Estimating the changing disease burden attributable to smoking in South Africa for 2000, 2006 and 2012

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Background. Ongoing quantification of the disease burden attributable to smoking is important to monitor and strengthen tobacco control policies.
Objectives. To estimate the attributable burden due to smoking in South Africa for 2000, 2006 and 2012.
Methods. We estimated attributable burden due to smoking for selected causes of death in South African (SA) adults aged ≥35 years for 2000, 2006 and 2012. We combined smoking prevalence results from 15 national surveys (1998 - 2017) and smoking impact ratios using national mortality rates. Relative risks between smoking and select causes of death were derived from local and international data.
Results. Smoking prevalence declined from 25.0% in 1998 (40.5% in males, 10.9% in females) to 19.4% in 2012 (31.9% in males, 7.9% in females), but plateaued after 2010. In 2012 tobacco smoking caused an estimated 31 078 deaths (23 444 in males and 7 634 in females), accounting for 6.9% of total deaths of all ages (17.3% of deaths in adults aged ≥35 years), a 10.5% decline overall since 2000 (7% in males; 18% in females). Age-standardised mortality rates (and disability-adjusted life years (DALYs)) similarly declined in all population groups but remained high in the coloured population. Chronic obstructive pulmonary disease accounted for most tobacco-attributed deaths (6 373), followed by lung cancer (4 923), ischaemic heart disease (4 216), tuberculosis (2 326) and lower respiratory infections (1 950). The distribution of major causes of smoking-attributable deaths shows a middle- to high-income pattern in whites and Asians, and a middle- to low-income pattern in coloureds and black Africans. The role of infectious lung disease (TB and LRIs) has been underappreciated. These diseases comprised 21.0% of deaths among black Africans compared with only 4.3% among whites. It is concerning that smoking rates have plateaued since 2010.
Conclusion. The gains achieved in reducing smoking prevalence in SA have been eroded since 2010. An increase in excise taxes is the most effective measure for reducing smoking prevalence. The advent of serious respiratory pandemics such as COVID-19 has increased the urgency of considering the role that smoking cessation/abstinence can play in the prevention of, and post-hospital recovery from, any condition.

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The article in context

Evidence before this study. The prevalence of tobacco smoking has been declining since the introduction of comprehensive tobacco control legislation in 1993 (the Tobacco Products Control Act No. 83 of 1993). However, monitoring of smoking prevalence and trends has been challenging. Several national surveys collected information on current smoking using different methods. In 2000, the first South African Comparative Risk Assessment (SACRA1) study was conducted and assessed the attributable burden due to tobacco smoking. Smoking ranked third in terms of mortality among 17 risk factors evaluated, and accounted for 8.0 - 9.0% of total adult deaths and 3.7 - 4.3% of total adult disability-adjusted life years.
Added value of this study. This study applied updated Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) methods to estimate the smoking-attributable burden from selected health-related outcomes in adults aged ≥35 years for three time points, 2000, 2006 and 2012. The number of data sources increased. Smoking prevalence estimates for 2000, 2006 and 2012, by population group, age and sex, were obtained from a pooled meta-regression analysis of 15 national surveys between 1998 and 2017. Smoking prevalence declined between 1998 and 2010, but has plateaued since then. Smoking caused 31 078 deaths in 2012, accounting for 7% of total deaths (17% of total deaths in adults aged ≥35 years). This is a decline of 10.5% in smoking-attributable burden since 2000.
Implications of all the available evidence. Despite gains in tobacco control in SA, smoking prevalence and smoking-attributable burden remains high. Rates of decline in smoking prevalence plateaued between 2010 and 2012, suggesting that tobacco control measures need review and strengthening. Increasing excise taxes is the most effective measure to reduce smoking prevalence, and this should be implemented. In addition, brief interventions encouraging patients to quit smoking during clinic or hospital visits should target high-risk patients.

Smoking tobacco is one of the main risk factors for morbidity and mortality globally, with enormous economic and health costs.[1,2] Smoking considerably increases the risk of death from lung and other cancers, heart disease, stroke, chronic respiratory disease and other conditions.[3] In 2019, the World Health Organization (WHO) estimated that tobacco use was responsible for 8 million deaths worldwide per year, with many of these occurring prematurely, and smoking prevalence was estimated at 19.2% worldwide (37.2% males and 5.8% females).[1] In 2019, the Global Burden of Diseases, Injuries and Risk Factors Study (GBD)[4] ranked tobacco exposure the second leading cause of death out of 87 risk factors, accounting for 7.7 million deaths worldwide. Tobacco use accounted for 6.2 million deaths in males (20.2% of all male deaths) and 1.5 million deaths in females (5.8% of all female deaths). A number of studies have demonstrated that long-term sustainable public health interventions can reduce smoking prevalence.[4-6] GBD 2019 estimates that globally, government interventions including taxation and tobacco regulatory policy reduced the prevalence of smoking by almost 1% per year between 2010 and 2019. However, despite a decline of 15.7% in age-standardised smoking-attributable death rates between 2010 and 2019, smoking remains the second leading risk factor for deaths.

South Africa (SA) was an early adopter of the WHO Framework Convention on Tobacco Control.[7] In 1994, SA enacted comprehensive tobacco control legislation measures (the Tobacco Products Control Act No. 83 of 1993), including increases in excise taxes and an advertising ban.[8] The prevalence of smoking decreased from 32.6% in 1993 to 28.5% in 1998.[9] The Global Youth Tobacco Surveys (GYTSs) conducted in SA in 1999, 2002, 2008, and 2011[10,11] show the positive impact of tobacco control policies on youth smoking over a 12-year period.[12]

According to the South African National Health and Nutrition Examination Survey (SANHANES-1),[13] 17.6% of South Africans aged ≥15 years were smokers in 2012.[14] This decline (from 32% in 1993) has been largely attributed to an increase in excise taxes, stricter smoking legislation and control over advertising.[8,10] Despite these achievements, smoking rates in SA (especially for black African males (28.5%) and females (3.3%)) are higher than those of most other African countries.[1] Global Adult Tobacco Survey data from 8 other African countries range from 7.2% - 23.9% in males and 0.2% - 2.8% in females,[15] and there are also concerns that smoking prevalence has plateaued at 20% of the adult population since 2010.[16]

Since smoking is a major public health issue in SA, ongoing quantification of smoking prevalence and the smoking-attributable disease burden is important for monitoring and strengthening tobacco control policies. In 2000 the first South African Comparative Risk Assessment Study (SACRA1)[17] conducted by the South African Medical Research Council (SAMRC) found that smoking ranked third (after unsafe sex/sexually transmitted disease and high blood pressure) in terms of mortality among the 17 risk factors evaluated. Furthermore, smoking accounted for 8.0% - 9.0% of deaths and 3.7% - 4.3% of disability-adjusted life years (DALYs).[18]

Local mortality surveillance on smoking-attributed risks (1997 - 2013), derived from the Smoking and Death Notification South Africa (S&DNSA) study[19] and mortality trends in lung cancer, suggests that the relative risks (RRs) (although they measured diluted RRs of current smoker v. ex-/never-smokers) for smoking-related deaths in some SA population groups (see disclaimer) are heterogeneous and differ from the American Cancer Society Prevention Study, Phase II cohort (CPS-II cohort).[20] Methods were therefore adapted for the second SACRA[21] to account for available local smoking prevalence and RR data. The aim of the present study was to estimate the burden attributable to smoking in SA over time (for 2000, 2006 and 2012), incorporating improved methods, updated information on prevalence of smoking and revised RRs for smoking-attributable deaths by population group. The results presented in this article supersede the previously published SACRA1 estimates.

Methods

The GBD updates its comparative risk assessment (CRA) methods regularly, including new smoking-related outcomes, revision of the RRs of smoking in relation to these outcomes and updated local smoking prevalence estimates.[22,23] GBD 2017[24] used a new measure of exposure to smoking that takes duration as well as consumption into account, namely pack years of exposure. Such data are not available in SA, so a modified CRA methodology from the GBD 2016[23] was used for this study.

We followed the hybrid method used in the GBD 2010 study,[22] which used a combination of the smoking impact ratio (SIR) method[25] and the smoking prevalence method to calculate population-attributable fractions (PAFs). The SIR method was used for conditions where the long-term lag between smoking prevalence and eventual hazards is well described and homogeneous (e.g. lung, certain cancers, chronic obstructive pulmonary disease (COPD). The prevalence method was used for conditions where the relationship with smoking is more heterogeneous (e.g. cardiovascular disease, stroke, tuberculosis (TB), other respiratory diseases, diabetes and other conditions), as reported below. Attributable burden due to smoking was estimated for adults aged ≥35 years by population group by applying the PAF for each health outcome to burden of disease estimates from the Second SA National Burden of Disease Study (SANBD2) for the respective years.[21,26]

Estimating exposure to tobacco smoking

Smoking prevalence

Smoking prevalence estimates from 1998 until 2012 were obtained from a pooled meta-regression analysis of 15 national surveys that included data on smoking status.[27] These surveys were *a priori* reviewed for risk of bias based on a standardised assessment tool[28] that evaluated the wording of the smoking question and the representativeness of the sample (see Table S1 in appendix: https://www.samedical.org/file/1841). Each survey was weighted by the risk of bias score and the sample size. Prevalence estimates for each sex, population and age group were normalised to represent the SA population (Table S2 in appendix).

The smoking prevalence method uses the current prevalence of smoking applied to RRs to calculate PAFs. The disease burden attributable to tobacco smoking was estimated by comparing the current local smoking exposure with the theoretical minimum risk exposure level (TMREL), defined as the counterfactual exposure or distribution with the lowest possible risk (never smoking).

