Estimating the burden of disease attributable to high cholesterol in South Africa in 2000

Rosana Norman, Debbie Bradshaw, Krisela Steyn, Thomas Gaziano and the South African Comparative Risk Assessment Collaborating Group

Objectives. To estimate the burden of disease attributable to high cholesterol in adults aged 30 years and older in South Africa in 2000.

Design. World Health Organization comparative risk assessment (CRA) methodology was followed. Small community studies were used to derive the prevalence by population group. Population-attributable fractions were calculated and applied to revised burden of disease estimates for the relevant disease categories for each population group. The total attributable burden for South Africa in 2000 was obtained by adding the burden attributed to high cholesterol for the four population groups. Monte Carlo simulation-modelling techniques were used for uncertainty analysis.

Setting. South Africa.

Subjects. Black African, coloured, white and Indian adults aged 30 years and older.

Outcome measures. Mortality and disability-adjusted life years (DALYs) from ischaemic heart disease (IHD) and ischaemic stroke.

Results. Overall, about 59% of IHD and 29% of ischaemic stroke burden in adult males and females (30+ years) were attributable to high cholesterol (≥ 3.8 mmol/l), with marked variation by population group. High cholesterol was estimated to have caused 24 144 deaths (95% uncertainty interval 22 404 - 25 286) or 4.6% (95% uncertainty interval 4.3 - 4.9%) of all deaths in South Africa in 2000. Since most cholesterol-related cardiovascular disease events occurred in middle or old age, the loss of life years comprised a smaller proportion of the total: 222 923 DALYs (95% uncertainty interval 206 712 - 233 460) or 1.4% of all DALYs (95% uncertainty interval 1.3 - 1.4%) in South Africa in 2000.

Conclusions. High cholesterol is an important cardiovascular risk factor in all population groups in South Africa.

S Afr Med J 2007; 97: 708-715.

The value of abnormal blood lipids and apo-lipoprotein levels to predict ischaemic heart disease (IHD) has been studied for decades, with the initial focus shifting from studying the relationship with total blood cholesterol (TC) to that of the individual components associated with TC. TC is a composite measure of the cholesterol content of lipoprotein particles such as low-density lipoprotein cholesterol (LDLC) and high-density lipoprotein cholesterol (HDLC). The dyslipidaemic patterns of high levels of LDLC and/or low HDLC have been found to impart high risk for developing IHD, and justify aggressive treatment to reduce the risk.[1] Recent data suggest that levels of the actual apo-lipoproteins such as ApoB and ApoA1 are the most powerful lipid predictors for IHD.[2]

Burden of Disease Research Unit, Medical Research Council of South Africa, Tygerberg, Cape Town
Rosana Norman, PhD
Debbie Bradshaw, DPhil (Oxon)

Chronic Diseases of Lifestyle Research Unit, Medical Research Council of South Africa and Department of Medicine, University of Cape Town
Krisela Steyn, MD, MSc, NED

Divisions of Cardiovascular and Social Medicine and Health Inequalities, Brigham and Women's Hospital, Harvard Medical School, Boston, USA
Thomas Gaziano, MD, MSc

Corresponding author: R Norman (rosana.norman@mrc.ac.za)

In most developing countries the only lipid-related population-based data available are TC levels. However, TC data can be used effectively as a proxy measure of other dyslipidaemic markers of risks for IHD, ischaemic stroke and other vascular diseases. The risks of TC are continuous and occur even in populations with TC levels much lower than those experienced in North American and European populations.[3,4] The level of TC usually increases with age in populations with a westernised lifestyle. High TC levels are associated with a diet high in fat (particularly saturated animal fat), with cholesterol in the diet, and with lack of fibre.

Cardiovascular disease (CVD) risk factors, including high TC, are already prevalent in the South African population, and are set to increase with growing urbanisation of the black African population.[5-7] (Population group classification is used in this article to demonstrate differences in risk-factor profile and the subsequent burden. Data are based on self-reported categories according to the population group categories used by Statistics South Africa. Mentioning such differences allows for a more accurate estimate of the overall burden and may assist in higher effectiveness of future interventions. The authors do not subscribe to this classification for any other purpose.) In the black African population currently the predominant CVD is cerebrovascular disease (stroke).[8] However, as the TC levels increase, the CVD pattern will shift towards higher rates of IHD. It is already consistently reported that the caseload of IHD is on the increase in the black

African population, particularly in urban hospitals. It has been suggested that the incidence of IHD in the urban black African population may even be as high as in the white population.[9]

Nine community studies[10-19] have been conducted in South Africa, but there are no nationally representative data on TC levels. This article aimed to use the community study data to derive estimates of national prevalence of exposure to high TC in adults aged 30 years and older by sex, age and population group. It also aimed to quantify the adverse health consequences associated with high TC by population group, and to estimate the burden of disease attributed to high TC by sex, population and age group in South Africa for the year 2000.

