Second Comparative Risk Assessment for South Africa (SACRA2) highlights need for health promotion and strengthened surveillance

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Background. South Africa (SA) faces multiple health challenges. Quantifying the contribution of modifiable risk factors can be used to identify and prioritise areas of concern for population health and opportunities for health promotion and disease prevention interventions.
Objective. To estimate the attributable burden of 18 modifiable risk factors for 2000, 2006 and 2012.
Methods. Comparative risk assessment (CRA), a standardised and systematic approach, was used to estimate the attributable burden of 18 risk factors. Risk exposure estimates were sourced from local data, and meta-regressions were used to model the parameters, depending on the availability of data. Risk-outcome pairs meeting the criteria for convincing or probable evidence were assessed using relative risks against a theoretical minimum risk exposure level to calculate either a potential impact fraction or population attributable fraction (PAF). Relative risks were sourced from the Global Burden of Disease, Injuries, and Risk Factors (GBD) study as well as published cohort and intervention studies. Attributable burden was calculated for each risk factor for 2000, 2006 and 2012 by applying the PAF to estimates of deaths and years of life lost from the Second South African National Burden of Disease Study (SANBD2). Uncertainty analyses were performed using Monte Carlo simulation, and age-standardised rates were calculated using the World Health Organization standard population.
Results. Unsafe sex was the leading risk factor across all years, accounting for one in four DALYs (26.6%) of the estimated 20.6 million DALYs in 2012. The top five leading risk factors for males and females remained the same between 2000 and 2012. For males, the leading risks were (in order of descending rank): unsafe sex; alcohol consumption; interpersonal violence; tobacco smoking; and high systolic blood pressure; while for females the leading risks were unsafe sex; interpersonal violence; high systolic blood pressure; high body mass index; and high fasting plasma glucose. Since 2000, the attributable age-standardised death rates decreased for most risk factors. The largest decrease was for household air pollution (–41.8%). However, there was a notable increase in the age-standardised death rate for high fasting plasma glucose (44.1%), followed by ambient air pollution (7%).
Conclusion. This study reflects the continued dominance of unsafe sex and interpersonal violence during the study period, as well as the combined effects of poverty and underdevelopment with the emergence of cardiometabolic-related risk factors and ambient air pollution as key modifiable risk factors in SA. Despite reductions in the attributable burden of many risk factors, the study reveals significant scope for health promotion and disease prevention initiatives and provides an important tool for policy makers to influence policy and programme interventions in the country.

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The article in context

Evidence before the study. The first South African Comparative Risk Assessment (SACRA1) study showed a distinct risk factor profile in 2000 that was dominated by unsafe sex (31.5% of total DALYs) and interpersonal violence (8.4%). The risk factor profile reflected a combination of risks related to poverty and underdevelopment – such as indoor smoke from solid fuels, undernutrition, and unsafe water, sanitation and hygiene – as well as risks associated with a 'Western' or middle-to-high income lifestyle, including high blood pressure, high cholesterol, diabetes, tobacco smoking and alcohol consumption. The second National Burden of Disease Study (SANBD2) described the country's mortality trends, outlining the trajectory of the four colliding epidemics, i.e. 'maternal, new-born and child health', 'HIV/AIDS

and tuberculosis (TB)', 'non-communicable diseases' and 'violence and injury', with receding trends in age-standardised rates by 2012. The Global Burden of Disease, Injuries, and Risk Factors (GBD) study provides country estimates up to 2019. For the period 2000 - 2012, the GBD estimates for South Africa (SA), based on models incorporating global trends and DALYs calculated using different assumptions, indicate that unsafe sex dominated the risk factor profile. This was followed by child and maternal malnutrition, a decreasing burden attributable to tobacco and alcohol and an increased burden attributable to high body mass index, high systolic blood pressure and high fasting plasma glucose.

Added value of the study. The study provides estimates of the attributable burden of 18 risk factors, which unlike the GBD estimates are based on local empirical data only, avoiding influences of trends from other countries. Discounting years of life lost (YLLs; 1.5% per annum) allows higher weighting for the non-fatal burden than the DALY used in the GBD studies and provides estimates that are consistent with SANBD2. The risk factors have been selected on six criteria, and bring interpersonal violence into consideration. This study confirms the continued contribution of unsafe sex but highlights the sustained contribution of interpersonal violence together with a rapid increase in high fasting plasma glucose. Little change has been observed in the other metabolic risk factors except for a decline in low-density lipoprotein (LDL) cholesterol. Improvements have been made in poverty-related risk factors (water, sanitation and hygiene, household air pollution and childhood undernutrition) and the addictive substance use risk factors (smoking and alcohol), but these improvements have been accompanied by a small but steady increase in the attributable burden associated with ambient air pollution.

Implications of all the available evidence. In-depth understanding of trends in exposures and their contributions to the burden of disease between 2000 and 2012 provides pointers towards prioritising health promotion and disease prevention interventions. Despite some improvements in health, this study highlights substantial scope to reduce the disease burden in SA by reducing the prevalence of modifiable risk factors. Intersectoral and multipronged approaches that operate at multiple levels, including the individual, family and community level involving institutional or organisational structures and the macro level, including public policy and legislation, need to be strengthened and further developed. SA needs to build its national health surveillance system – it is critical that quality population health surveys are conducted routinely, and appropriate data reported timeously. In addition, the available technical capacity to synthesise such data and generate timely estimates to guide policy needs to be strengthened.

Informed by the findings of the initial Burden of Disease Study for South Africa,[1] the *Lancet* series for South Africa[2] highlighted that the country was amid four colliding epidemics, i.e. 'maternal, newborn and child health conditions', 'HIV/AIDS and tuberculosis (TB)', 'non-communicable diseases' and 'violence and injury', with an anomalously high disease burden given its per capita expenditure on healthcare. Reviewing the situation in 2009, Mayosi *et al*.[3] sounded the alarm about stasis in the management of health services in the country and limited health data. The second National Burden of Disease Study (SANBD2)[4] addressed cause-of-death data limitations and documented rapid changes in mortality between 1997 and 2012, with the beginnings of reversals in some of the epidemics becoming apparent. These reversals were largely through the prevention of mother-to-child transmission of HIV and roll-out of antiretroviral therapy (ART), but also the extension of childhood vaccinations and reductions in violence and injuries. Estimates of amenable mortality, however, identified the fact that the country's health challenges were exacerbated by an underperforming healthcare system and insufficient effort to address preventable mortality.[5]

The World Health Organization (WHO)'s thirteenth general work programme (GWP 13) for the period 2019 - 2023 identifies three interconnected strategic priorities to ensure healthy lives and wellbeing for all across the life course: achieving universal health coverage, addressing health emergencies and promoting healthier populations.[6] In order to prioritise health promotion, it is useful to undertake a comparative risk assessment (CRA), which provides estimates of the relative contribution of individual risk factors. Such information can be used to guide a health sector-led response to promote health and prevent disease and injury. In combination with information on the effectiveness, cost-effectiveness and local applicability and appropriateness of interventions, a CRA can contribute to the more rational use of limited resources to affect the risk factors that determine the health of the nation.

The first South African (SA) CRA study (SACRA1) estimated the contribution of 17 selected risk factors for the year 2000[7] using the CRA approach developed by the WHO[8] and the Global Burden of Disease (GBD) Studies.[9] This provides an overarching framework for population risk assessment by estimating the contributions of risk factors to the burden of disease.[10] Criteria for inclusion were on the basis of being among the leading causes of burden and injury, evidence of causality, being potentially modifiable and availability of data. SACRA1 showed a distinct risk factor profile in 2000, with a combination of risk factors related to poverty and underdevelopment – such as indoor smoke from solid fuels, undernutrition, and unsafe water, sanitation and hygiene – as well as risk factors associated with a 'Western' or middle-to-high income lifestyle, including high blood pressure, high levels of LDL cholesterol, type 2 diabetes, tobacco smoking, and alcohol consumption.[7] The study showed that unsafe sex dominated the attributable burden (accounting for 31.5% of total DALYs and 26.3% of total deaths in SA in 2000), followed by interpersonal violence (8.4%), alcohol use (7.0%), tobacco smoking (4.0%) and high body mass index (BMI), accounting for 2.9% of total DALYs in SA in 2000. The GBD 2019 study showed that for SA,[11] unsafe sex still dominated, followed by child and maternal malnutrition, high BMI, high fasting blood glucose and high blood pressure. Although the GBD study provides an updated risk factor profile for SA and the provinces, its estimates rely on models based on international data. A rigorous integration of local data promises to provide estimates that are more accurate with regard to the country context.