Smoking impact ratio (SIR) (long lag conditions)

The SIR method uses lung cancer mortality as a marker of cumulative population exposure to smoking to calculate the PAF. Current smoking is a poor proxy for the cumulative hazards of smoking, as some of the negative effects of smoking take time to manifest. The cumulative hazards of smoking depend on several factors: smoking onset age, smoking duration, smoking intensity, degree of inhalation and cigarette characteristics, such as tar and nicotine content and the type of filter. To overcome this problem for conditions where there is a long lag between exposure and disease outcome, and the long-term hazards are well documented, the SIR method, which estimates excess lung cancer mortality, was used as a marker for accumulated smoking risk.[29] In the present study, the SIR is defined as the observed SA

lung cancer mortality in excess of never-smokers, relative to excess lung cancer mortality for the reference group of smokers in the American Cancer Society Prevention Study, (CPS-II).[20]

$$SIR = \frac{C_{LC} - N_{LC}}{S^*_{LC} - N^*_{LC}} \times \frac{N^*_{LC}}{N_{LC}}$$

where C_{LC} is the observed population group-age-sex-specific lung cancer mortality rate in SA for 2000, 2006 and 2012, N_{LC} is the non-smoker lung cancer mortality rate in the SA population, and S^*_{LC} and N^*_{LC} are the smoker and non-smoker lung cancer mortality rates in the reference population CPS-II (which is not categorised by population group). The numerator and denominator are normalised with the respective non-smoker lung cancer mortality rates.[30]

The non-smoker lung cancer mortality rates (N_{LC}) estimated for the SA population (Asians excluded because of small sample size) from the S&DNSA data (Table S3 in appendix: www.samedical.org/file/1841) are higher than in the CPS-II population because they include ex-smokers (Fig. 1). Therefore the non-smoker lung cancer mortality rates in the reference population CPS-II were substituted for the N_{LC} in the SIR formula.[25] The observed lung cancer mortality rates (C_{LC}) by population group from the most recent SA burden of disease estimates for 2000, 2006 and 2012 were used in the SIR calculations.[21]

Smoking-related causes of death

The smoking-related medical causes of death used in GBD 2016[23] were included: cancers of mouth, oro- and nasopharynx, oesophagus, stomach, colorectal, liver, pancreas, lung, breast, cervix uteri, prostate, kidney and bladder, leukaemia, COPD, other chronic respiratory diseases, asthma, TB, lower respiratory infections (LRIs), ischaemic heart disease (IHD), stroke, hypertensive heart disease, other cardiovascular disease, peptic ulcer, gallbladder and biliary disease, Alzheimer's disease, multiple sclerosis, diabetes mellitus (DM) and rheumatoid arthritis (Table 1). GBD 2016 included Parkinson's disease, low back pain, cataract and macular degeneration. These conditions were not included because of the low mortality attributable to these conditions and uncertainties regarding the extent of the morbidity data. While GBD 2016 attributed a small number of deaths to unintentional injuries (road traffic injuries and falls) we did not, owing to likely confounding by alcohol.

Relative risks for smoking

Comparison of lung cancer mortality rates from the CPS-II and from the S&DNSA study[19] indicated that there are marked differences in the tobacco epidemic between population groups in SA, particularly in the black African population (Fig. 1). Lung cancer mortality rates among white and coloured male smokers are comparable with or higher than those for smokers in CPS-II, while those for black African male smokers are lower than the other population groups, probably as a result of later age of initiation,[31] lower daily consumption of cigarettes[32-37] and shorter duration of smoking.[32]

For conditions with a long lag from exposure to outcome (lung and certain other cancers, COPD and other chronic respiratory conditions), the GBD 2016 RRs that were based upon the CPS-II RRs were used for all population groups (Table 1), because conceptually the SIR is already converting the smokers from the four SA population groups with different smoking histories into equivalents of smokers in the CPS-II reference population, where risks for smoking-related diseases have been measured.[29]

For other conditions where the RRs are more heterogenous (acute respiratory infections including TB, cardiovascular diseases (IHD, stroke and others), peptic ulcer, gallbladder and biliary disease, multiple sclerosis, Alzheimer's disease, rheumatoid arthritis and DM), the RRs from CPS-II as used in GBD 2016 were applied for whites, coloureds and Asians.

For historical reasons, black Africans appear to have lower risks due to smoking, so the GBD 2016 RRs for the other conditions were adjusted using the ratio of black African to white RR from updated S&DNSA estimates.[19] The RRs and adjustment factors for black African RRs are set out in Table 1. Meta analyses of RRs for TB mortality due to smoking revealed heterogeneity across populations,[38] whereas a meta-analysis of smoking in relation to community-acquired pneumonia mortality yielded more homogenous results.[39] For this reason, RRs for TB mortality from the S&DNSA data and RRs for infectious respiratory disease from GBD 2016 were used (Table 1).

Following the hybrid method, exposure was measured by the SIR method for conditions that have a long lag from exposure to disease outcome and by current smoking prevalence for other conditions. The estimated SIRs for each population group, sex and age group are shown in Fig. S1 in the appendix (www.samedical.org/file/1841).

Lung cancer

The absolute difference between the observed lung cancer death rate and the level in never/ex-smokers in the CPS-II was used to directly estimate the proportion of lung cancer attributable to smoking (PAF).

COPD, other chronic respiratory diseases and cancers other than lung cancer

The estimated SIRs using never-smoker lung cancer mortality rates from CPS-II and CPS-II RRs were used in the classic PAF formula[25] to calculate attributable burden for 2000, 2006 and 2012 for deaths, premature mortality (years of life lost (YLLs)), years lived with a disability (YLDs) and DALYs, as follows:

$$AB = \sum_j \frac{SIR_j\left(RR^*_j - 1\right)}{SIR_j\left(RR^*_j - 1\right) + 1} \times B_j$$

where RR^*_j is the relative risk and B_j is the estimated burden of disease for age group j. The latest burden of disease estimates for SA for 2000, 2006 and 2012 were used for B_j.

Other conditions

Current smoking prevalences for 2000, 2006 and 2012 were estimated from local nationally representative surveys, and the RRs from CPS-II, with adjustment for black Africans, were used in the classic PAF formula to calculate the attributable burden for 2000, 2006 and 2012 for deaths, YLLs, YLDs and DALYs as follows:

$$AB = \sum_j \frac{P_j\left(RR^*_j - 1\right)}{P_j\left(RR^*_j - 1\right) + 1} \times B_j$$

where P_j is the prevalence, RR_j is the relative risk and B_j is the burden from age group j.

Age-standardised death rates were calculated using alternative SA mid-year population estimates[40] and the WHO standard population.[41]

Uncertainty analysis

We used Monte Carlo simulation modelling to present uncertainty intervals (UIs) around point estimates reflecting the main sources of sampling uncertainty in the calculations using the Ersatz software version 1.35,[43] and normal distribution was specified for smoking prevalence based on

Table 1. Disease outcomes, ICD-10 codes and relative risks by sex and age for estimating smoking attributable burden by method

Disease outcome (group and individual)	ICD-10 codes	RR source	Relative risks: Age group, years	Male RR	Male LL	Male UL	Male SE	Female RR	Female LL	Female UL	Female SE	Black African male RR	Black African male Adjustment	Black African female RR	Black African female Adjustment
SIR method															
Mouth, oropharynx and larynx cancers	C00-C14, C32	Kontis *et al.*, 2014;[30] GBD 2013[31]	All	8.10	5.70	11.70	0.18	6.00	4.30	8.50	0.17	-	-	-	-
Oesophagus cancer	C15	GBD 2016[23]	All	6.68	3.92	10.00	0.24	6.36	4.40	8.79	0.18	-	-	-	-
Stomach cancer	C16	-	All	1.93	1.41	2.50	0.15	1.57	1.23	1.95	0.12	-	-	-	-
Colorectal cancer	C18-C21	-	All	1.33	1.20	1.50	0.06	1.42	1.30	1.60	0.05	-	-	-	-
Liver cancer	C22	-	All	2.54	1.62	3.73	0.21	1.72	1.22	2.25	0.16	-	-	-	-
Pancreas cancer	C25	-	All	2.51	1.99	3.06	0.11	2.10	1.85	2.37	0.06	-	-	-	-
Lung cancer	C33-C34	-	All	22.51	18.90	26.80	0.09	14.10	13.00	15.30	0.04	-	-	-	-
Breast cancer	C50	-	All	1.29	1.08	1.55	0.09	1.29	1.08	1.55	0.09	-	-	-	-
Cervix cancer	C53	-	All	-	-	-	-	1.68	1.19	2.25	0.16	-	-	-	-
Prostate cancer	C61	-	All	1.24	1.17	1.31	0.03	-	-	-	-	-	-	-	-
Kidney cancer	C64-C66, C68	-	All	2.29	1.64	3.06	0.16	1.52	1.18	1.87	0.12	-	-	-	-
Bladder cancer	C67	-	All	3.33	2.35	4.51	0.17	2.58	1.87	3.40	0.15	-	-	-	-
Leukaemia	C91-C95	-	All	2.01	1.32	2.83	0.19	1.16	0.89	1.49	0.13	-	-	-	-
Chronic obstructive pulmonary disease	J40-J44, J47	-	All	11.55	9.01	14.40	0.12	15.26	13.60	17.10	0.06	-	-	-	-
Other chronic respiratory diseases	J30-J35, J37-J39, J66-J68, J70, J82, J91-J92, J95, J98, J99	-	All	2.08	1.76	2.46	0.09	1.98	1.79	2.18	0.05	-	-	-	-
Smoking prevalence method															
Asthma	J45-46	GBD 2016[23]	All	2.10	1.76	2.46	0.09	1.98	1.79	2.18	0.05	-	-	-	-
Tuberculosis black African	A15-A19, B90, U51, U52	S&DNSA[19]	All	1.22	1.20	1.25	0.01	1.21	1.17	1.26	0.02	-	-	-	-
Tuberculosis Asian				1.61	1.33	1.95	0.10	2.02	1.42	2.86	0.18	-	-	-	-
Tuberculosis coloured				1.84	1.64	2.07	0.06	1.92	1.70	2.16	0.06	-	-	-	-
Tuberculosis white				1.97	1.63	2.38	0.10	2.16	1.63	2.87	0.14	-	-	-	-
Lower respiratory infections	J09-J18, J20-J22, P23>6 yrs, J86	Baskaran *et al.*, 2019[32]	All	2.17	1.70	2.76	0.12	2.17	1.70	2.76	0.12	1.69	0.779	1.48	0.681
Ischaemic heart disease	I20-I25	GBD 2016[23]	35 - 44	3.75	3.31	5.16	0.11	5.16	4.16	7.55	0.15	2.88	0.769	2.54	0.493
			45 - 59	2.96	2.35	2.94	0.06	3.86	2.83	3.57	0.06	2.28	0.769	1.90	0.493
			60 - 69	2.33	1.69	2.01	0.04	2.87	2.41	2.80	0.04	1.79	0.769	1.41	0.493
			70 - 79	1.93	1.22	1.54	0.06	2.27	1.72	1.99	0.04	1.48	0.769	1.12	0.493
			≥80	1.60	0.88	1.68	0.16	1.79	1.17	1.53	0.07	1.23	0.769	1.00	0.493