Methods

Using World Health Organization (WHO) comparative risk assessment (CRA) methodology[3,20] the disease burden attributable to a particular risk factor is estimated by comparing current local health status with a theoretical minimum counterfactual with the lowest possible risk. The attributable fraction of disease burden in a population is determined by prevalence of exposure to the risk factor in the population and the relative risk (RR) of disease occurrence given exposure. Cholesterol was defined as a continuous variable with mean and standard deviation (SD) values of total serum cholesterol expressed in millimoles per litre of serum (mmol/l).

The outcomes assessed were IHD and ischaemic stroke. IHD was chosen in the WHO CRA study[4] on the basis of clear and consistent positive associations observed in cohort studies, as well as on the evidence of reversibility in clinical trials of treatments to lower cholesterol levels. There is a positive association between cholesterol and ischaemic stroke, but there is a qualitatively different association with haemorrhagic stroke.[4] As the endpoints had to be mapped to the South African burden of disease study classification system, total stroke (which includes both stroke subtypes) was used in this analysis. It was necessary, however, to adjust stroke burden by the proportions of total fatal and non-fatal stroke that were ischaemic stroke, using the proportions by stroke subtype for the WHO African subregion AFR-E, which includes South Africa.[4] Although cholesterol has been shown to be inversely associated with cancer and chronic respiratory disease, evidence suggests that these associations were rather due to the effects of the diseases on cholesterol levels, and hence these outcomes were not included in the analysis.[4]

Estimates of mean TC levels and SDs by age and sex for adults aged 30 years and older were obtained by pooling data from the nine available studies[10-19] of randomly selected subjects conducted between 1980 and 2000. The means and SDs were weighted according to the number of observations of each study and the SD also took into account the difference between the means of the studies. The pooled TC mean was calculated as $m=\Sigma\omega_i m_i$ and the pooled SD as

$$\sqrt{\sum \omega_i sd_i^2 + \sum \omega_i (m_i - m)^2}$$

where ω_i was a proportional weight based on the number of subjects in each study and m_i and sd_i were the study mean and SD respectively.

Owing to differences in prevalence of CVD in the four population groups, the analysis was carried out separately for each. Age- and sex-related population group-specific mean cholesterol levels from these community studies were weighted according to the size of the population in each age-sex group in South Africa in 2000.[21]

Cholesterol values for those aged 70 - 79 years and > 80 years were assumed to be the same as for the 60 - 69-year age group, owing to the extremely limited availability of cholesterol levels in community studies for adults older than 65. This may have led to a slight overestimate in the white population, as the association between age and cholesterol is non-linear.[4] In high-cholesterol regions, cholesterol levels for females increase between the ages of 30 and 65 years, and then fall slightly. In males, levels increase between the ages of 30 and 50 years, and then flatten before declining slightly in older age.[4] Lawes *et al*.[4] did not assume a decline in older ages in the low-cholesterol AFR-E region.

A comprehensive review of the literature by Lawes *et al*.[4] identified the Asia-Pacific Cohort Studies Collaboration analysis of 1999 (APCSC 1999)[22] as the primary data source for RR estimates of IHD and ischaemic stroke. APCSC 1999 analyses offered greater sample size, and while other available meta-analyses used tabular data, APCSC analyses were based on individual participant data and provided age-specific analyses of total stroke and stroke subtypes. These analyses could therefore more reliably adjust for confounding and provide more reliable estimates of hazard ratios.[4]

In this analysis we used risk ratios based on more recent analyses of the APCSC data, which reflect a smoother estimate of the attenuation of RRs across age, as shown in Table I (S Vander Hoorn, University of Auckland – personal communication, 2005). These same risk ratios were used across population groups. Related health outcomes and ICD-10[23] codes are also presented in Table I.