The Second Comparative Risk Assessment for SA (SACRA2) aimed to update the work of SACRA1 and to estimate the temporal trend between 2000 and 2012. Since the methods have evolved and more data sources have become available, it was important to re-estimate 2000 estimates to ensure comparability, and the results presented in this article supersede the previously published SACRA1 estimates. Thus estimates of the burden contribution of 18 modifiable risk factors are now available using the same method for 2000 and 2012, with the profile in 2006 to indicate trends.

Methods

Comparative risk assessment methodology

The CRA method is a standardised and systematic approach to estimate the contribution of individual risk factors to the observed burden of disease. It compares the observed burden of disease due to exposure with a hypothetical distribution in a population, making use of the level of exposure in the population and the epidemiological relationship between a risk factor and health outcomes.[12]

Selection of risk factors for the SA study

The focus in this study was on proximal risk factors including behavioural, physiological and environmental risks considered modifiable, as opposed to the more distal risk factors such as poverty and inequality, which have complex relationships with health. With input from health and environmental stakeholders, a list of 18 risk factors (Table 1) was selected for inclusion based on the following criteria: (*i*) likely to be among the leading causes of burden of disease and injury nationally in SA; (*ii*) potentially modifiable; (*iii*) availability of sufficient evidence for causal effects; (*iv*) availability of sufficient data to enable the estimation of exposure distributions by specified age-groups and sex; (*v*) availability of relative risks (RRs) or hazard ratios per unit of exposure for each risk factor-outcome pair by age and sex; and (*vi*) evidence or expert advice to support the generalisability of RRs to the SA population. We considered including climate change in SACRA2, but concluded that CRA methodology was not appropriate, as it would be ideal to quantify future avertable burden rather than consider the current burden that could be attributed to previous exposures. Furthermore, there is a need for more primary data to quantify the impact of excessive heat and extreme weather on health. Vitamin A deficiency and lead exposure, previously included in SACRA1, were omitted because of the low attributable burden, which has been reduced further by interventions.[17,18] Illicit drug use was omitted after expert consultation pointed to the lack of robust national epidemiological data. Non-optimal breastfeeding and sugar-sweetened beverages were not included owing to limited capacity of the study team.

Estimation of exposure levels

We used a consistent approach to identify local data that could provide estimates of the population distribution of risk factors for the study period. Primary data were sparse (rarely directly available for all 3 reference years) and of varying, and generally modest, quality. For most risk factors, there was large heterogeneity in terms of measurement methods, sampling design and realisation and, in some cases, exposure definition and target population. Some data were only accessible in aggregate form, with grouping not always matching the level of disaggregation needed for our study. To address these limitations, for the majority of risk factors (high systolic blood pressure, tobacco smoking, high fasting plasma glucose, alcohol use, high BMI, low fruit and vegetable intake, high LDL cholesterol, high sodium intake, iron deficiency) we adopted a meta-regression approach to the estimation of the parameters of the exposure distribution within each subgroup (age, sex and, for some risk factors, population group, province or urban/rural).[19-27]

The modelling and estimation details varied across risk factors – depending on the characteristics of the exposure and the available data – but in all cases the procedure involved two separate steps. In the first step, we used all available microdata and applied standard estimation methods (weighted estimators with robust standard error) to recover age, sex and survey-specific estimates of the parameters of interest (e.g. mean and standard deviation for normally distributed continuous exposures, and proportions for categorical exposures). In the second step, these estimates were used as inputs to generalised additive linear models to recover trends of the parameters over the whole study period, and to predict the values for the years 2000, 2006 and 2012. For the estimation of exposure to alcohol, we implemented the second step in a Bayesian framework. This allowed for the joint estimation of the prevalence of drinkers and the average consumption among drinkers, and the use of aggregate administrative data on alcohol sales and import/export at country level to adjust for under-reporting. Details on the estimation procedure are provided elsewhere.[28]

Advantages of the meta-regression approach were the ability to extract estimates from data not directly collected in the reference years, to include estimates available in the literature only in aggregated form and/or for specific subpopulations, and to introduce covariates in the regression models to adjust for known confounders. The procedures also allowed for taking into account heterogeneity of the data sources in terms of both precision (quantified by the inverse of the variance of the first-step estimates) and potential bias (summarised by the risk of bias score[29]) through the use of weighted estimators, with weights calculated according to the ‘quality-effects’ approach of Doi and Talib.[30]

In cases where the characteristics of the exposure and/or the availability of data made the meta-regression approach unsuitable or unnecessary (namely for low physical activity, childhood undernutrition, interpersonal violence, household air pollution, and unsafe water, sanitation and hygiene) we recovered the estimates of interest directly from data collected on, or close to, the reference years.[31-35] For the estimation of concentrations of ambient air pollution (particulate matter with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) and ozone) in 2012, we employed a regionally optimised fully coupled climate-chemistry model along with locally informed model forcing datasets.[36] Fine-scale regional models allow for the generation of more realistic small-scale climate information, chemical processes and patterns compared with global coarse-resolution models.[37] To further enhance the quality of modelled values and ensure their reliable applicability for regional exposure studies, bias corrections were performed using regionally obtained and quality-controlled surface observation datasets. Subsequently, for exposure and population-weighted analysis, the bias-corrected gridded distribution of $PM_{2.5}$ and ozone were transferred into small area level population census polygons using a polygonal size-dependent multi-gridpoint weighted average matrix method, which has more than 99% transformation accuracy.[36]

Heterogeneity in the type of measures (i.e. cases where the different sources reported on multiple related indicators for the same exposure) were addressed by converting all data to a common ‘reference’ format using empirically observed relationships between the reference format and the non-standard indicators. When possible, we directly estimated these relationships (*cross-walk* equations) from SA data, and otherwise we applied equations recovered from global studies. For example, we used the first method to obtain fruit and vegetable intake in a common metric (g/day) from widely different self-report dietary questionnaires.[18] We used an externally estimated *cross-walk* equation to recover distributional parameters of fasting plasma glucose from the prevalence of diabetes,[15] and average blood concentration of haemoglobin in women of reproductive age from estimates referring to pregnant women only.[21]

Burden of disease estimates

The foundation of the burden of disease estimates used in SACRA2 are the mortality estimates from the SANBD2 for a list of 140 single causes, structured to reflect conditions of public health importance for 2000, 2006 and 2012.[4,38] The year 2006 was selected as the turning point in the rapidly changing levels of mortality in SA. Data were sourced from the national statistical office, Statistics South Africa, and adjusted for completeness of death registration,

Table 1. Selected modifiable risk factors

Risk factor	Exposure measure	Theoretical minimum risk exposure level
Non-communicable disease cluster		
High systolic blood pressure	Systolic blood pressure in mmHg	110 - 115 mmHg*
High BMI	BMI in kg/m^2	20 - 25 kg/m^2*
High fasting plasma glucose	Serum fasting plasma glucose measured in mmol/L	4.5 - 5.4 mmol/L*
High LDL cholesterol	Serum LDL cholesterol measured in mmol/L	0.7 - 1.3 mmol/L*
Low fruit intake	Average usual daily consumption of fruits (fresh, frozen, cooked, canned or dried, excluding fruit juices and salted or pickled fruits) in g/day	200 - 300 g per day*
Low vegetable intake	Average usual daily consumption of fresh, frozen, cooked, canned or dried vegetables, and excluded legumes, salted or pickled vegetables, juices, nuts, seeds and starchy vegetables such as potatoes or corn measured in g/day	288 - 432 g per day*
High sodium intake	Sodium intake mediated through high blood pressure	1 g/day†
Low physical activity	Average weekly physical activity at work, at home, transport-related, sport-related and recreational measured by MET min per week	≥8 000 MET-min per week‡
Addictive substance use		
Tobacco smoking	For short-lag conditions: proportion of the population with cumulative exposure to tobacco smoking; proportion of the population who currently smoke For long-lag conditions: smoking impact ratio method: cumulative exposure to smoked tobacco products, proxied by excess lung cancer mortality; direct smoking: proportion of the population who currently smoke daily	Never smoked tobacco*
Alcohol consumption	Average daily consumption of pure alcohol (measured in g/day) in current drinkers who had consumed alcohol during the past 12 months	Lifetime abstinence§
	In addition, for selected outcomes, consumption of 60 g (men)/48 g (women) or more of alcohol in a single drinking occasion (binge drinking pattern) in the last 30 days	Non-binge drinking§
Undernutrition cluster		
Childhood undernutrition	Proportion of children:	
Child underweight	Mild (−2 - ≤1), moderate (−3 - ≤−2), or severe (≤−3) lower than the WHO 2006 standard weight-for-age curve	All children are <1 SD below the WHO 2006 standard weight-for-age curve*
Child wasting	Mild (−2 - ≤−1), moderate (−3 - ≤−2), or severe (≤−3) lower than the WHO 2006 standard weight-for-length curve	All children are <1 SD below the WHO 2006 standard weight-for-length curve*
Child stunting	Mild (−2 - ≤−1), moderate (−3 - ≤−2), or severe (<−3) lower than the WHO 2006 standard height-for-age curve	All children are <1 SD below the WHO 2006 standard height-for-age curve*
Iron deficiency	Peripheral blood haemoglobin concentration in g/L for all iron-responsive causes	The counterfactual haemoglobin distribution that would have been observed among women of reproductive age in the absence of iron deficiency for all iron-responsive causes*