(continued)

Table 1. (continued) Disease outcomes, ICD-10 codes and relative risks by sex and age for estimating smoking attributable burden by method

Disease outcome			Relative risks													
			Age group,	Male				Female				Black African male		Black African female	
(group and individual)	ICD-10 codes	RR source	years	RR	LL	UL	SE	RR	LL	UL	SE	RR	Adjustment	RR	Adjustment
Stroke	I60-I69, G81	GBD 2016[23] (Asian, coloured, white)	35-44	3.64	1.94	6.86	0.32	5.06	3.01	6.40	0.19	1.00	-	1.00	-
			45-59	2.89	2.10	4.04	0.17	3.79	2.75	4.15	0.10	1.00	-	1.00	-
		S&DNSA[19] (black African only)	60-69	2.29	1.61	2.50	0.11	2.83	2.50	3.25	0.07	1.00	-	1.00	-
			70-79	1.90	1.31	2.01	0.11	2.25	1.54	1.95	0.06	1.00	-	1.00	-
			≥80	1.58	0.41	1.51	0.33	1.78	0.84	1.30	0.11	1.00	-	1.00	-
Hypertensive heart disease	I11	GBD 2016[23] (Asian, coloured, white); S&DNSA[19] (black African only)]	35-44	3.62	1.60	3.10	0.17	3.57	1.21	2.32	0.17	1.93	0.533	1.81	0.506
			45-59	2.88	2.18	3.20	0.10	2.83	2.26	3.22	0.09	1.53	0.533	1.43	0.506
			60-69	2.28	1.96	2.63	0.08	2.25	2.71	3.51	0.07	1.22	0.533	1.14	0.506
			70-79	1.90	1.77	2.51	0.09	1.87	2.07	2.67	0.06	1.01	0.533	1.00	0.506
			≥80	1.58	0.77	1.85	0.22	1.56	1.07	1.76	0.13	1.00	0.533	1.00	0.506
Other cardiovascular and circulatory diseases	I27, I28, I30-I31, I34-I37, I44-I45, I47, I72, I77, I78, I80, I82-I84, I86-I89, I95-I98	GBD 2016[23] (Asian, coloured, white); S&DNSA[19] (black African only)	35-44	3.62	1.60	3.10	0.17	3.57	1.21	2.32	0.17	2.67	0.737	2.29	0.640
			45-59	2.88	2.18	3.20	0.10	2.83	2.26	3.22	0.09	2.12	0.737	1.81	0.640
			60-69	2.28	1.96	2.63	0.08	2.25	2.71	3.51	0.07	1.68	0.737	1.44	0.640
			70-79	1.90	1.77	2.51	0.09	1.87	2.07	2.67	0.06	1.40	0.737	1.20	0.640
			≥80	1.58	0.77	1.85	0.22	1.56	1.07	1.76	0.13	1.16	0.737	1.00	0.640
Peptic ulcer	K25-K28, K31	GBD 2016[23]	All	2.04	1.68	2.48	0.10	2.04	1.68	2.48	0.10				
Gallbladder and biliary tract disease	K80-K83		All	1.19	1.11	1.29	0.04	1.19	1.12	1.26	0.03				
Alzheimer's disease	F00-F03, G30-G31		All	1.41	1.11	1.74	0.11	1.40	1.13	1.18	0.01				
Multiple sclerosis	G35		All	1.57	1.27	1.91	0.10	1.57	1.28	1.90	0.10				
Diabetes mellitus	E10-E14		All	1.42	1.10	1.83	0.13	1.10	0.95	1.28	0.08				
Rheumatoid arthritis	M05-M06, M08		All	1.38	1.14	1.65	0.09	1.38	1.14	1.65	0.09				

RR = relative risk; LL = lower 95% confidence limit; UL= upper 95% confidence limit; SE = standard error; GBD = Global Burden of Diseases, Injuries and Risk Factors study; S&DNSA = Smoking and Death Notification South Africa study.

standard errors from the meta-regression analysis of 16 surveys. We used the Ersatz function ErRelativeRisk for the RR variables. Standard errors were derived from the published 95% confidence intervals (CIs). We modelled the uncertainty around the CPS-II smoker and non-smoker lung cancer mortality rates using a gamma distribution. For the output variables (attributable burden and attributable burden as a percentage of total burden in SA), 95% CIs were calculated bounded by the 2.5th and 97.5th percentiles of the 2000 iterative values generated.

Results

Smoking prevalence

Smoking prevalence estimates declined from 25.0% in 1998 to 19.4% in 2012. Male smoking prevalence declined from 40.5% to 31.9%, and females from 10.8% to 7.9%, during the same period. Smoking prevalence estimates for South Africans between 1998 and 2012 are shown by population group and sex in Fig. 2. Smoking prevalence was highest among Asian and coloured males followed by white males, coloured females, black African males, white females, Asian females and black African females. A declining trend was visible between 1998 and 2010, with plateauing after 2010 for all population groups except for Asians (declining trend continuing at a slower rate) and black African females (remained flat throughout).

SIRs by age and population group are shown in Fig. S1 in the appendix (www.samedical.org/file/1841). Coloured males and females had the highest SIR, particularly in the younger age groups.

Population-attributable fractions and attributable burden

The estimated PAFs for grouped conditions included in the study are shown in Table 2 (PAFs and the number of smoking-attributable deaths for single causes can be found in Table S4 in the appendix: www.samedical.org/file/1841). In 2012, lung cancer had the highest attributable fraction (75.8%) followed by chronic respiratory disease (42.0%). Seven percent of TB deaths and 11.5% of LRIs were attributed to tobacco smoking. Overall, the PAFs were three times higher in males than females. PAFs for all causes except chronic respiratory disease showed a declining trend between 2000 and 2012 (Fig. S2 in appendix).

In 2000, smoking caused an estimated 34 739 deaths among those aged ≥35 years. Of these, 25 415 deaths were among males (9.6% of total male deaths of all ages) and 9 324 among females (3.9%

Table 2. Population attributable fractions and burden attributable to smoking in males and females by disease categories in South Africa for 2000, 2006 and 2012