Similar to the case of blood pressure, regression dilution bias must be taken into account when observational data are used to estimate the association between cholesterol and cardiovascular endpoints. This bias occurs as baseline or 'one-off' measures of TC are subject to random fluctuations, due partly to the measurement process and partly to real but temporary deviations at a single time-point from the 'usual' exposure level. The measured values have a wider distribution than the 'usual' values, and with repeated measures result in

Table I. Age-specific hazard ratios (95% CI) for 1 mmol/l difference in usual total cholesterol

Related health outcome (ICD-10)[23]	30 - 44 yrs	45 - 59 yrs	60 - 69 yrs	70 - 79 yrs	80+ yrs
Ischaemic heart disease (I20-I25)	0.27 (0.20 - 0.38)	0.48 (0.44 - 0.52)	0.64 (0.62 - 0.67)	0.70 (0.66 - 0.75)	0.70 (0.67 - 0.73)
Ischaemic stroke (I63)	0.61 (0.32 - 1.18)	0.69 (0.59 - 0.80)	0.76 (0.64 - 0.90)	0.82 (0.68 - 0.99)	0.90 (0.75 - 1.08)

Source: S Vander Hoorn, University of Auckland – personal communication, 2005; more recent reanalysis of Asia-Pacific Cohort Studies Collaboration (APCSC)[22] data.
95% CI = 95% confidence interval.

'regression to the mean' of values, whereby an initially extreme observation tends to become less abnormal with replication. Since this bias is accounted for in the estimates of RR, it also needs to be reflected in a narrower distribution around the estimated mean TC levels.[24,25] A correction for regression dilution resulting from the 'time-dependent' variation from the usual level is made by multiplying the SDs across all age-sex categories by a factor of 0.625 (S Vander Hoorn – personal communication).

Customised MS Excel spreadsheets based on templates used in the Clinical Trial Research Unit at the University of Auckland (S Vander Hoorn – personal communication, 2005) as well as Australian studies (T Vos, University of Queensland – personal communication, 2005) were used to calculate the attributable burden using a discrete version of the general potential impact fraction (see below), taking into account continuous risk factor disease exposures compared with a theoretical minimum distribution (conferring the lowest possible risk), on a categorical scale.

$$PAF = \frac{\sum_{i=1}^{n} P_i\, RR_i - \sum_{i=1}^{n} P'_i\, RR_i}{\sum_{i=1}^{n} P_i\, RR_i}$$

where n = the number of exposure categories; P_i = the proportion of the population in exposure category i; RR_i = the RR for exposure category i; and P'_i = the proportion of the population in exposure category i in the counterfactual distribution.

The theoretical minimum exposure distribution is zero in most cases, since zero exposure reflects minimum risk (e.g. no smoking). For TC, however, zero exposure would be physiologically impossible, and therefore is an inappropriate choice as the theoretical minimum. Lawes *et al*.[4] examined data from 'unacculturated' populations which included hunter-gatherer societies where mean values were as low as 3.0 - 3.5 mmol/l. With diets low in salt and animal fat, the prevalence of CVD is very low in these 'low-cholesterol' populations. In populations such as China, data suggest that the relationship between cholesterol and cardiovascular endpoints may continue, without a threshold, below cholesterol levels of about 4.0 mmol/l. Based on this evidence, the theoretical minimum of usual cholesterol was set at a mean of 3.8 mmol/l (SD 0.6 mmol/l – 'usual'), for all age, sex and population groups.[4]

PAFs were then applied to revised South African burden of disease estimates for 2000 for each population group,[21] deaths, premature mortality or years of life lost (YLL), years lived with disability (YLD), and disability-adjusted life years (DALYs) for the relevant disease categories, to calculate attributable burden. The total attributable burden for South Africa in 2000 was obtained by adding the burden attributed to high cholesterol for the four population groups.

Monte Carlo simulation-modelling techniques were used to present uncertainty ranges around point estimates that reflect all the main sources of uncertainty in the calculations. We used the @RISK software version 4.5 for Excel,[26] which allows multiple recalculations of a spreadsheet, each time choosing a value from distributions defined for input variables. Normal probability distributions were specified around the mean TC levels by age, sex and population group. For the RR input variables a normal distribution was specified, with the natural logarithm of the RR estimates as the entered means of the distribution and the standard errors of these estimates. For each of the output variables (namely attributable burden as a percentage of total burden in South Africa, 2000), 95% uncertainty intervals were calculated bounded by the 2.5th and 97.5th percentiles of the 2000 iteration values generated.