...continued

Table 1. (continued) Selected modifiable risk factors

Risk factor	Exposure measure	Theoretical minimum risk exposure level
Social behaviour cluster		
Unsafe sex	Proportion of the population with exposure to sexual encounters that convey the risk of disease	No exposure to disease-causing pathogen through sex*
Interpersonal violence	Intentional use of physical force or power against other persons by an individual or small group of individuals and nature of the violence may be physical, sexual, or psychological/emotional, and it may involve deprivation and neglect. Acts are divided into family (child maltreatment and intimate partner violence) and community (bullying, assault, rape by non-partners, etc.) violence	No exposure to these interpersonal violence risk factors in the population*
Environmental cluster		
Ambient air pollution – $PM_{2.5}$	Annual average daily exposure to outdoor air concentration of $PM_{2.5}$ in μg/m^3.	2.4 - 5.9 μg/m^3*
Ambient air pollution – ozone	Mean of the 6-month period (July - December) with highest mean 8-hour daily maximum ozone concentrations (ppb)	29.1 - 35.7 ppb*
Household air pollution	The (*i*) proportion of households using solid cooking fuels, which include coal, wood, charcoal, dung and agricultural residues; and (*ii*) 'individual exposure' to $PM_{2.5}$ due to use of solid cooking fuel	2.4 - 5.9 μg/m^3*
Unsafe water, sanitation and hygiene	Unsafe water and unimproved sanitation: proportion of population with access to different water sources and sanitation facilities (improved and an unimproved water source (rainwater tank or dam, pool, stagnant water, or river, stream or water on community stand: distance >200 m) and improved and unimproved sanitation (dry toilet or pit toilet with ventilation or pit toilet without ventilation or bucket system or none)	All households use an improved water source (piped water inside the household) and improved sanitation (flush toilet connected to sewerage system)*

BMI = body mass index; LDL = low-density lipoprotein; MET = metabolic equivalent of time; WHO = World Health Organization; SD = standard deviation; $PM_{2.5}$ = particulate matter with an aerodynamic diameter ≤2.5 μm.
*Global Burden of Disease Study 2017.[13]
†Zhang *et al.*[14]
‡Global Burden of Disease Study 2016.[15]
§Sherk *et al.*[16]

as well as the under-reporting of HIV/AIDS, the relatively large proportion of unusable International Classification of Disease and Injury (ICD) cause-of-death codes and misclassification of cause of death for injury deaths. The estimates of the numbers of deaths and YLLs by age and sex were used for SACRA2.

In addition, we used DALYs as a comprehensive measure combining information on both fatal and non-fatal health outcomes to determine the number of years lost due to ill-health, disability or early death. This is a time-based summary metric that requires several value choices. We used a hybrid DALY[39] as introduced in the GBD studies since 2010, making use of prevalence-based years lived with disability (YLDs) rather than the incidence-based YLDs that were used in SACRA1. As described in detail elsewhere,[40] we used the West Model level 26 standard life table, considered an achievable target for SA, as the normative standard against which to measure YLLs. We did not apply age weighting due to ethical concerns about valuing the life of young adults above older adults and young children. Unlike the GBD study where the use of both age weighting and discounting has been discontinued in recent iterations, we used a discounting rate so that the loss of healthy life that occurs in the future can be equated to a current loss. We selected a 1.5% discounting rate, since it maintains a better balance of giving less weight to causes of death at younger ages as well as not being too far removed from the ranking of causes when not discounting compared with the 3% and 4.5% discounting rate.[40]

Given the limited availability of nationally representative disease prevalence data, we used a prevalence YLD estimated by applying the ratio of the GBD estimates for SA of the non-fatal burden to the fatal burden (YLDs/YLLs) to the SANBD estimates of YLLs, as recommended following an exploratory study.[41] A mapping of the causes in the SANBD list with the GBD list identified 123 common cause groupings[42] to facilitate the extrapolation, and these were proportionally divided by applying the GBD breakdown for specific causes required by the SACRA2 study (e.g. ischaemic and haemorrhagic stroke), and provided estimates that would be consistent with the SANBD estimates of deaths and YLLs (further details in section S2.2 of appendix, https://www.samedical.org/file/1954). The all-cause mortality rates changed profoundly during the period 2000 to 2012 owing to the effect of the HIV/AIDs pandemic, peaking in 2006, and then decreasing. Male death rates were considerably higher than female rates, while the estimated DALY rates for the period reflect a similar time trend but have a much-reduced gender differential (Fig. S1 in appendix: https://www.samedical.org/file/1954).

Population attributable fractions and attributable burden

The PAF for each risk factor has been calculated independently of others. In the case of unsafe sex, we used a categorical attribution approach to calculate the attributable burden, and assigned the total burden due to HIV/AIDS and cervical cancer to unsafe sex. In addition, the interpersonal violence injury burden was also directly attributable to interpersonal violence as a risk factor. However, for all other risk factors, including non-injury consequences of interpersonal violence, we estimated attributable burden by multiplying the burden metric (deaths and DALYs) by the PAF for the risk-outcome pair for each age, sex and year (2000, 2006 and 2012). The PAF is the proportion by which the outcome would be reduced in the SA population and in a given year, if past exposure to the risk factor were reduced to the counterfactual level of the theoretical minimum risk exposure level (TMREL). This was estimated by a generalised potential impact fraction (PIF)[43] for continuous exposures, with the usual attributable fraction formula for binary exposure, or with a multi-level extension of the latter when the exposure variable had several categories. PAFs have been calculated for each risk factor from the estimates of the exposure distribution and the RR associated with each exposure level.

Modelling uncertainty

We used Monte Carlo simulation to present uncertainty ranges around point estimates of the PAFs, reflecting the level of uncertainty in the exposure, the RR functions and the TMREL, using Ersatz software version 1.35 (EpiGear, Australia) as an add-in to Excel (Microsoft Corp., USA). Separately for each year, sex, age group and health outcome, we drew repeated random samples from the distributions of the parameters of the exposure distribution, the RR functions and the TMREL, and repeated the calculation of the PAF. We used the mean of the distribution of the replicates as the point estimate of the PAF, and the 2.5th and 97.5th percentiles as the bounds of the 95% uncertainty interval (UI).

Results

In 2012, unsafe sex was the leading risk factor, with just over one in four DALYs attributable to unsafe sex, accounting for 26.6% of the estimated 20.6 million DALYs (Fig. 1). Interpersonal violence ranked second, accounting for 8.5% of DALYs. Metabolic risks were prominent, with high BMI (6.9%), high systolic blood pressure (5.8%) and high fasting plasma glucose (5.1%) ranking 3rd, 4th and 6th, respectively. The substance use risk factors, i.e. alcohol use and tobacco smoking, as well as the environmental risk factors, i.e. water, sanitation and hygiene and ambient air pollution, each had a significant contribution to DALYs. These attributable burdens, however, are independent contributions, and cannot be added together for risk factors that share common causal pathways. This applies to risk factors such as high systolic blood pressure, high LDL cholesterol, low physical activity, low fruit intake, low vegetable intake and tobacco smoking, which are all risks for cardiovascular disease. Similarly, the attributable burden for interpersonal violence includes the contribution resulting from alcohol-associated violence, and the attributable burdens of underweight and micronutrient deficiencies are not additive. Environmental risk factors such as unsafe water, sanitation and hygiene and ambient air pollution may also work synergistically with others such as tobacco smoking to increase incidence and effects of diseases such as respiratory infection and diarrhoeal diseases in children.

The ranking of the risk factors alongside the ranking of the leading causes of death is shown in Table 2A and DALYs in Table 2B for 2012. In terms of deaths, cardiometabolic risks were prominent, with high systolic blood pressure (12.4%), high BMI (11.1%), high fasting plasma glucose (8.8%) and LDL cholesterol (2.7%) ranking 2nd, 3rd, 4th and 10th, respectively. Substance use risk factors, i.e. alcohol use (7.1%) and tobacco smoking (5.9%), also ranked high at 5th and 7th, respectively, while interpersonal violence (6.9%) ranked 6th.