	Males			Female			Persons		
Disease outcome	**AF (%)**	**Deaths**	**DALYs**	**AF (%)**	**Deaths**	**DALYs**	**AF (%)**	**Deaths**	**DALYs**
2000									
Cardiovascular disease*	17.1	6 638	138 112	9.1	4 530	77 801	12.6	11 168	215 913
Lung cancer	84.8	3 384	61 342	58.3	909	16 765	77.4	4 294	78 107
Other cancers	33.6	4 298	86 220	8.5	1 054	21 653	21.2	5 352	107 872
Chronic respiratory disease†	50.5	6 022	152 009	24.1	1 889	63 169	40.0	7 911	215 178
Tuberculosis	10.5	2 369	64 838	3.3	289	8 457	8.5	2 658	73 295
Lower respiratory infections	22.2	1 638	28 853	6.6	407	5 491	15.1	2 045	34 343
Digestive diseases‡	26.5	303	7 671	8.5	88	2 656	18.0	391	10 327
Neurological disease§	11.6	78	2 819	7.6	82	1 675	9.1	160	4 494
Diabetes mellitus	14.3	648	14 968	0.9	64	1 398	6.1	712	16 366
Rheumatoid arthritis	13.0	36	6 533	3.6	12	1 481	7.9	48	8 014
Total attributable burden	-	**25 415**	**563 365**	-	**9 324**	**200 545**	-	**34 739**	**763 910**
95% UI	-	(22 130 - 28 033)	(502 680 - 609 232)	-	(8 848 - 9 674)	(191 975 - 206 668)	-	(33 173 - 35 714)	(701 571 - 807 339)
% of total deaths in adults ≥35 years	-	**24.4**	**26.4**	-	**9.7**	**10.6**	-	**17.3**	**19.0**
95% UI	-	(21.3 - 26.9)	(23.5 - 28.5)	-	(9.2 - 10.1)	(10.2 - 10.9)	-	(15.6 - 18.6)	(17.4 - 20.1)
% of total deaths all ages	-	**9.6**	**5.8**	-	**3.9**	**2.1**	-	**6.9**	**4.0**
95% UI	-	(8.4 - 10.6)	(5.2 - 6.3)	-	(3.7 - 4.1)	(2.0 - 2.2)	-	(6.2 - 7.4)	(3.7 - 4.2)
2006									
Cardiovascular disease*	15.7	6 740	141 518	4.9	2 762	54 018	9.5	9 502	195 536
Lung cancer	83.1	3 244	56 824	62.4	1 155	19 859	76.4	4 399	76 683
Other cancers	28.2	3 612	69 594	8.3	1 110	20 004	18.0	4 722	89 598
Chronic respiratory disease†	48.2	6 011	159 250	25.0	2 155	66 035	38.7	8 166	225 285
Tuberculosis	9.6	2 133	56 784	2.9	248	7 647	7.7	2 381	64 431
Lower respiratory infections	20.0	1 654	28 169	4.1	308	3 671	12.4	1 962	31 840
Digestive diseases‡	23.1	309	7 831	5.4	79	2 508	13.9	387	10 339
Neurological disease§	10.0	76	2 170	3.9	55	1 450	6.1	131	3 620
Diabetes mellitus	12.8	790	18 001	0.6	59	1 394	5.3	848	19 395
Rheumatoid arthritis	11.1	11	2 003	2.9	6	850	5.6	17	2 853
Total attributable burden	-	**24 578**	**542 144**	-	**7 937**	**177 435**	-	**32 515**	**719 580**
95% UI	-	(22 954 - 25 657)	(509 648 - 563 194)	-	(7 636 - 8.176)	(171 754 - 181 760)	-	(30 883 - 33 550)	(686 404 - 740 058)
% of total deaths in adults ≥35 years	-	**22.1**	**24.6**	-	**7.2**	**8.4**	-	**14.7**	**16.6**
95% UI	-	(20.7 - 23.1)	(23.1 - 25.5)	-	(7.0 - 7.4)	(8.1 - 8.4)	-	(14.0 - 15.2)	(15.9 - 17.1)
% of total deaths (all ages)	-	**7.2**	**4.4**	-	**2.4**	**1.3**	-	**4.8**	**2.8**
95% UI	-	(6.7 - 7.5)	(4.1 - 4.4)	-	(2.3 - 2.4)	(1.3 - 1.4)	-	(4.6 - 5.0)	2.7 - 2.9)

(continued)

Table 2. (continued) Population attributable fractions and burden attributable to smoking in males and females by disease categories in South Africa for 2000, 2006 and 2012

	Males			Female			Persons		
Disease outcome	**AF (%)**	**Deaths**	**DALYs**	**AF (%)**	**Deaths**	**DALYs**	**AF (%)**	**Deaths**	**DALYs**
2012									
Cardiovascular disease*	2012	5 704	121 830	4.5	2 434	48 651	8.7	8 138	170 481
Lung cancer	84.0	3 736	63 283	58.0	1 187	19 940	75.8	4 923	83 224
Other cancers	26.7	3 681	66 949	7.7	1 123	21 272	16.9	4 804	88 221
Chronic respiratory disease†	50.9	5 389	158 560	29.3	2 163	105 478	42.0	7 552	264 038
Tuberculosis	9.1	2 078	59 208	2.7	248	9 113	7.2	2 326	68 321
Lower respiratory infections	18.8	1 651	28 790	3.7	299	3 815	11.5	1 950	32 605
Digestive diseases‡	21.5	280	6 932	4.4	68	2 513	12.2	348	9 445
Neurological diseases§	8.9	74	1 920	3.5	50	1 098	5.5	124	3 018
Diabetes mellitus	11.8	844	20 672	0.5	59	1 763	4.9	902	22 435
Rheumatoid arthritis	10.6	7	1 426	2.9	4	783	5.2	11	2 209
Total attributable burden	-	**23 444**	**529 572**	-	**7 634**	**214 425**	-	**31 078**	**743 997**
95% UI	-	(22 005 - 24 571)	(499 902 - 551 860)	-	(7 356 - 7 871)	(208 355 - 219 233)	-	(29 545 - 32 217)	(712 620 - 766 411)
% of total deaths in adults ≥35 years	-	**21.3**	**23.3**	-	**7.0**	**9.4**	-	**14.2**	**16.3**
95% UI	-	(20.0 - 22.3)	(22.0 - 24.2)	-	(6.7 - 7.2)	(9.1 - 9.6)	-	(13.5 - 14.7)	(15.6 - 16.8)
% of total deaths (all ages)	-	**8.5**	**5.2**	-	**3.0**	**2.0**	-	**5.9**	**3.6**
95% UI	-	(8.0 - 8.9)	(4.9 - 5.4)	-	(2.9 - 3.1)	(2.0 - 2.1)	-	(5.6 - 6.1)	(3.4 - 3.7)

AF = attributable burden; UI = uncertainty interval.
*Cardiovascular disease includes ischaemic heart disease, stroke, hypertensive heart disease and other cardiovascular conditions.
†Chronic respiratory disease includes COPD, other chronic respiratory diseases and asthma.
‡Digestive diseases include peptic ulcer and gallbladder and biliary diseases.
§Neurological diseases include Alzheimer's disease and multiple sclerosis.

of total female deaths of all ages). This declined in 2012 to 31 078 or 6.9% of total deaths (all ages) or 17.3% of the total deaths in adults ≥35 years. Of these, 23 444 (8.5%) deaths were among males and 7 634 (3.0%) among females. The 95% UIs are presented in Table 2.

In 2012, the proportion of DALYs attributable to smoking was lower (5.2% for males and 2.0% for females) than for deaths, as most deaths attributable to smoking occur in middle and old age. Overall, cardiovascular deaths (8 138) accounted for the majority of smoking-attributable deaths, followed by chronic respiratory disease including asthma (7 552), lung cancer (4 923), other cancers (4 802), TB (2 326) and LRIs (1 950) (Table 2).

The top 10 individual causes of smoking-attributable deaths for adult males and females aged ≥35 years are shown in Fig. 3. COPD accounted for the majority of deaths (6 373), followed by lung cancer (4 923), IHD (4 216), TB (2 326) and LRIs (1 950).

The relative proportions of smoking-attributable deaths by major cause in 2012 are shown in Fig. 4 for each population group. While the leading cause of death attributed to smoking is COPD, followed by cardiovascular diseases, there are at least two epidemiological patterns evident, illustrated by differences in infectious respiratory disease. Among black Africans, TB and infectious respiratory disease comprise 21.0% of smoking-attributed deaths, compared with only 4.3% among whites. Lung cancer, on the other hand, comprised 12.5% of all deaths in black Africans v. 17.7% - 19.9% in the other groups, reflecting the longer and more intense smoking history of the latter groups. The relative proportions of smoking-attributable deaths in 2012 by major cause are shown by sex for each population group in Fig. S3 in the appendix (www.samedical.org/file/1841).

Smoking-attributable deaths by age

At all ages there were significantly more deaths among males than females (Fig. 5). Smoking-attributable deaths peaked in the 45 - 59-year age group, in line with the historically high smoking prevalence in those age groups. A decline in PAFs between 2000 and 2012 in younger populations is encouraging and suggests a current cohort effect of prior reductions in smoking prevalence.

Age-standardised smoking-attributable mortality rates (ASDR) varied markedly by population group and sex (Fig. 6). Coloured males had the highest ASDR, followed by Asian males and coloured females, black African males and then white males. White female ASDR smoking-attributable rates were about half those of coloured females. In comparison, rates for black African and Asian females were low. Smoking-attributable burden decreased in all population and sex groups between 2000 and 2012.

Discussion

Smoking prevalence declined from 25% to 19.4% between 1998 and 2012. Similarly, smoking-attributable deaths declined from 34 739 (6.9%) in 2000 to 31 078 (5.9%) in 2012. Despite gains in tobacco control in SA, smoking prevalence and smoking-attributable burden remain high. In addition, rates of decline in smoking