Results

Table II shows the estimated mean TC levels, which were highest in the white population group, followed closely by the coloured and Indian groups. The black African population had the lowest mean levels for males and females at all ages, with levels in urban areas only slightly (but not significantly) higher than rural levels. Mean TC levels in women were higher than in men above 45 years of age in all population groups. In the youngest age group, however, levels in men were higher than in women in the Indian, coloured and white population groups. TC levels in white women increased between the ages of 30 and 65 years, and were then assumed to remain flat – although they should fall slightly afterwards. In white males, levels increased between the ages of 30 and 50 years and then flattened, although they are also supposed to decline slightly in older age groups. Similar age patterns were observed in Indian and coloured males and females, but not in the black African population. In the black African population the increases between the 30 - 44-year and 45 - 59-year age groups were not as marked as in the other population groups, and in black African men the levels appeared to continue increasing between ages of 30 and 65 years.

Table II. Estimates of age-specific mean total cholesterol levels and standard deviations (SDs) (mmol/l) for males and females by population group, South Africa, 2000

			Age groups (yrs)					Data sources		
Population	Sex	Parameter	30 - 44	45 - 59	60 - 69	70 - 79	80+	Study site	Year	*N*
Urban black African*	Males	Mean	4.4	4.5	4.7	4.7	4.7	Cape Town (Western Cape)[12]	1990	665
		SD†	0.8	0.7	0.7	0.7	0.7	Mangaung (Free State)[10‡]	1990/1	758
	Females	Mean	4.5	5.0	5.1	5.1	5.1	Durban (KwaZulu-Natal)[13]	1986	232
		SD†	0.6	0.7	0.6	0.6	0.6			
Rural black African*	Males	Mean	4.4	4.6	4.6	4.6	4.6	QwaQwa (Free State)[10‡]	1990/1	853
		SD†	0.7	0.6	0.7	0.7	0.7	Dikgale (Limpopo)[11§]	1997/8	1 494
	Females	Mean	4.4	4.7	5.0	5.0	5.0			
		SD†	0.6	0.7	0.7	0.7	0.7			
Black African	Males	Mean	4.4	4.5	4.7	4.7	4.7	Weighted estimate		
		SD†	0.7	0.7	0.7	0.7	0.7			
	Females	Mean	4.4	4.9	5.1	5.1	5.1			
		SD†	0.6	0.7	0.7	0.7	0.7			
Coloured	Males	Mean	5.7	5.8	5.6	5.6	5.6	Cape Town (Western Cape)[14]	1982	779
		SD†	0.8	0.8	0.7	0.7	0.7	Mamre (Western Cape)[15]	1996	646
	Females	Mean	5.3	6.2	6.4	6.4	6.4			
		SD†	0.7	0.8	0.7	0.7	0.7			
White	Males	Mean	5.8	6.3	6.2	6.2	6.2	Durban (KwaZulu-Natal)[17‡]	1987	354
		SD†	0.9	0.8	0.7	0.7	0.7	Robertson, Swellendam,	1983	2 722
	Females	Mean	5.5	6.4	7.2	7.2	7.2	Riversdal (Western Cape)[18¶]		
		SD†	0.7	0.8	0.9	0.9	0.9	Riversdal, Caledon, Bredasdorp (Western Cape)[19‖]	1993	327
Asian/Indian	Males	Mean	5.8	6.1	5.6	5.6	5.6	Durban (KwaZulu-Natal)[16‡]	1984/6	601
		SD†	0.8	0.8	0.7	0.7	0.7			
	Females	Mean	5.3	5.9	6.1	6.1	6.1			
		SD†	0.7	0.8	0.8	0.8	0.8			
South Africa*	Males	Mean	4.8	5.0	5.2	5.2	5.2	Weighted estimate		
		SD†	0.8	0.9	0.8	0.8	0.8			
	Females	Mean	4.6	5.3	5.7	5.7	5.7			
		SD†	0.7	0.9	0.9	0.9	0.9			

*Rural black African, urban black African and South African average estimates are presented but were not used in the calculations.
†Corrected for regression dilution resulting from time-dependent change in 'usual' level (ratio = 0.625).
‡Oldest age category in study is 55 - 69 years.
§Data of Dikgale study extracted from data from reference 11, youngest age group, 30 - 34 years.
¶Data for men of the CORIS study extracted from data from reference 18.
‖Age group 35 - 44 years.