Figs 2A and B present the changes in leading risk factors for DALYs between 2000 and 2012 by sex. The top five leading risk factors for males and females remained the same between 2000 and 2012. For males, the leading risks were (in order of descending rank) unsafe sex, alcohol consumption, interpersonal violence, tobacco smoking and high systolic blood pressure, while for females the leading risks were unsafe sex, interpersonal violence, high systolic blood pressure, high BMI and high fasting plasma

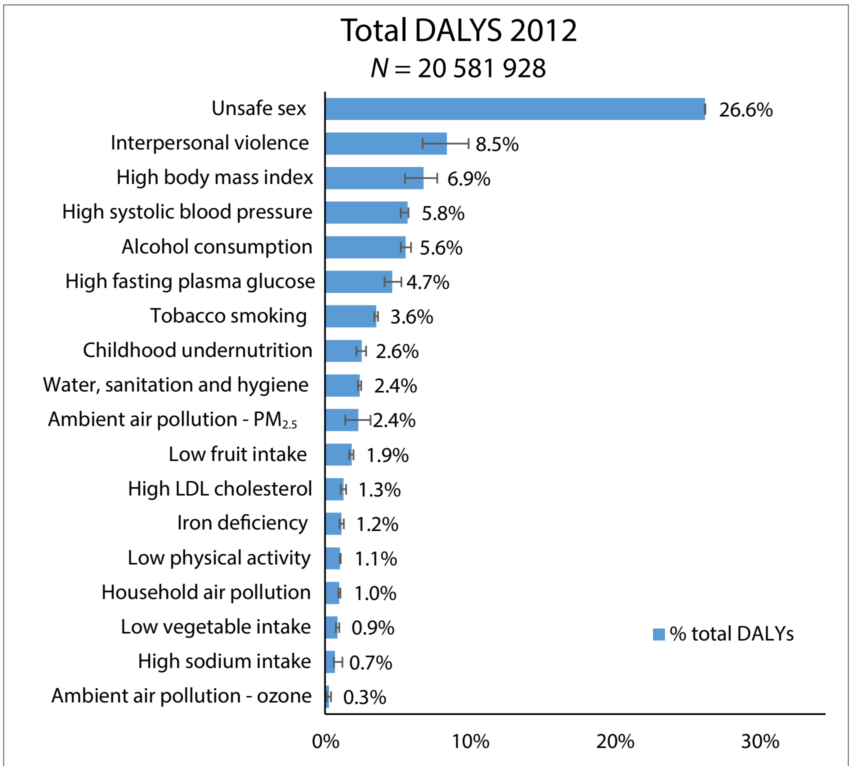

Fig. 1. Proportion of total disability-adjusted life years attributable to selected risk factors for persons in South Africa in 2012.

Table 2A. Deaths attributable to selected risk factors compared with the underlying causes of death, 2012

Rank	Risk factor	Total deaths, %*	Rank	Disease, injury or condition	Total deaths, %*
1	Unsafe sex	29.9	1	HIV/AIDS	29.1
2	High systolic blood pressure	12.4	2	Cerebrovascular disease	7.5
3	High body mass index	11.1	3	Lower respiratory infections	4.9
4	High fasting plasma glucose	8.1	4	Ischaemic heart disease	4.7
5	Alcohol	7.1	5	Tuberculosis	4.5
6	Interpersonal violence	6.9	6	Diabetes mellitus	3.6
7	Tobacco smoking	5.9	7	Interpersonal violence injuries (homicides)	3.5
8	Ambient air pollution – $PM_{2.5}$	3.8	8	Hypertensive heart disease	3.5
9	Low fruit intake	3.6	9	Road and other transport injuries	3.3
10	High LDL cholesterol	2.7	10	Diarrhoeal diseases	3.1
11	Water, sanitation and hygiene	2.6	11	Genito-urinary diseases	2.8
12	Low physical activity	2.1	12	Cardiovascular diseases	2.3
13	Childhood undernutrition	2.0	13	Chronic obstructive pulmonary disease	2.0
14	Low vegetable intake	1.8	14	Meningitis and encephalitis	1.3
15	Household air pollution	1.7	15	Asthma	1.2
16	High sodium intake	1.5	16	Trachea, bronchi and lung cancers	1.2
17	Ambient air – ozone	0.3	17	Other infectious diseases	1.2
18	Iron deficiency	0.1	18	Self-inflicted injuries (suicides)	1.2

Table 2B. DALYs attributable to selected risk factors compared with the underlying causes of DALYs, 2012

Rank	Risk factor	Total DALYs, %*	Rank	Disease, injury or condition	Total DALYs, %*
1	Unsafe sex	26.6	1	HIV/AIDS	26.0
2	Interpersonal violence	8.5	2	Tuberculosis	4.2
3	High body mass index	6.9	3	Back and neck pain	3.5
4	High systolic blood pressure	5.8	4	Lower respiratory infections	3.2
5	Alcohol	5.6	5	Interpersonal violence injuries	3.2
6	High fasting plasma glucose	4.7	6	Genito-urinary diseases	3.1
7	Tobacco smoking	3.6	7	Road and other transport injuries	3.1
8	Childhood undernutrition	2.6	8	Cerebrovascular disease	3.1
9	Water, sanitation and hygiene	2.4	9	Diarrhoeal diseases	2.9
10	Ambient air – $PM_{2.5}$	2.4	10	Diabetes mellitus	2.5
11	Low fruit intake	1.9	11	Depressive disorder	2.2
12	High LDL cholesterol	1.3	12	Upper respiratory infections	2.2
13	Iron deficiency	1.2	13	Ischaemic heart disease	2.1
14	Low physical activity	1.1	14	Chronic obstructive pulmonary disease	1.9
15	Household air pollution	1.0	15	Asthma	1.7
16	Low vegetable intake	0.9	16	Skin diseases	1.6
17	High sodium intake	0.7	17	Other musculo-skeletal disorders	1.6
18	Ambient air – ozone	0.3	18	Cardiovascular diseases	1.5

DALY = disability-adjusted life year; cardiovascular diseases include cardiomyopathy, myocarditis, endocarditis, atrial fibrillation and other dysrhythmias, among others; LDL = low=density lipoprotein; $PM_{2.5}$ = particulate matter with an aerodynamic diameter ≤2.5 µm.
*Percentages are rounded to one decimal place but the ranking is based on two decimal places.

glucose. Two of the five leading risks for males were substance use risk factors, i.e. tobacco smoking and alcohol consumption, whereas three of the five leading risks for females were diet-related cardiometabolic risk factors such as high systolic blood pressure, high BMI and high fasting plasma glucose. For males, the undernutrition risk factors, i.e. childhood undernutrition and iron deficiency, dropped in rank from 7th to 8th and 14th to 16th, respectively. The three risk factors that rose in rank for males are all related to the non-communicable cluster of disease, i.e. high fasting plasma glucose (9th to 7th), low fruit intake (15th to 14th) and low physical activity (16th to 15th). For females, the change in rank seems to be more heterogeneous within clusters. For instance, among the environmental risk factors, ambient air pollution ($PM_{2.5}$) rose in rank (11th to 7th), whereas household air pollution (12th to 15th) and water, sanitation and hygiene (7th to 8th) dropped in rank. For persons, shown in Fig. S7 of the appendix (https://www. samedical.org/file/1867), unsafe sex was consistently responsible for the highest proportion of DALYs across 2000 (29.4%), 2006 (42.4%) and 2012 (26.6%). Figs. S8 and S9 of the appendix (https://www.samedical.org/file/1954) contrast the 2000 risk factor profile from SACRA2 with those from the SACRA1.

Fig. 3 presents the percentage change in the risk factor-attributable age-standardised death (A) and DALY (B) rates (ASRs) between 2000 and 2012 for persons. The attributable ASRs decreased for most risk factors. The largest decrease was for household air pollution (–41.8%). For the other environmental

A. Males

2000

Risk factor	Rank	Male DALYs (95% UI)	% total DALYs (95% UI)
Unsafe sex	1	2 649 422 (2 646 634-2 652 062)	27.4 (27.3-27.4)
Alcohol consumption	2	1 057 871 (935 048-1 174 205)	10.9 (9.7-12.1)
Interpersonal violence	3	939 628 (901 092-990 308)	9.7 (9.3-10.2)
Tobacco smoking	4	563 365 (502 680-609 232)	5.8 (5.2-6.3)
High systolic blood pressure	5	432 061 (403 856-435 422)	4.5 (4.2-4.5)
High body mass index	6	361 948 (253 528-464 269)	3.7 (2.6-4.8)
Childhood undernutrition	7	309 193 (257 493-348 653)	3.2 (2.7-3.6)
Water, sanitation and hygiene	8	296 836 (282 252-307 667)	3.1 (2.9-3.2)
High fasting plasma glucose	9	220 417 (178 977-281 978)	2.3 (1.8-2.9)
Ambient air pollution - $PM_{2.5}$	10	179 796 (106 109-248 658)	1.9 (1.1-2.6)
Low fruit intake	11	173 171 (154 062-190 313)	1.8 (1.6-2.0)
Low density lipoprotein cholesterol	12	141 940 (124 444-156 590)	1.5 (1.3-1.6)
Household air pollution	13	128 190 (118 272-137 163)	1.3 (1.2-1.4)
Iron deficiency	14	108 478 (86 803-133 396)	1.1 (0.9-1.4)
Low vegetable intake	15	87 278 (70 570-102 290)	0.9 (0.7-1.1)
Low physical activity	16	82 344 (78 325-85 968)	0.9 (0.8-0.9)
High sodium intake	17	68 880 (60 002-107 281)	0.7 (0.6-1.1)
Ambient air pollution - ozone	18	19 589 (7 889-27 849)	0.2 (0.1-0.3)