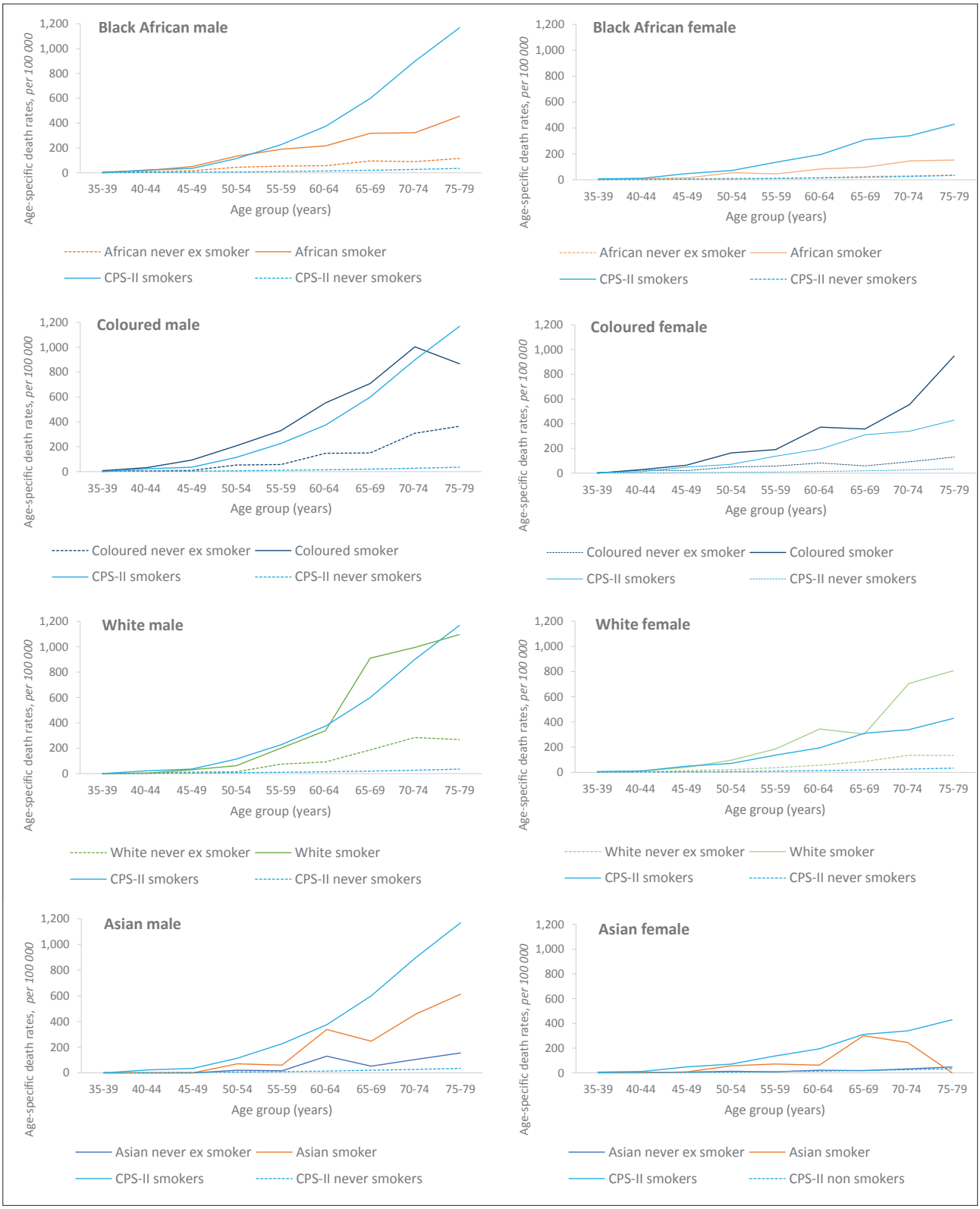

Fig. 1. South African smoker and never/ex-smoker lung cancer mortality rates compared with Cancer Prevention Study II (CPS-II) smokers and never-smokers by population group and sex.[20]

prevalence plateaued between 2010 and 2012, suggesting that tobacco control measures need review and strengthening.

In refining national 'working' estimates of deaths attributed to smoking, we took account of absolute risks calculated from locally available data on the S&DNSA death notification forms in SA smokers in comparison with the CPS-II data. While absolute risks for white, coloured and Asian populations were similar to CPS-II, data from black African populations were markedly different. Lower smoking risks in black African populations are a likely consequence of historically low smoking prevalence among black African women, and among black

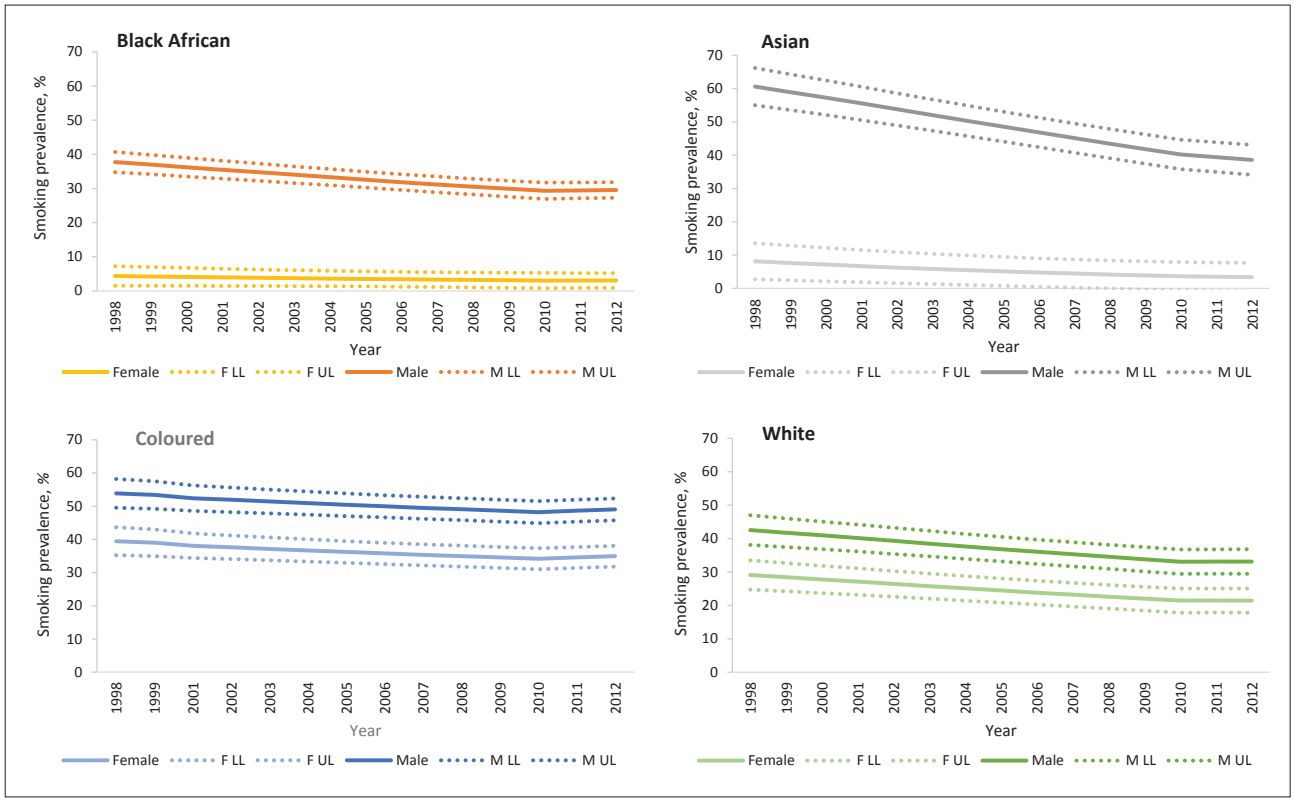

Fig. 2. Smoking prevalence based on pooled meta-regression analysis of 15 national surveys by population group and sex, South Africa 1998 - 2012. (F = female; M = male; LL = lower 95% confidence interval; UL = upper 95% confidence interval.)

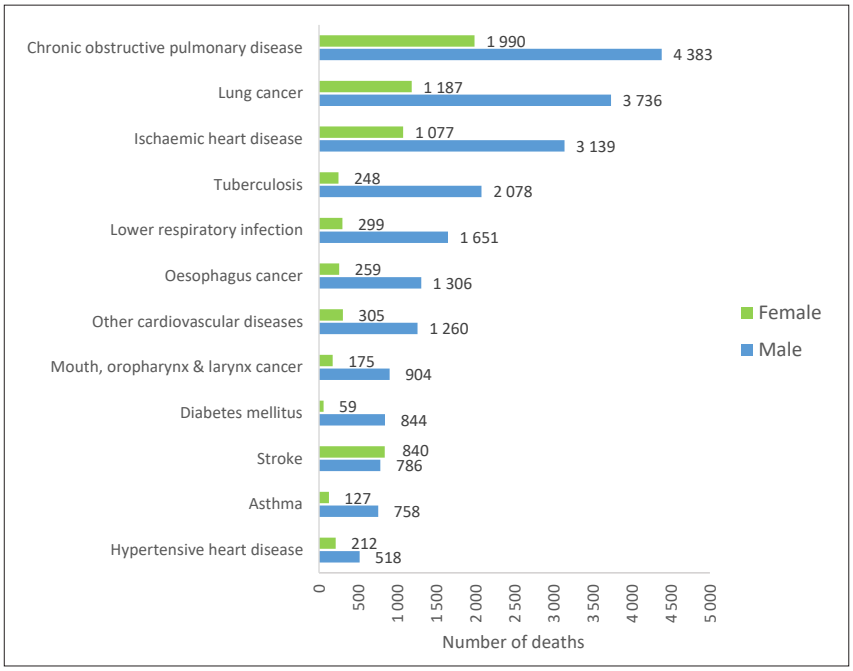

Fig. 3. Top 10 causes of smoking-attributable deaths by sex (age ≥35 years) in South Africa for 2012. Twelve causes shown to encompass top 10 for males and females separately.

African men, historically lower smoking prevalence, lower amounts smoked and later age of initiation than other groups. In view of this, RRs for LRIs, IHD, hypertensive heart disease and other cardiovascular diseases for black Africans were adjusted downwards.

With the understanding that RRs on smoking and deaths derived from the S&DNSA study are attenuated (but with no evidence of systematic biases), we retained some of these to inform risks for diseases for which there is large international heterogeneity in risks. This was particularly the case for TB, where the background incidence and mortality from the disease is high, and RRs from international studies are very heterogeneous. The PAFs calculated here are thus higher than reported in the S&DNSA study but more realistic, and the rankings of causes of deaths remained broadly similar, aside from a reduction of the relative effect of TB and infectious respiratory disease (see later) and stroke. Peculiarly, possibly due to differences in diet, the S&DNSA and a systematic review in sub-Saharan Africa found no association between smoking and stroke in black African populations,[19,42] so we set RRs for black Africans to 1.0. This apparent variation from the international norm is worthy of further investigation.