Table III. Prevalence with serum cholesterol values above 5 mmol/l* by population group, age and sex, South Africa, 2000

		Proportion (%) with serum cholesterol ≥ 5 mmol/1		
Population group	Age group (yrs)	Males	Females	Persons
Black African	30 - 44	21.5	17.4	19.4
	45 - 59	24.5	43.5	34.5
	60+	32.2	54.1	44.9
	30+	23.8	30.9	27.6
Coloured	30 - 44	80.8	66.9	73.6
	45 - 59	84.5	94.8	90.0
	60+	79.6	97.9	90.4
	30+	81.7	79.9	80.7
White	30 - 44	83.9	75.0	79.5
	45 - 59	93.8	95.3	94.6
	60+	96.0	99.4	97.9
	30+	90.0	88.4	89.2
Asian/Indian	30 - 44	84.9	65.1	74.9
	45 - 59	92.3	87.8	89.9
	60+	78.4	90.3	85.2
	30+	86.5	77.4	81.7
South Africa	30 - 44	38.9	30.3	34.4
	45 - 59	50.5	63.2	57.4
	60+	58.0	78.7	70.7
	30+	45.2	49.6	47.6

*Current clinical cut-off for hypercholesterolaemia.

The estimated prevalence of hypercholesterolaemia (TC ≥ 5 mmol/l, the current clinical cut-off) by population group in the age groups 30 years and older is shown in Table III. The differences between the prevalence rates in the black African population and the other three groups are striking, and are consistent with the lower levels of urbanisation and concomitant incomplete adoption of Western lifestyles in this group.

The PAFs for high cholesterol for males, females and adults of 30+ years are shown in Table IV. Attributable fractions were higher in females for all related outcomes and in all population groups. Overall, about 59% of IHD and 29% of ischaemic stroke burden in adult males and females (30+ years of age) were attributable to high cholesterol (≥ 3.8 mmol/l).

High cholesterol was estimated to cause 24 144 deaths (95% uncertainty interval 22 404 - 25 286) or 4.6% (95% uncertainty interval 4.3 - 4.9%) of all deaths in South Africa in 2000. There are more female than male attributable deaths, with attributable deaths from ischaemic stroke in females double those in males (Table IV). Since most cholesterol-related CVD events occurred in middle or old age, the loss of life years comprises a smaller proportion of the total: 222 923 DALYs (95% uncertainty interval 206 712 - 233 460) or 1.4% of all DALYs (95% uncertainty interval 1.3 - 1.4%) in South Africa in 2000.

Age-standardised attributable mortality rates by population group are presented in Fig. 1. Large population group differences were observed, with the highest rates seen in Indian males and females, followed by white males and females. Coloured adults had intermediate rates, with very low rates observed in the black African population group. It is interesting to note that in the Indian and white groups, age-standardised cholesterol-attributable mortality rates in males were higher than in females. However, in the black African and coloured groups the rates in females were slightly higher than in males.

The contribution of IHD and ischaemic stroke to total attributable burden by population group is shown in Fig. 2. While ischaemic stroke and IHD accounted for similar proportions of total burden in the black African population group, IHD accounted for the majority of the burden in the Indian and white population groups, with a very small contribution from ischaemic stroke.

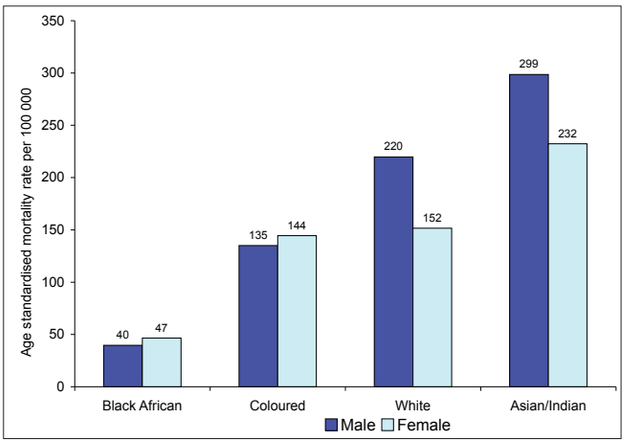

Fig. 1. Age-standardised cholesterol-attributable mortality rates by population group and sex, South Africa, 2000.