2012

Risk factor	Rank	Male DALYs (95% UI)	% total DALYs (95% UI)
Unsafe sex	1	2 563 672 (2 560 910-2 566 506)	25.3 (25.3-25.4)
Alcohol consumption	2	963 111 (895 117-1 036 975)	9.5 (8.8-10.2)
Interpersonal violence	3	750 302 (699 121-804 316)	7.4 (6.9-7.9)
Tobacco smoking	4	529 572 (499 902-551 860)	5.2 (4.9-5.4)
High systolic blood pressure	5	493 779 (463 740-497 209)	5.1 (4.8-5.1)
High body mass index	6	457 157 (319 942-580 349)	4.5 (3.2-5.7)
High fasting plasma glucose	7	381 354 (322 584-456 886)	3.8 (3.2-4.5)
Childhood undernutrition	8	266 585 (226 358-296 925)	2.6 (2.2-2.9)
Water, sanitation and hygiene	9	250 253 (236 857-260 204)	2.5 (2.3-2.6)
Ambient air pollution - $PM_{2.5}$	10	229 632 (139 777-312 492)	2.3 (1.4-3.1)
Low fruit intake	11	180 469 (158 316-195 791)	1.8 (1.6-1.9)
Low density lipoprotein cholesterol	12	134 544 (114 622-151 090)	1.3 (1.1-1.5)
Household air pollution	13	91 835 (85 216-97 794)	0.9 (0.8-1.0)
Low vegetable intake	14	90 165 (73 388-106 069)	0.9 (0.9-1.2)
Low physical activity	15	86 549 (82 237-90 209)	0.9 (0.8-0.9)
Iron deficiency	16	75 581 (58 878-95 431)	0.7 (0.6-0.9)
High sodium intake	17	65 337 (57 345-104 757)	0.6 (0.6-1.0)
Ambient air pollution - ozone	18	29 350 (12 311-40 612)	0.3 (0.1-0.4)

B. Females

2000

Risk factor	Rank	Female DALYs (95% UI)	% total DALYs (95% UI)
Unsafe sex	1	3 275 614 (3 272 671-3 278 444)	34.8 (34.8-34.8)
Interpersonal violence	2	1 089 392 (677 793-1 466 997)	11.6 (7.2-15.6)
High body mass index	3	695 717 (582 424-773 027)	6.6 (5.6-7.4)
High systolic blood pressure	4	537 994 (484 017-544 349)	5.7 (5.1-5.8)
High fasting plasma glucose	5	313 979 (260 157-385 655)	3.3 (2.8-4.1)
Childhood undernutrition	6	305 495 (255 166-344 372)	3.2 (2.7-3.7)
Water, sanitation and hygiene	7	290 273 (276 011-300 864)	3.1 (2.9-3.2)
Alcohol consumption	8	222 367 (201 511-246 643)	2.4 (2.1-2.6)
Tobacco smoking	9	200 545 (191 975-206 668)	2.1 (2.0-2.2)
Low fruit intake	10	184 421 (162 004-201 531)	2.0 (1.7-2.1)
Ambient air pollution - $PM_{2.5}$	11	178 857 (103 288-246 865)	1.9 (1.1-2.6)
Household air pollution	12	152 486 (141 241-161 637)	1.6 (1.5-1.7)
Iron deficiency	13	152 042 (128 479-178 187)	1.6 (1.4-1.9)
Low density lipoprotein cholesterol	14	144 773 (122 951-163 479)	1.5 (1.3-1.7)
Low physical activity	15	111 940 (107 148-116 219)	1.2 (1.1-1.2)
High sodium intake	16	79 721 (64 945-137 568)	0.8 (0.7-1.5)
Low vegetable intake	17	76 922 (62 681-90 437)	0.8 (0.7-1.0)
Ambient air pollution - ozone	18	16 497 (6 644-23 453)	0.2 (0.1-0.2)

2012

Risk factor	Rank	Female DALYs (95% UI)	% total DALYs (95% UI)
Unsafe sex	1	2 906 988 (2 904 252-2 909 703)	27.8 (27.8-27.8)
Interpersonal violence	2	1 006 567 (674 083-1 318 340)	9.6 (6.4-12.6)
High body mass index	3	965 881 (829 368-1 042 859)	9.2 (7.9-10.0)
High systolic blood pressure	4	611 370 (547 673-619 836)	6.5 (5.8-6.6)
High fasting plasma glucose	5	589 809 (506 883-681 109)	5.6 (4.8-6.5)
Childhood undernutrition	6	264 337 (224 171-294 536)	2.5 (2.1-2.8)
Ambient air pollution - $PM_{2.5}$	7	254 174 (150 701-344 645)	2.4 (1.4-3.3)
Water, sanitation and hygiene	8	253 323 (239 762-263 396)	2.4 (2.3-2.5)
Tobacco smoking	9	214 425 (208 355-219 233)	2.0 (2.0-2.1)
Low fruit intake	10	205 839 (178 495-227 765)	2.0 (1.7-2.2)
Alcohol consumption	11	198 264 (181 817-215 933)	1.9 (1.7-2.1)
Iron deficiency	12	164 070 (141 045-188 800)	1.6 (1.3-1.8)
Low density lipoprotein cholesterol	13	136 286 (112 499-156 501)	1.3 (1.1-1.5)
Low physical activity	14	133 302 (127 730-137 914)	1.3 (1.2-1.3)
Household air pollution	15	116 981 (109 149-123 950)	1.1 (1.0-1.2)
Low vegetable intake	16	91 883 (75 342-107 593)	0.9 (0.7-1.0)
High sodium intake	17	81 988 (68 439-149 455)	0.8 (0.7-1.4)
Ambient air pollution - ozone	18	31 781 (13 323-43 993)	0.3 (0.1-0.4)

Fig. 2. Ranking of risk factors based on attributable disability-adjusted life years (DALYs) for (A) males and (B) females in South Africa in 2000 and 2012. (Social behaviour risk factors are coloured red, non-communicable disease clusters are blue, undernutrition-related risk factors are green, addictive substances are light green and environmental risk factors are beige; risks are connected by lines between time periods; solid lines are increases and dashed lines are decreases. (UI = uncertainty interval.)

risk factors, water, sanitation and hygiene also decreased (–25.3%), while ambient air pollution ($PM_{2.5}$; 6.7%) and ozone (6.6%) increased. The ASRs decreased notably for substance use and nutritional risk factors as well as interpersonal violence. The most notable increase in the ASR was for high fasting plasma glucose (44.1%). Some risk factors within the non-communicable disease cluster showed little change (high systolic blood pressure (1.1%) and high BMI (0.2%)), while the others decreased. The pattern for the change in age-standardised DALYs is very similar to the pattern for age-standardised deaths. Trends in age-standardised rates for males and females for the three time points are provided in section 3.2 of the appendix (https://www.samedical.org/file/1954).

A. Death	ASRs 2000	ASRs 2012	% change ASR 2000-2012
High fasting plasma glucose	153.7	203.5	32.4%
Ambient air pollution - $PM_{2.5}$	49.6	52.9	6.7%
Ambient air pollution - ozone	7.8	8.3	6.6%
High systolic blood pressure	328.9	301.3	-8.4%
High body mass index	240.2	240.5	0.2%
Unsafe sex	351.8	330.2	-6.2%
Low physical activity	60.9	53.8	-11.6%
Low fruit intake	107.6	93.1	-13.5%
High sodium intake	49.3	38.7	-21.4%
Low vegetable intake	73.8	56.5	-23.4%
High LDL cholesterol	89.6	67.0	-25.2%
Water, sanitation and hygiene	37.7	28.1	-25.3%
Iron deficiency	1.5	1.1	-25.9%
Interpersonal violence	100.9	70.7	-30.0%
Tobacco smoking	232.6	164.5	-29.3%
Alcohol consumption	333.5	235.4	-29.4%
Childhood undernutrition	59.0	39.6	-32.9%
Household air pollution	39.2	22.8	-41.8%