These refinements to the RRs for black Africans account for the lower number of smoking-attributable deaths estimated for 2000 (34 739) in this study v. 44 000 in SACRA1. Using a standard estimation technique for 2000, 2006 and 2012 we have documented a 7.8% relative decline in smoking-attributed deaths in males and an 18.1% decline in females, so long-term investment into tobacco control appears to show positive results. However, we note that smoking prevalence has plateaued since 2010. It is worth noting that the PAFs in SA

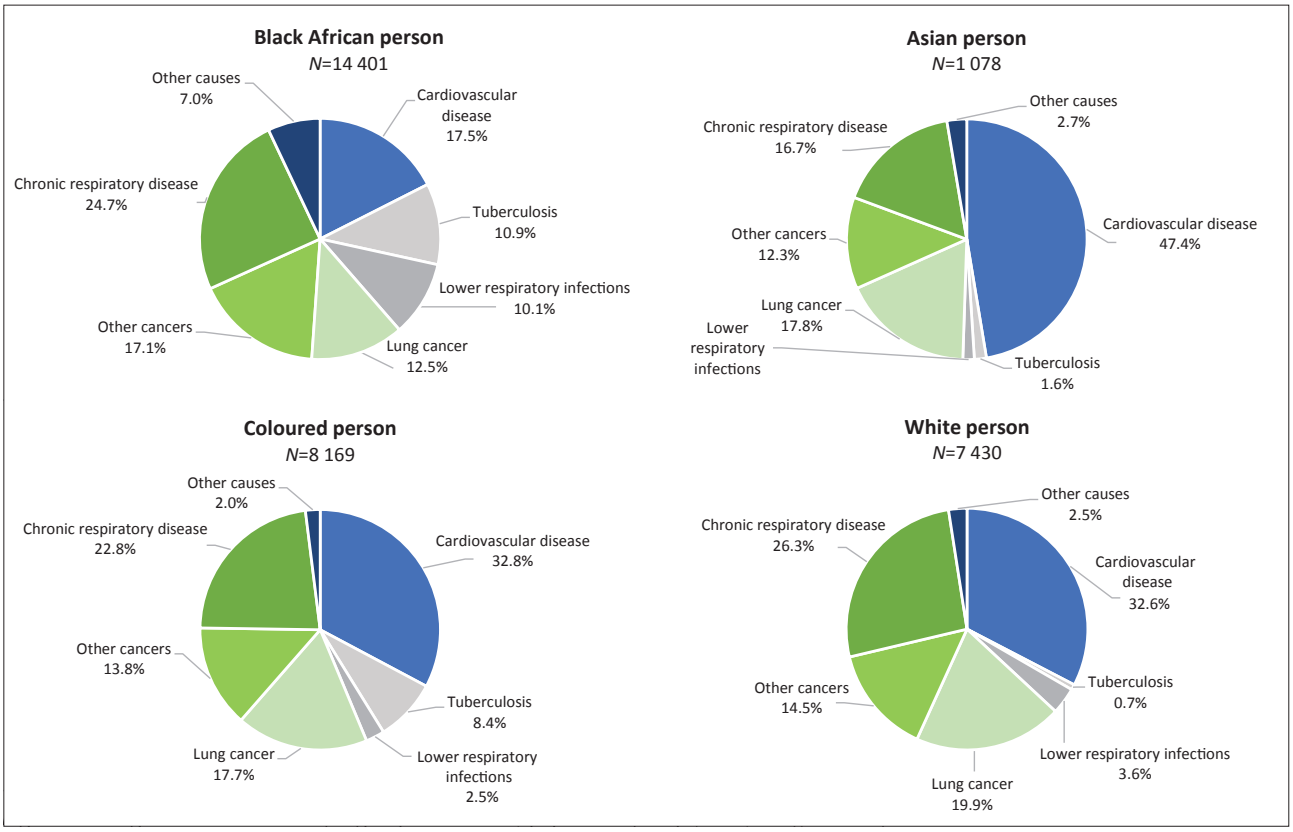

Fig. 4. Smoking-attributable deaths for grouped causes by population group (≥35 years), South Africa 2012.

are lower than the worldwide average estimate of 15%.[4] This is likely to be because the worldwide estimate is dominated by data from high-income countries where smoking peaked after World War II and the 1960s.[43] With such high smoking prevalence, especially in males, it is therefore possible that the future effects of these current smoking patterns may increase if young generations with heavier consumption of tobacco replace the older generations with lower consumption.

The distribution of major causes of deaths attributed to smoking clearly shows at least two epidemiological patterns, a well-described middle- to high-income pattern observed in developed countries,[43] illustrated among whites and Asians where chronic diseases (IHD, COPD and lung cancer) are the predominant causes of death from smoking, and a less described middle- to low-income pattern, illustrated among coloureds and black Africans where the contribution of infectious respiratory diseases is significant. The coloured population has been highlighted previously as a population at risk, with smoking prevalence estimates exceeding 40% and showing the highest population-attributed mortality rates (Fig. 6).[19]

While deaths from chronic disease rank high in importance in all population groups, the proportion of deaths due to infectious respiratory disease (mainly TB and LRIs) has been underappreciated in tobacco control, despite clear causal relationships documented by US Surgeon General reports.[3] The contrast of smoking-attributed proportions of deaths due to infectious respiratory disease of 21.0% in black Africans v. 4.3% in whites (with the proportion for coloureds being in the middle at 10.9%) is remarkable, and reflects the persistent historical socioeconomic differences between SA's population groups (Fig. 4).

It is also important to conduct research to identify groups using more modern population classifications that are least responsive to current interventions, and to co-design more targeted campaigns. It is worth noting that (using such crude population groupings) smoking rates for so-called black African and Asian females have remained historically low, and both groups have benefited from low rates of smoking-attributed disease. Setting such low rates as a target for all population groups and genders (or plausibly even lower rates) would be a desirable outcome in tobacco control.

The COVID-19 pandemic has increased scientific appreciation of the potential role that smoking has on infectious respiratory diseases. There is emerging evidence of the role smoking may play in increasing COVID-19 infection, transmission,[44] worsening of clinical symptoms[45] and death[46] in those infected, and the role smoking reductions can play in the prevention of future respiratory infections.[47,48] While much of the educational messaging around smoking focuses on the risk of developing chronic disease, consideration should be given to broadening the message to include infectious respiratory disease. Brief interventions motivating smokers on TB daily observed treatment (DOT) programmes to quit could be implemented quite easily.

The attributable fractions are likely to be a minimal estimate because they exclude conditions for which there may be confounding or reverse causation, such as HIV/AIDS, mental and behavioural conditions, cirrhosis and injuries. Smoking rates in such groups (e.g. in people living with HIV (PLWH)) are high.[49] The crude RR between smoking and mortality from these 'excluded' conditions in males was 1.32 (95% CI 1.29 - 1.35).[19] Even assuming smoking has little to no effect, it can certainly exacerbate the outcomes of people with these conditions. For example, hospitalised HIV/AIDS patients would be expected to have total mortality risks that would be related to that condition, multiplied by the risks of smoking.[50] In the USA, PLWH have poorer smoking-associated outcomes than HIV-related outcomes,[51] and international studies of PLWH who quit smoking show beneficial reductions in smoking-related cancer and cardiovascular disease mortality.[52,53] Hence smoking cessation should be encouraged in all

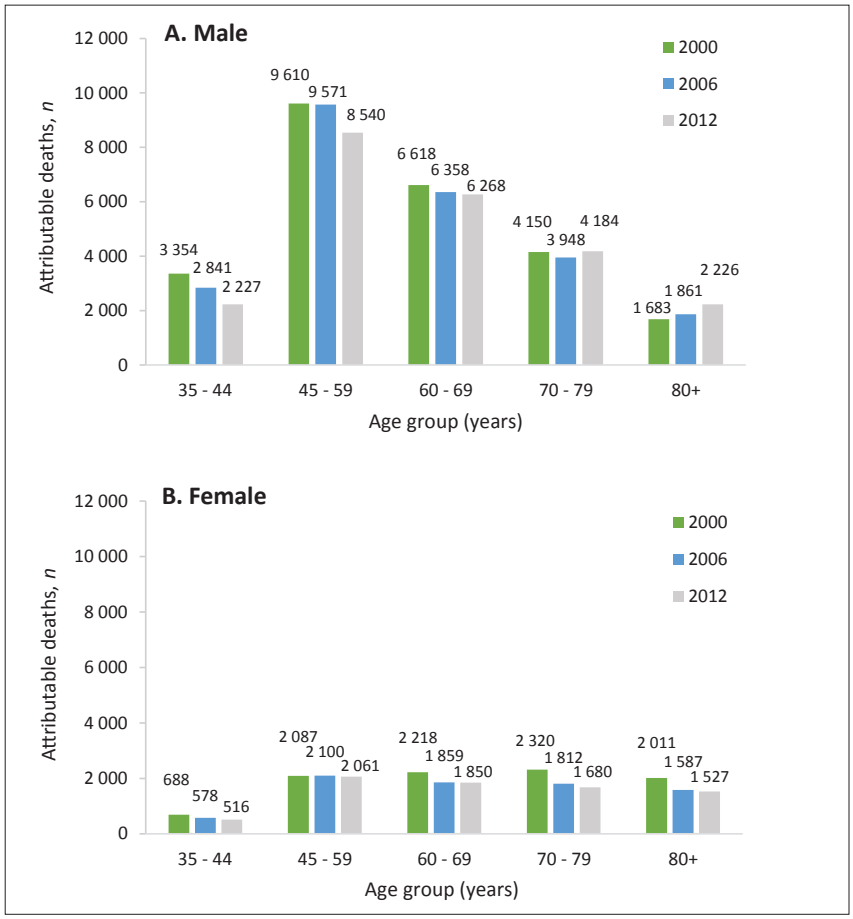

Fig. 5. Smoking-attributable deaths by sex and age group in South Africa for 2000, 2006 and 2012.