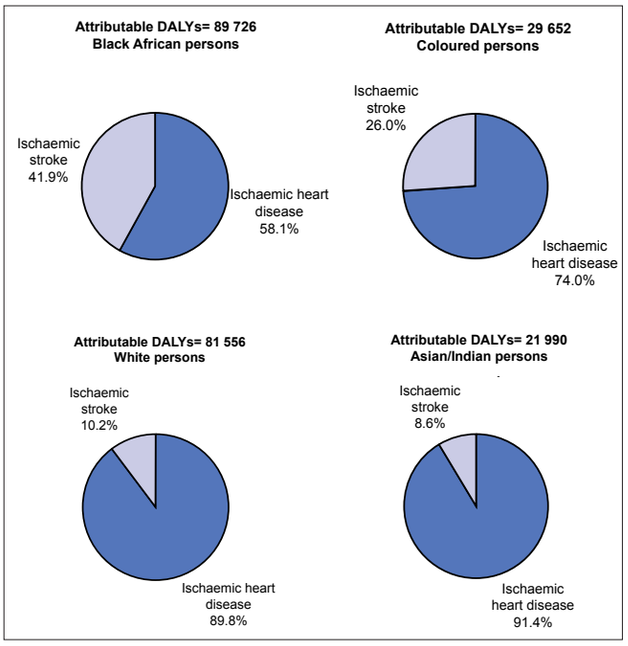

Fig. 2. Burden attributable to high cholesterol by population group, South Africa, 2000.

Discussion

Overall, the results suggest that a considerable proportion of CVD in South Africa can be attributed to non-optimal cholesterol levels, which translates into a high proportion of deaths and disability. Worldwide, 56% of IHD mortality and disease burden was attributable to cholesterol levels of more than 3.8 mmol/l, which translated to 3.6 million deaths in the year 2000.[4] In South Africa, 59% of IHD was attributable to raised cholesterol. In addition, 29% of ischaemic stroke was attributable to raised cholesterol, which compares with the worldwide estimate of 32% (range 25 - 45% by subregion).[4] Overall, 4.4 million deaths (about 7.9% of the total) and 40.4 million DALYs (2.8% of the total) worldwide were estimated to be due to non-optimal cholesterol levels. About 40% of the cholesterol-related attributable burden occurred in developed subregions, 20% in low-mortality developing sub-regions, and a further 40% in high-mortality developing subregions. The relative impact of attributable deaths and DALYs was highest in the European subregions, with the highest mean cholesterol levels.[4]

In South Africa, although the national IHD PAFs (59%) were similar to the global average, there were marked population group differences, ranging from 42% of IHD in the black African population to 73% in the white population. Similarly, PAFs for ischaemic stroke were as low as 26% of disease burden in the black African population and as high as 48% in the white population, giving an overall average of 29%, which is similar to the global average.

The attributable mortality by population group spanned the full spectrum observed globally. Cholesterol-attributable mortality was highest in the Indian population, where it accounted for 22.2% (95% uncertainty interval 20.7 - 23.3%) of all deaths, followed by the white population, where it accounted for 20.5% (95% uncertainty interval 18.5 - 21.8%) of all deaths in 2000. Attributable mortality was lowest in the black African group, accounting for only 1.8% (95% uncertainty interval 1.5 - 2.0%) of all deaths. In the coloured population, 8.8% (95% uncertainty interval 7.9 - 9.5%) of all deaths in 2000 could be attributed to non-optimal cholesterol levels.

The TC values (Table II) in the black African population group were generally lower than the levels found in the other three population groups, with differences being larger in older participants than in younger ones. This may suggest that the younger black African participants have already adopted a more westernised diet and lifestyle. The ratio of HDLC to TC has generally been found to be higher in the studies conducted in the black African population group[10,12] than in the other three groups. This suggests that the black African population group with its lower TC levels is experiencing additional protection against atherosclerosis-related diseases by virtue of its relatively higher proportion of protective HDLC.[27] The implication of this is that the real estimated impact of high TC in the black African population might have been overestimated in the data presented.