B. DALY	ASRs 2000	ASRs 2012	% change ASR 2000-2012
High fasting plasma glucose	2 999.6	4 312.1	43.8%
Ambient air pollution - ozone	196.1	263.9	34.6%
Ambient air pollution - $PM_{2.5}$	1 041.7	1 149.6	10.4%
High body mass index	5 064.9	5 454.7	7.7%
High systolic blood pressure	5 507.4	5 077.7	-7.8%
Low physical activity	1 090.3	991.0	-9.1%
High sodium intake	832.4	668.6	-19.7%
Low fruit intake	2 007.8	1 730.4	-13.8%
Iron deficiency	523.4	450.0	-14.0%
Unsafe sex	13 440.2	10 900.6	-18.9%
Tobacco smoking	5 309.9	4 159.7	-21.7%
Low vegetable intake	1 288.6	997.2	-22.6%
Water, sanitation and hygiene	1 209.5	911.9	-24.6%
High LDL cholesterol	1 594.4	1 201.5	-24.6%
Interpersonal violence	4 568.5	3 332.7	-27.1%
Alcohol consumption	9 183.6	6 677.7	-27.3%
Childhood undernutrition	2 879.6	1 990.6	-30.9%
Household air pollution	790.6	478.7	-39.4%

Fig. 3. Percentage change in attributable death (A) and disability-adjusted life year (DALY) and (B) age-standardised rates (ASRs) for persons between 2000 and 2012 for selected risk factors. Social behaviour risk factors are red, non-communicable disease cluster are blue, undernutrition-related risk factors are green, addictive substances are light green and environmental risk factors are yellow). (LDL = low-density lipoprotein.)

The detailed evaluation of each risk factor and the quantification of the resultant attributable burden[19-27,31-36] revealed insights into trends. Key observations for each risk factor are summarised in Table 3.

Discussion

Compared with other countries in the world, SA, alongside countries in the southern African region, has an unusual risk factor profile dominated by the contribution of unsafe sex associated with the HIV/AIDS epidemic. In 2012, unsafe sex contributed more than a quarter of the 20 million DALYs lost in SA. Interpersonal violence, together with alcohol in the case of males, have been the 2nd and 3rd leading risk factors for loss of health during this study period, reflecting social pathologies associated with high inequalities and unemployment as well as sociocultural norms and values.[73] The remaining risk factor profile depicts two distinct types of risk factors: those usually associated with a 'Western' or middle-to-high income lifestyle, such as tobacco smoking, diabetes, high BMI and high LDL cholesterol, and those related to poverty and underdevelopment, such as unsafe water and sanitation and household air pollution from solid fuels.

Our study shows slight shifts in the risk factor profile between 2000 and 2012, reflecting the increased impact of ambient air pollution accompanied by reductions in household air pollution and improvements in water and sanitation on the one hand, and the shifts in cardiometabolic risk factors, particularly the rapid emergence of high fasting plasma glucose accompanied by increases in high systolic blood pressure and high BMI, on the other. The attributable burden due to unsafe sex increased to a peak in 2006 and declined thereafter. The roll-out of antiretroviral treatment since 2004 for the management of HIV infection is a large contributor to the reduction in attributable burden due to unsafe sex.[74] Other reductions in risk-attributable burdens are possibly linked to strengthening the provision of primary healthcare through the development of non-communicable disease programmes and long-standing maternal and child health programmes. The latter include efforts to improve child and maternal survival through (*i*) improved nutrition and expansion of the childhood vaccination programme; (*ii*) healthier pregnancies and safer births; and (*iii*) social safety nets such as the child and foster care grants. Other initiatives beyond the primary healthcare sector that contributed to declines in risk-attributable burdens include public works development initiatives ensuring increased access to piped and in-house water, and improved sanitation and hygiene infrastructure. Policies such as tobacco control legislation and food regulation also likely contributed to improvements in health. The decrease in the ASR for overall interpersonal violence since 2000 accompanies the reduction in homicide rates over time during this period.[4]

A major limitation of SACRA2 is the fact that the results reflect the 2012 status, as this is the latest year for which burden of disease estimates are available for SA. The country has very limited epidemiological data on non-fatal burden, making it necessary to estimate this from the relationship of non-fatal to fatal burden from the GBD study. In addition, due to scarcity of data, the same prevalence levels of exposure were assumed for interpersonal violence across the three time points, and in the case of ambient air pollution, the exposure was modelled for 2012 and then applied to estimate levels for 2006 and 2000. Nonetheless, the study does provide an in-depth and empirically grounded understanding of the trends in risk factors that can be derived from SA data, and the insights gained should be used to influence policy. Without contemporary data, it is impossible to know how different the current risk factor profile might be, or the impact that COVID-19 would have had. The Thembisa model,[75] drawing on 2017 survey data[76,77] suggests considerable decrease in AIDS mortality in recent years, raising the possibility that unsafe sex would currently no longer be the single leading risk factor. However, the 2016 SADHS,[64] suggests that many of the trends in the exposures to risk factors observed in SACRA2 have continued beyond 2012.

The mere force of premature death and disability burden reported in 2012, however, indicates the necessity of expanding health promotion and disease prevention actions in the country. Health behaviours are the product of individual, interpersonal, community, societal and cultural influences, and it is critical to make use of behavioural sciences to identify effective interventions within this complexity.[78] While each risk factor requires specific intervention, there is a continued need to develop and strengthen intersectoral and

Table 3. Key observations about each modifiable risk factor in the SACRA2 study

Rank	Risk factor	Observations
1	Unsafe sex	• The incidence of HIV has declined considerably since 2006, largely as a result of access to ART and the use of male condoms, which have reduced the transmission of HIV.[38] • A model[44] of the prevalence and incidence of HIV shows that the provinces of SA differ in the timing and magnitude of their HIV epidemics. Most of the heterogeneity in HIV prevalence is attributable to differences in the prevalence of male circumcision and the frequency of non-marital sexual activity. • It is important that these epidemic drivers are not neglected in the push towards meeting the 90-90-90 management targets by 2022 and the 95-95-95 targets by 2030.[45] HIV communication programmes should continue to promote male circumcision and risk awareness in the context of non-marital relationships to prevent HIV transmission.[21] • SA included HPV vaccination for girls in Grade 4 in the national vaccination programme in 2014[46] but needs to increase the coverage[47] and urgently review the cervical cancer screening and treatment programme in light of the WHO goal to eliminate cervical cancer by the year 2030.[48]
2	Interpersonal violence[33]	• The age-standardised attributable death rates for interpersonal violence decreased from 100 to 71 per 100 000 population between 2000 and 2012. • Interpersonal violence ranked as the second leading risk, after unsafe sex, for attributable DALYs in 2000, 2006 and 2012 in SA. • Despite a decline in interpersonal violence, the exceedingly high burden indicates that SA requires further reinforcement and strengthening of existing laws on and responses to gender-based violence, child protection and firearm use, and other prevention programmes to address the burden of violence,[44] and achieve SDG 16 (among other targets which also call for the elimination of violence).[49] • Owing to the lack of epidemiological data, the estimate of the attributable burden in males, although exceedingly high, remains an underestimate. There is a need to improve the epidemiological data on the prevalence and risks for the different types of interpersonal violence.
3	High BMI[22]	• Average BMI increased between 2000 and 2012 and accounted for a growing proportion of total attributable deaths and DALYs. • The SA government has taken bold steps in introducing taxation of sugar-sweetened beverages and is urged to implement the other strategies outlined in its 2015 Obesity Prevention and Control Strategy,[50] including population-wide initiatives to encourage physical activity and reduce childhood obesity. Such policies and programmes must be supported by sound scientific evidence with ongoing surveillance and monitoring to evaluate their effectiveness. • However, the country needs to adopt a comprehensive framework to target underlying determinants such as food systems, urban systems and economic systems to stem the increasing prevalence of obesity.[51]
4	High systolic BP[19]	• Despite an increase in the prevalence of hypertension over the study period, there was no change in mean systolic BP; this may be related to an increase in the treatment of hypertension with antihypertensive medication.[52] • Nonetheless, the burden attributable to high BP remained substantial and unacceptably high, particularly in adults <60 years old. This underscores the need for preventive strategies, and improved diagnosis and care of hypertension and CVDs, the main sequelae of high BP, to prevent morbidity and mortality.[53]
5	Alcohol consumption[23]	• Alcohol continues to contribute substantially to SA's disease burden, which in 2012 was split three ways almost equally across major infectious diseases, NCDs and injuries. • The study improves on the previous estimates by applying updated exposure estimation methods and relative risk functions for a wider range of alcohol-related health outcomes, including HIV/AIDS and TB. Further, it identifies frequent heavy episodic (i.e. binge) drinking as a main contributor to the unusually large share of injuries and infectious diseases in the alcohol-attributable burden of disease profile.[23] • Interventions that underpin successful harm reduction are diverse and have previously been communicated to the government by the SAMRC, e.g. increasing alcohol excise taxes and/or imposing minimum unit pricing on alcohol products;[54] implementing further restrictions on alcohol marketing;[55] tightening up on various aspects of the retail sale of alcohol products, including a track-and-trace system on alcohol products;[56] implementing screening and brief interventions to address heavy drinking in certain healthcare settings;[57] and intensifying drink-driving countermeasures.[59] The inability to reduce alcohol harm successfully is therefore not due to any uncertainty as to which strategies to apply, but rather to a lack of political will.
6	High fasting plasma glucose[21]	• There has been a 5% increase in mean fasting plasma glucose and a 75% increase in diabetes prevalence, resulting in an unacceptable 56% increase in attributable DALY rates between 2000 and 2012. • Our study reports a changing age pattern over time among females, where more women ≥80 years are dying from CVD and CKD; there is a concerning 139% increase in DALY rates from CKD. • A multipronged approach is needed to mitigate the impact of raised glucose and BP levels. This approach should include mass screening of high-risk individuals and health promotion activities that encourage the uptake of healthy lifestyles.[58] Strategies need to prevent the development of impaired glucose tolerance and improve management, i.e. screening, diagnosis, treatment and control of diabetes.