hospital discharge settings, as hospitalised patients (for any condition) may be amenable to quitting. In SA, for example, 89.3% of smokers in HIV/TB clinics were motivated to quit,[54] and such interventions are proven to be effective.[55]

The most effective tobacco control policy to decrease smoking prevalence is to increase excise taxes.[56] Excise tax increases have successfully been used, both in SA and globally, to reduce smoking prevalence.[57,58] Smoking prevalence decreases that occurred in the 1990s and 2000s are attributed mainly to increases in the retail price of cigarettes, driven by increases in the excise tax and tobacco industry prices.[59] The largest excise tax growth occurred between 1995 and 2011, when the real excise tax increased at an average rate of 9.7% per year, but it slowed markedly to 1% per year between 2011 and 2017.[59] An increase in excise taxation needs urgent consideration. However, given that illicit trade in cigarettes increased from ~5% to 30% between 2009 and 2017,[60] stricter controls of illicit trade are also required. The SA Revenue Service should implement a track and trace system to improve tax compliance, which may reduce the availability of cheap cigarettes.

Much could be done in the meanwhile to streamline research and monitoring by using more standardised questions to measure the

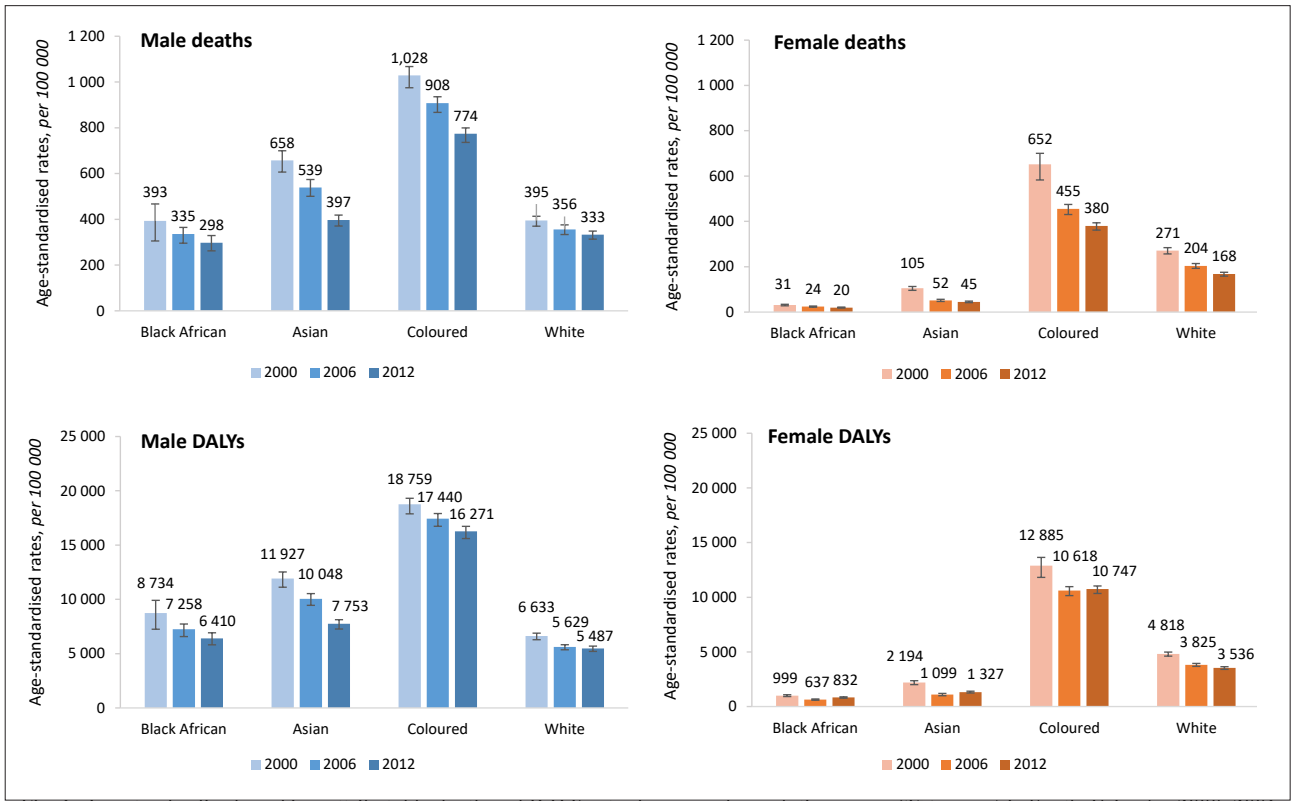

Fig. 6. Age-standardised smoking-attributable death and disability-adjusted life-year (DALY) rates by sex and population group (≥35 years) in South Africa for 2000, 2006 and 2012.

prevalence of smoking and modifying the death notification forms to discern never-smokers from former smokers. In this way the current working estimates of smoking-attributed mortality can be further refined to measure the impact of the tobacco epidemic in SA.

Conclusions

Deaths attributable to smoking decreased from 34 739 in 2000 to 31 078 in 2012, but smoking remained a leading cause of attributable deaths in 2012. Multi-institutional efforts are needed to reduce smoking prevalence to maintain and improve the early successes in tobacco control and reduce these avoidable deaths.

Disclaimer. The population group classification 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 as it has important correlates of lifestyle, culture and socioeconomic conditions that impact on health and health-related behaviours. The authors do not subscribe to this classification for another purpose.

Declaration. None.

