies in post-apartheid South Africa. BMC Public Health 2018;18(Suppl 1):956. https://doi.org/10.1186/s12889-018-5832-8
54. National Department of Health, South Africa. National Strategic Plan for the Prevention and Control of Non-communicable Diseases 2020 - 2025. 2019. https://www.sancda.org.za/wp-content/uploads/2020/05/17-May-2020-South-Africa-NCD-STRATEGIC-PLAN_For-Circulation.pdf (accessed 4 June 2022).
55. Juma PA, Mapa-Tassou C, Mohamed SF, et al. Multi-sectoral action in non-communicable disease prevention policy development in five African countries. BMC Public Health 2018;18(Suppl 1):953. https://doi.org/10.1186/s12889-018-5826-6
56. Department of Sport and Recreation, South Africa. National Recreation Day. 2014. https://www.srsa.gov.za/content/national-recreation-day (accessed 22 December 2020).
57. Department of Sport and Recreation, South Africa. The Big Walk. 2012. https://www.srsa.gov.za/content/big-walk (accessed 22 December 2020).
58. South African Government. The Move for Health Day. https://www.gov.za/world-move-health-day (accessed 22 December 2020).
59. Department of Basic Education, South Africa. National School Nutrition Programme. https://www.education.gov.za/Programmes/NationalSchoolNutritionProgramme.aspx (accessed 22 December 2020).
60. Western Cape Government. Western Cape on Wellness. https://www.westerncape.gov.za/westerncape-on-wellness/about-us (accessed 22 December 2020).
61. Lambert EV, Kolbe-Alexander TL. Innovative strategies targeting obesity and non-communicable diseases in South Africa: What can we learn from the private healthcare sector? Obesity Rev 2013;14(Suppl 2):141-149. https://doi.org/10.1111/obr.12094
62. Boulle A, Davies MA, Hussey H, et al. Risk factors for COVID-19 death in a population cohort study from the Western Cape Province, South Africa. Clin Infect Dis 2021;73(7):e2005-e2015. https://doi.org/10.1093/cid/ciaa1198
63. Pillay-van Wyk V, Bradshaw D, Groenewald P, et al. COVID-19 deaths in South Africa: 99 days since South Africa's first death. S Afr Med J 2020;110(11):1093-1099. https://doi.org/10.7196/SAMJ.2020.v110i11.15249
64. Patel P, Rose CE, Collins PY, et al. Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: A systematic review and meta-analysis. AIDS 2018;32 (Suppl 1):S5-S20. https://doi.org/10.1097/QAD.0000000000001888
65. Nansseu JR, Bigna JJ, Kaze AD, et al. Incidence and risk factors for prediabetes and diabetes mellitus among HIV-infected adults on antiretroviral therapy: A systematic review and meta-analysis. Epidemiology 2018;29(3):431-441. https://doi.org/10.1097/EDE.0000000000000815

66. Njuguna B, Kiplagat J, Bloomfield GS, et al. Prevalence, risk factors, and pathophysiology of dysglycemia among people living with HIV in sub-Saharan Africa. J Diabetes Res 2018;2018:6916497. https://doi.org/10.1155/2018/6916497
67. Prioreschi A, Munthali RJ, Soepnel L, et al. Incidence and prevalence of type 2 diabetes mellitus with HIV infection in Africa: A systematic review and meta-analysis. BMJ Open 2017;7(3):e013953. https://doi.org/10.1136/bmjopen-2016-013953
68. Erzse A, Stacey N, Chola L, et al. The direct medical cost of type 2 diabetes mellitus in South Africa: A cost of illness study. Glob Health Action 2019;12(1):1636611. https://doi.org/10.1080/16549716.2019.1636611

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