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Table 3. Key observations about each modifiable risk factor in the SACRA2 study (continued)

Rank	Risk factor	Observations
7	Tobacco smoking[20]	• Despite gains in tobacco control in SA, smoking prevalence and smoking-attributable burden remains high. Rates of decline in smoking prevalence have plateaued between 2010 and 2012, suggesting that tobacco control measures need review and strengthening.[59] • The distribution of the smoking-attributable cause of death clearly shows two epidemiological patterns, the typical high-income pattern where NCDs predominate among whites and Asians, and a middle-to-low-income pattern where infectious respiratory diseases, such as TB, make a significant contribution among coloureds and black Africans. • Increasing excise taxes is the most effective measure to reduce smoking prevalence and should be implemented along with a track-and-trace system to improve tax compliance and reduce illicit trade.[60] In addition, brief interventions during clinic or hospital visits should encourage all patients who smoke to quit smoking, and should refer high-risk patients, including TB and HIV/AIDS patients, for more intensive cessation support.[61]
8	Childhood undernutrition[32]	• The study revealed little change in the prevalence of stunting, wasting and underweight between 2000 and 2012, and that in 2012 an estimated 33% of child deaths in SA were attributable to undernutrition.[32] • In order to reduce the prevalence of child undernutrition, a multisectoral approach is needed.[62] Aside from input from the health sector, addressing undernutrition must include measures that address household poverty and food security, fixing prices of basic foodstuffs and ensuring nutrition as a basic human right as enshrined in the Constitution. • A second essential component to improving nutritional status of children is strengthening the health sector response, particularly at primary healthcare level. Evidence has highlighted the need to monitor the nutritional status of children routinely, as well as to evaluate the programmes currently in place.[63]
9	Unsafe WASH[34]	• In 2011, 41% of South Africans lived with poor water and sanitation conditions; however, wide provincial inequalities exist. In 2012 it was estimated that 84.1% of all deaths due to diarrhoeal disease were attributable to unsafe WASH; this equates to 13 757 deaths (95% UI: 13 015 - 14 300). Of these diarrhoeal disease deaths, 48.2% occurred in children under 5 years of age, accounting for 13.9% of all deaths in this age group (95% UI: 13.1 - 14.4). • The study demonstrates stark provincial inequalities in attributable burden, mediated through good v. poor water and sanitation supply and unequal improvement in water and sanitation supply across provinces. • High priority needs to be given to improving access to safe and sustainable sanitation and water supply, particularly in underserved urban and rural communities in SA.[64] The high burden attributable to unsafe WASH, especially in children, provides a strong public health justification for prioritisation of this problem. Additionally, there are strong development, equity and human rights reasons for improving access and achieving the water-related SDGs[60] and to address the right to water and sanitation services for all.[64] Policy makers need to pay attention to the promotion of handwashing with soap and other hygiene behaviours.[66]
10, 18	Ambient air pollution – $PM_{2.5}$ and ozone[36]	• In 2012, approximately 97.6% of people in South Africa were exposed to $PM_{2.5}$ at levels above the 2005 WHO guideline: 10 μg/m^3 annual mean. • In 2012, deaths attributed to $PM_{2.5}$ were 19 507 (95% UI: 11 318 - 27 111) and ozone were 1 734 (95% UI: 727 - 2 399). • Efforts are needed to reduce the concentrations of ambient air pollution in the country. In the short term, proactive enforcement of air quality standards and minimum emission standards is needed.[67] Also, it is significant to promote the implementation of technological tools that have a capacity to render the intended service while reducing emissions and increase awareness in the communities and decision-makers. In the long term, the country needs to employ alternative strategies[68] to eliminate reliance on fossil fuels, to ensure industrial and domestic energy needs are met in an environmentally sustainable manner.
11, 16	Low fruit and vegetable intake[24]	• Between 2000 and 2012 the average intake of fruit and vegetables in the SA population (>25 years) decreased by 7% and 25%, respectively. The number of deaths and DALYs attributable to low fruit consumption increased by 7.3% and 8%, respectively. The number of deaths and DALYs attributable to low vegetable consumption increased by a greater extent (13.6% and 10.8%, respectively). • Despite the reduction of fruit and vegetable consumption, age-standardised death rates were lower in 2012 than in 2000 (–9% among males and –12% among females). This apparent contradiction can be explained by the reduction in death rates due to cardiovascular diseases observed in this period as a result of other unrelated factors in combination with increased fruit and vegetable consumption in some older age categories in whom there is a high CVD burden. • While the reduction in death rates and the progress in fruit and vegetable consumption among some age categories is a positive sign, the absolute burden of disease attributable to a diet low in fruits and vegetables remains high. Effective interventions supported by legislation and policy are needed to reverse the declining trends in fruit and vegetable consumption observed in most age categories.[24]

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Table 3. Key observations about each modifiable risk factor in the SACRA2 study (continued)

Rank	Risk factor	Observations
12	High LDL cholesterol[25]	• Mean LDL cholesterol in SA declined from 2.74 mmol/L in 2000 to 2.58 mmol/L in 2012 for males, while in females it declined from 3.05 mmol/L in 2000 to 2.91 mmol/L in 2012, resulting in declines in the LDL cholesterol-attributable burden. • Nonetheless, mean population LDL cholesterol values remain high and can be lowered further through nationwide nutrition education programmes, and collaboration with the food industry to improve labelling that would enable consumers to make informed healthier choices as well as stimulate product reformulation.[69] Legislation is likely required to promote such initiatives. Further, there is a need to ensure the cheaper pricing of healthy foods compared with their unhealthy alternatives through legislation.
13	Iron deficiency[27]	• Although there has been a slight decrease in the prevalence of iron-deficiency anaemia in women of reproductive age from about 11.9% in 2000 to 10.0% in 2012, the prevalence of overall anaemia in SA increased over the same period (25.5% - 33.2%) with a peak in 2006. • Our study shows a decline over time in the proportion of maternal deaths attributable to iron deficiency from 38.2% (95% UI: 29.0 - 46.1%) in 2000 to 26.6% (95% UI: 10.3 - 40.2%) in 2012. Furthermore, there has been a decrease (0.15% (95% UI: 0.10% - 0.18%) to 0.12% (95% UI: 0.05% - 0.19%)) in the percentage of all female deaths attributable to iron deficiency between 2000 and 2012. • Between 2000 and 2012, the age-standardised DALY rate from iron-deficiency anaemia attributable to iron deficiency markedly decreased by 33% in males and increased by 3% in females of all ages. About 1.1 - 1.4% of all DALYs in SA from 2000 to 2012 were attributable to iron deficiency. • Iron-deficiency anaemia prevalence can be markedly reduced if iron deficiency is eliminated. Hence, it is essential to encourage, reappraise and strengthen the measures that have been implemented to address iron deficiency, including food fortification and the iron supplementation programme for infants >6 months old and women of reproductive age.[27] In addition, iron supplementation in young infants (<6 months old) requires attention and policy direction. The reported increase in anaemia prevalence and its impact in pregnant women could possibly be due to other causes such as HIV infection. The role of HIV infection *per se*, ART and the dietary requirements of HIV-positive pregnant females need to be evaluated.
14	Low physical activity[31]	• The prevalence of physical inactivity (<600 MET-min/week) decreased by 16% for females and 8% for males, while high activity (>8 000 MET-min/week) increased by 10% and 13%, respectively, between 2000 and 2012. The number of deaths and DALYs attributable to low physical activity (<8 000 MET-min/week) increased by 8.1% and 13.2%, respectively, due to a higher number of combined IHD, ischaemic stroke, breast cancer, colon cancer and type 2 diabetes mellitus deaths (~12 000) and DALYs (~210 000) in 2012 compared with 2000. • The attributable age-standardised death rate due to low activity decreased between 2000 and 2012 from 60/100 000 population in 2000 to 54/100 000 population in 2012. • While the decrease in physical inactivity has resulted in a reduction in attributable age-standardised death rates, the absolute burden remains high. This suggests that implementation of existing NCD policies needs better monitoring and evaluation. To encourage physical activity, the SA National Development Plan recommended universal access to sports and recreational facilities, and encouraged local authorities to promote physical activity by creating walkable communities.[70] Monitoring of physical activity levels through surveys is needed in order to evaluate the success of such initiatives and to reach set physical activity targets.
15	Household air pollution[35]	• In 2012, an estimated 17.6% of the SA population was exposed to HAP. This was estimated to have caused 8 862 deaths (95% UI: 8 413 - 9 251) and 1.7% (95% UI: 1.6% - 1.8%) of all deaths in SA. • While electrification rates have improved over the past two decades, many people still use solid fuels for cooking owing to energy poverty. The prevalence of HAP due to cooking and the disease burden attributable to this risk factor has decreased. However, more work is needed to lower and eventually eradicate the use of solid fuels for cooking. • A multipronged approach must be taken that involves legislation and interventions[71] to reduce the use of solid fuels for cooking in SA.
16	High sodium intake[26]	• High sodium intake from processed foods as well as discretionary use of salt, mediated through raised BP, accounted for a sizeable burden of disease in 2012 having declined by 14% since 2000. • The study suggests that the regulation to reduce the salt content of selected processed foods,[72] which came into effect in 2016, could decrease the burden of CVD by almost 3 000 deaths yearly. • National monitoring programmes of sodium consumption and the content in selected processed foods need to be developed by government to inform strategies to reduce CVD further.