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Author contributions. Conceived and designed the study: PG, RP, FS and DB. Provided input on risk exposure: CJvR, RL, DB, SM, OA, BN, JJ, PG, FS, NV, ET, DL and OA-O. Provided input on the burden of disease estimates: VPvW, RR, NA and IN. Analysed data: PG and RP. Checked the worksheets: VPvW, IN, NA, ET, BN and OA. Reviewed results: FS and DB. Drafted manuscript: PG, RP and FS. 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. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2019: Offer Help to Quit Tobacco. Geneva: WHO, 2019.
2. World Health Organization. The Global Status Report on Non-communicable Diseases 2014. Attaining the nine global non-communicable diseases targets; a shared responsibility. Geneva: WHO, 2014.
3. US Department of Health and Human Services. The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004.
4. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2020. http://ghdx.healthdata.org/gbd-results-tool (accessed 25 March 2021).
5. Levy DT, Tam J, Kuo C, Fong GT, Chaloupka F. The impact of implementing tobacco control policies: The 2017 Tobacco Control Policy Scorecard. J Pub Health Management Practice: 2018;24(5):448-457. https://doi/org/10.1097/PHH.0000000000000780
6. Levy DT, Ellis JA, Mays D, Huang AT. Smoking-related deaths averted due to three years of policy progress. Bull World Health Organ 2013;91(7):509-518. https://doi.org/10.2471/BLT.12.113878
7. World Health Organization. WHO Framework Convention on Tobacco Control. Article 8(2). https://www.who.int/fctc/text_download/en (accessed 25 March 2021).
8. Van Walbeek CP. Tobacco excise taxation in South Africa. Published report for the Tobacco Free Initiative of the World Health Organization. Report WHO/NMH/TFI/FTC/03.4. Geneva: WHO, 2003.
9. Van Walbeek CP. Recent trends in smoking prevalence in South Africa – some evidence from AMPS data. S Afr Med J 2002;92(6):462-468.
10. Swart D, Reddy P, Ruiter RAC, de Vries H. Cigarette use among male and female grade 8 - 10 students of different ethnicity in South African schools. Tob Control 2003;12(1):e1-e1. https://doi.org/10.1136/tc.12.1.e1
11. Reddy SP, James S, Sewpaul R, Koopman F. The 2008 Global Youth Tobacco Survey: The 3rd GYTS in South Africa. Cape Town: South African Medical Research Council, 2010.
12. Reddy P, James S, Sewpaul R, et al. A decade of tobacco control: The South African case of politics, health policy, health promotion and behaviour change. S Afr Med J 2013;103(11):835-840.
13. Shisana O, Labadarios D, SANHANES-1 Team. South African National Health and Nutrition Examination Survey (SANHANES-1). Cape Town: HSRC Press, 2013.
14. Reddy P, Zuma K, Shisana O, Jonas K, Sewpaul R. Prevalence of tobacco use among adults in South Africa: Results from the first South African National Health and Nutrition Examination Survey. S Afr Med J 2015;105(8):648-655. https://doi/org/10.7196/SAMJnew.7932
15. WHO Africa. Tobacco Control. https://www.afro.who.int/health-topics/tobacco-control (accessed 27 August 2021).
16. Groenewald P, Nojilana B, Janse van Rensburg C, et al. The impact of tobacco control policy interventions on the prevalence of tobacco smoking in South Africa, 1998 - 2017. NCD Symposium, Stellenbosch University, 4 March 2020.
17. Norman R, Bradshaw D, South African Comparative Risk Assessment Collaborating Group. A comparative risk assessment for South Africa in 2000: Towards promoting health and preventing disease. S Afr Med J 2007;97(8):637.
18. Groenewald P, Vos T, South African Comparative Risk Assessment Collaborating Group. Estimating the burden of disease attributable to smoking in South Africa in 2000. S Afr Med J 2007;97(8):674-681.
19. Sitas F, Egger S, Bradshaw D, et al. Differences among the coloured, white, black, and other South African populations in smoking-attributed mortality at ages 35 - 74 years: A case-control study of 481 640 deaths. Lancet 2013;382(9893):685-693. https://doi.org/10.1016/S0140-6736(13)61610-4.
20. Garfinkel L. Selection, follow-up, and analysis in the American Cancer Society prospective studies. Nat Cancer Inst Mongr 1985;67:49-52.
21. 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). https://doi.org/10.1016/S2214-109X(16)30113-9
22. 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
23. GBD 2016 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990 - 2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390(10100):1345-1422. https://doi.org/10.1016/S0140-6736(17)32366-8
24. 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. Erratum in: Lancet 2019;393(10167):132. Erratum in: Lancet 2019;393(10190):e44.
25. Peto R, Lopez AD, Boreham J, Thun M, Heath C Jr. Mortality from tobacco in developed countries: Indirect estimation from national vital statistics. Lancet 1992;339(8804):1268-1278.
26. Pillay van Wyk et al. 2nd Comparative Risk Assessment for South Africa (SACRA2) highlights need to strengthen health promotion and surveillance (in this issue).
27. Janse van Rensburg C, Groenewald P, Awotiwon O, et al. Trends in smoking prevalence in South Africa for 1988 - 2014: Overcoming the challenge of multiple data sources. Tob Induc Dis 2018;16(Suppl 1):A780. https://doi.org/10.18332/tid/84201
28. Pillay-van Wyk V, Roomaney RA, Awotiwon OF, et al. Burden of disease review manager for systematic review of observational studies: Technical report and user guide. Cape Town: South African Medical Research Council, 2018.
29. Ezzati M, Lopez AD. Measuring the accumulated hazards of smoking: Global and regional estimates for 2000. Tob Control 2003;12(1):79-85.
30. Kontis V, Mathers CD, Rehm J, et al. Contribution of six risk factors to achieving the 25×25 non-communicable disease mortality reduction target: A modelling study. Lancet 2014;384(9941):427-437. https://doi.org/10.1016/S0140-6736(14)60616-4
31. GBD 2013 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990 - 2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386(10010):2287-2323. https://doi.org/10.1016/S0140-6736(15)00128-2
32. Baskaran V, Murray RL, Hunter A, Lim WS, McKeever TM. Effect of tobacco smoking on the risk of developing community acquired pneumonia: A systematic review and meta-analysis. PLoS ONE 2019;14(7):e0220204. https://doi.org/10.1371/journal.pone.0220204
33. National Department of Health, Statistics South Africa, South African Medical Research Council and ICF. South Africa Demographic and Health Survey 2016. Pretoria, South Africa, and Rockville, Maryland, USA: NDoH, Stats SA, SAMRC, ICF, 2019.
34. Department of Health, South Africa and Macro International. South Africa Demographic and Health Survey 1998. Pretoria: DoH, 2002.
35. Department of Health, Medical Research Council, ORC Macro. South Africa Demographic and Health Survey 2003. Pretoria: DoH, 2003.
36. Southern Africa Labour and Development Research Unit. National Income Dynamics Study (NIDS) Wave 1, 2008. Version 6.1. Cape Town: Southern Africa Labour and Development Research Unit, 2016. Cape Town: DataFirst, 2016.
37. Southern Africa Labour and Development Research Unit. National Income Dynamics Study Wave 2, 2010 - 2011. Version 3.1. Cape Town: Southern Africa Labour and Development Research Unit, 2016.
38. Southern Africa Labour and Development Research Unit. National Income Dynamics Study Wave 3, 2012 . Version 3.0.0. Pretoria: SA Presidency; Cape Town: Southern Africa Labour and Development Research Unit, 2018. https://doi.org/10.25828/7pgq-q106.
39. Lin HH, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: A systematic review and meta-analysis. PLoS Med 2007;4(1):e20. https//:doi/org/10.1371/journal.pmed.0040020
40. Baskaran V, Murray RL, Hunter A, Lim WS, McKeever TM. Effect of tobacco smoking on the risk of developing community acquired pneumonia: A systematic review and meta-analysis. PLoS ONE 14(7):e0220204. https://doi.org/10.1371/journal.pone.0220204
41. Dorrington R. Alternative South African mid-year estimates, 2013. Cape Town: Centre for Actuarial Research, University of Cape Town, 2013.
42. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL, Lozano R, Inoue M. Age standardisation of rates: A new WHO standard. GPE Discussion Paper Series: No. 31 EIP/GPE/EBD. Geneva: World Health Organization, 2001.
43. Namale G, Kamacooko O, Kinengyere A, et al. Risk factors for hemorrhagic and ischemic stroke in sub-saharan Africa. J Trop Med 2018(2018):11. https://doi.org/10.1155/2018/4650851
44. Thun M, Peto R, Boreham J, Lopez AD. Stages of the cigarette epidemic on entering its second century. Tob Control 2012;21(2):96-101. https://doi.org/10.1136/tobaccocontrol-2011-050294
45. Gaiha SM, Cheng J, Halpern-Felsher B. Association between youth smoking, electronic cigarette use, and coronavirus disease 2019. J Adolesc Health 2020;67(4):519-523. https://doi.org/10.1016/j.jadohealth.2020.07.002

46. Li X, Zhong X, Wang Y, Zeng X, Luo T, Liu Q. Clinical determinants of the severity of COVID-19: A systematic review and meta-analysis. PLoS One 2021;16(5):e0250602. https://doi.org/10.1371/journal.pone.0250602
47. Xiang G, Xie L, Chen Z, et al. Clinical risk factors for mortality of hospitalised patients with COVID-19: Systematic review and meta-analysis. Ann Palliat Med 2021;10(3):2723-2735. https://doi.org/10.21037/apm-20-1278
48. Sitas F, Harris-Roxas B, Bradshaw D, Lopez A. Smoking and epidemics of respiratory infections. Bull WHO 2021;99(2):164-165. https://doi.org/10/2471/BLT.20.273052
49. World Health Organization. Smoking and COVID 19 scientific briefing. 30 June 2020. https://apps.who.int/iris/handle/10665/332895 (accessed 18 May 2022).
50. Mdege ND, Shah S, Ayo-Yusuf OA, Hakim J, Siddiqi K. Tobacco use among people living with HIV: Analysis of data from demographic and health surveys from 28 low-income and middle-income countries. Lancet Glob Health 2017;5(6):e578-e592. https://doi.org/10.1016/S2214-109X(17)30170-5
51. Reddy KP, Parker RA, Losina E, et al. Impact of cigarette smoking and smoking cessation on life expectancy among people with HIV: A US-based modeling study. J Infect Dis 2016;214(11):1672-1681. https://doi.org/10.1093/infdis/jiw430
52. Ashare RL, Bernstein SL, Schnoll R, et al. The United States National Cancer Institute's coordinated research effort on tobacco use as a major cause of morbidity and mortality among people with HIV. Nicotine Tob Res 2021;23(2):407-410. https://doi.org/10.1093/ntr/ntaa155
53. Shepherd L, Ryom L, Law M, et al. Data collection on adverse events of anti-HIV drugs (D:A:D) Study Group. Cessation of cigarette smoking and the impact on cancer incidence in human immunodeficiency virus-infected persons: The data collection on adverse events of anti-HIV drugs study. Clin Infect Dis 2019;68(4):650-657. https://doi.org/10.1093/cid/ciy508
54. Petoumenos K, Worm S, Reiss P, et al.; D:A:D Study Group. Rates of cardiovascular disease following smoking cessation in patients with HIV infection: Results from the D:A:D study. HIV Med 2011;12(7):412-421. https://doi.org/10.1111/j.1468-1293.2010.00901.x
55. Louwagie GM, Ayo-Yusuf OA. Tobacco use patterns in tuberculosis patients with high rates of human immunodeficiency virus co-infection in South Africa. BMC Public Health 2013;13(1):1031. https://doi.org/10.1186/1471-2458-13-1031
56. Pool ER, Dogar O, Lindsay RP, Weatherburn P, Siddiqi K. Interventions for tobacco use cessation in people living with HIV and AIDS. Cochrane Database Syst Rev 2016;13(6):CD011120. https://doi.org/10.1002/14651858.CD011120.pub2
57. International Agency for Research on Cancer. 2011. IARC Handbooks of Cancer Prevention, Tobacco Control, Volume 14: Effectiveness of Tobacco Tax and Price Policies for Tobacco Control. Lyon, France: IARC, 2011.
58. Chelwa, G, Van Walbeek, C, Blecher, E. Evaluating South Africa's tobacco control policy using a synthetic control method. Tob Control 2016; 26(5). https://doi.org/10.1136/tobaccocontrol-2016-053011
59. US National Cancer Institute and World Health Organization. The Economics of Tobacco and Tobacco Control. National Cancer Institute Tobacco Control Monograph 21. NIH Publication No. 16-CA-8029A. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, National Cancer Institute; Geneva, CH: World Health Organization, 2016.
60. Vellios N, Ross H, van Walbeek C. Illicit cigarette trade in South Africa: 2002 - 2017. Tob Control 2019;29(4). https://doi.org/10.1136/tobaccocontrol-2018-054798

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