ART = antiretroviral therapy; SA = South Africa; HPV = human papillomavirus; WHO = World Health Organization; DALY = disability-adjusted life year; BMI = body mass index; BP = blood pressure; CVD = cardiovascular disease; TB = tuberculosis; NCD = non-communicable disease; SAMRC = SA Medical Research Council; CKD = chronic kidney disease; WASH = water, sanitation and hygiene; LDL = low-density lipoprotein; UI = uncertainty interval; SDG = Sustainable Development Goal; $PM_{2.5}$ = particulate matter with an aerodynamic diameter ≤2.5 µm; MET = metabolic equivalent of time; IHD = ischaemic heart disease.

multipronged approaches that operate at multiple levels, including the individual and family level, the community level involving institutional or organisational structures and, at the macro level, public policy and legislation.[79] Acknowledging the socio-ecological model, the National Health Promotion Strategy 2015 - 2019 outlines steps for the country to build a healthy society and address risk factors and determinants of health at national and local level,[80] but its implementation requires financial and human resources, training and an information system to monitor and assess progress. A health promotion capacity mapping conducted in 2017/18 in SA[81] identified the need to overcome institutional barriers and strengthen health promotion capacities. It is also critical to recognise and systematically combat the commercial determinants of health in which strategies are used by the private sector and corporate actors to influence the lifestyles, choices and preferences of individuals, groups and populations without necessarily considering health outcomes.[82] Commercial determinants include promoting the purchase or use of unhealthy products, such as tobacco, ultra-processed food, obesogenic food, alcohol and sugary beverages, as well as promoting weaker governmental regulation.

Achoki *et al*.[11] utilised estimates from the GBD 2019 study[9] to assess national and provincial health trends in SA between 1990 and 2019, including attributable burden of selected risk factors. We note substantial differences in the ranking of the attributable burden of risk factors between the GBD and the SACRA2 studies, even considering that the study period differs. Unsafe sex is consistently the highest risk factor in both studies (although the Tembisa model[75] suggests that by 2019, the GBD study overstates the country's HIV burden, with HIV/AIDS accounting for 27.6% of all deaths, v. 10.4% of all deaths in the local model). Interpersonal violence and combined childhood malnutrition are not directly comparable between GBD and SACRA2 owing to differences in the level of aggregation of risk factors applied in the two studies. For childhood malnutrition, the GBD combines low birthweight and gestation, childhood growth failure (stunting, wasting and underweight), suboptimal breastfeeding, iron deficiency, vitamin A deficiency and zinc deficiency, whereas SACRA2 only assesses childhood stunting, wasting and underweight and iron deficiency. While suboptimal breastfeeding, iron deficiency, vitamin A deficiency and zinc deficiency account for <1% of total deaths, low birthweight and short gestation account for approximately 4% of deaths and 6.5% of DALYs for SA.[11] Currently for child maltreatment, global risk estimates are limited, as GBD only includes childhood sexual abuse and a few related health outcomes, with non-sexual child maltreatment (emotional and physical abuse, neglect and exposure to family violence) omitted. Additionally, for interpersonal violence, GBD also includes intimate partner violence (IPV) as a risk to health, and bullying victimisation has been included as the first risk factor for anxiety disorders since 2017. However, other forms of community violence are omitted for the global estimates. In this study we estimated the burden of disease attributable to exposure to interpersonal violence, including the contribution of IPV, all forms of child maltreatment, sexual violence by non-partners, bullying at school and other forms of community violence as risk factors for disease and injury in SA. Inevitably, the SACRA2 study ranks interpersonal violence high and childhood undernutrition low, while GBD 2019 ranks malnutrition high and the elements of interpersonal violence low. Another factor that contributes to the difference is the use of discounting of time lost in the future in the DALY metric used for SACRA2. SACRA2 has applied discounting to avoid the loss in the distant future outweighing the loss that occurs in the near future, at a reduced discounting rate of 1.5% compared with 3% used in earlier burden of disease studies.[1,10] Another important difference between the two studies is that SACRA2 made use of local data only, without using global or regional trends to infer missing information. While this has limited the risk factors that could be considered in SACRA2, as well as the scope to do provincial analyses for most of the risk factors, it is considered that robust analysis of local data can assist with building trust in the estimates and improve the quality and relevance of the data.

While the total numbers of deaths for the year 2000 from both SACRA1 and SACRA2 were reasonably similar (Fig. S8 in appendix: https://www. samedical.org/file/1867), SACRA2 was based on an estimate of 19.0 million DALYs compared with 16.1 million in SACRA1 (Fig. S9), due to the different assumptions made in the calculation of DALYs. The risk factor profiles shown in Fig. S9, however, had considerable similarity. Unsafe sex and interpersonal violence dominated in both studies. However, high BMI and high systolic blood pressure ranked higher in SACRA2 than they did in SACRA1, shifting tobacco smoking and childhood undernutrition lower down the list. For most risk factors, the attributable proportion of DALYs increased in SACRA2 when compared with SACRA1 owing to additional epidemiological evidence and enhancements in the methodology. Tobacco smoking and low physical activity, however, contributed lower proportions of the total burden owing to more stringent criteria being used for the risk-outcome pairs in SACRA2. High cholesterol also contributed to a lower proportion of the total burden in SACRA2 because of improved methodology that focused on the exposure to LDL cholesterol rather than total cholesterol.

SACRA2 has confronted the lack of consistent data to provide trend estimates for most risk factors. While meta-regression approaches could be used for some, it is of concern that measurement protocols have not been standardised for different surveys. It would also be ideal to be able to assess provincial variations. However, some risk factors still do not have national level estimates, necessitating reliance on extrapolating subnational data sources. SA needs to build its national health surveillance system based on locally relevant indicators. It is critical that quality population health surveys are conducted routinely, and appropriate data reported timeously. In addition, the available technical capacity needs to be strengthened to generate timely estimates and develop user-friendly platforms to communicate the findings. The COVID-19 pandemic has highlighted the urgency of providing timely burden of disease and risk factor data.

Conclusion

SACRA2 highlights considerable scope to reduce exposure to the range of modifiable risk factors and improve health. It also emphasises the need for better health surveillance and the critical role of health promotion, including age-appropriate interventions, to keep people healthy in SA. The National Public Health Institutes of South Africa (NAPHISA) Bill, enacted in 2020,[83] aims to provide health surveillance to guide health policy and planning; however, this has yet to be established and funded. The 2019 National Health Insurance NHI Bill[84] mentions health promotion, but Freeman *et al*.[85] warn that its lack of emphasis and the narrow approach proposed make it unlikely that health promotion will have significant impact on population health or reducing healthcare need. They, as others,[86] have called for the establishment of a multisectoral National Health Commission or an independent Health Promotion and Development Foundation, linked to the proposed NHI Fund, that includes several relevant government departments, civil society and researchers with a dedicated budget to promote health and prevent illness. Addressing many of these risk factors will require policies, legislation and budget allocation outside of the health sector. Following the devastating effects of COVID-19, well beyond numbers of deaths directly due to COVID, this call to consider the country's specific realities and needs, including poverty and its related behavioural impacts and health consequences, becomes even more relevant and urgent.

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 any other purpose.

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