Only six of the studies reported on the LDLC levels in the black African and coloured populations.[10-15] As would be expected, LDLC levels in the black African population group were significantly lower than in the coloured group, again pointing to the relatively lower level of risk in the black African group compared with others.[27]

Traditionally in the black African population TC levels were found to be low.[11,12] It is therefore an unexpected finding that about 3.5 million (28% of all) black African people 30 years and older were above the clinical cut-off for hypercholesterolaemia (TC level 5 mmol/l or higher), a prevalence rate similar to that for hypertension in this ethnic group. This suggests that health services should consider screening for high cholesterol in black African people aged 30 years or older with other cardiovascular risk factors. Furthermore, older women were found to have hypercholesterolaemia far more frequently than older men; this may be associated with the high obesity rates recorded in older black African women. In the other population groups hypercholesterolaemia in men occurred at least as frequently as in women, with younger women having lower prevalence rates than men and older women having much higher rates than men. By extrapolating the prevalence to all South Africans aged 30 years or older, these findings indicate that almost 8 million people carry a risk for a chronic disease of lifestyle by virtue of their total serum cholesterol level using the clinical cut-off of 5 mmol/l. However, it needs to be remembered that for the black African population the TC values represent a higher proportion of protective HDLC levels than in the other groups.

Interventions should follow a two-pronged approach: population-wide interventions aimed at lowering cholesterol levels and other cardiovascular risk factors among the whole population, and effective clinical management for individuals who are at high absolute risk for CVD.

High blood cholesterol can be treated effectively by lifestyle modification of diet and physical activity, combined with the use of medication if the lifestyle modification does not result in achieving normal blood cholesterol levels.[1] The lifestyle approach includes a diet with reduced intake of all

Table IV. Burden attributable to high cholesterol, South Africa, 2000

Outcome	Male			Female			Persons	
	PAF (%)	Deaths	DALYs	PAF (%)	Deaths	DALYs	PAF (%)	Deaths	DALYs
Ischaemic heart disease	57.7	9 265	94 234	61.2	9 868	73 166	59.2	19 133	167 401
Ischaemic stroke	26.3	1 711	20 835	31.7	3 300	34 688	29.4	5 011	55 523
Total		**10 976**	**115 069**		**13 168**	**107 855**		**24 144**	**222 923**
95% uncertainty interval		10 324 - 11 441	107 228 - 120 663		11 943 - 13 957	98 687 - 113 976		22 404 - 25 286	206 712 - 233 460
% of total burden		**4.0%**	**1.4%**		**5.3%**	**1.4%**		**4.6%**	**1.4%**
95% uncertainty interval		3.8 - 4.2%	1.3 - 1.4%		4.8 - 5.7%	1.3 - 1.5%		4.3 - 4.9%	1.3 - 1.4%

PAF = population-attributable fraction; DALYs = disability-adjusted life years.

fats, and replacement of saturated fats and trans-fatty acids with mono- and polyunsaturated fats. An increase of soluble fibre from unrefined cereals, fruits and vegetables also reduces blood cholesterol, as do plant sterols and stanols which are now added to some margarines.[28] Body mass should be reduced to normal levels along with maintaining a regular pattern of aerobic physical activity.[1] Cholesterol-lowering medication has been shown to save lives.[29]

Regardless of treatment choice, guidelines defining eligibility for medication use must focus on absolute or global clinical risk, in which high cholesterol is one of many CVD risk factors assessed, instead of individual risk factor approaches. There has been a shift away from considering the management of individual risk factors based on a single threshold. The review by Jackson *et al*.[30] shows that providing people at high absolute risk for CVD with blood pressure and cholesterol-lowering medications is a more effective approach than considering single risk factor thresholds in isolation. They argue that clinical management guidelines for the separate risk factors be replaced by an integrated management guideline for CVD.

In their review of cost-effective interventions for developing countries, Rogers *et al*.[31] conclude that providing people at high absolute risk for CVD with generic blood pressure and cholesterol-lowering agents is cost-effective. However, there remains an extensive research agenda for the development, implementation and evaluation of such a strategy. They argue that there must be parallel efforts to reduce the underlying risks for CVD. However, as the cost-effectiveness of population-wide initiatives is very sensitive to variations in the risk for CVD and the nature of the intervention, there is a need for further research.[31]

The experience internationally with highly active anti-retroviral treatment (HAART) has shown that these drugs may result in a metabolic syndrome qualitatively similar to that seen in obesity-related diabetes (diabesity).[32-34] These patients develop insulin resistance which is frequently severe enough to cause lipodystrophy,[35] which in turn is manifested by a central distribution of adiposity, but at other times by lipo-atrophy – an apparent paradox also seen in other causes of insulin resistance. The dyslipidaemia also manifests as a high-triglyceride/low-HDLC syndrome, and severe cases can present as a chylomicronaemia syndrome,[33] and is associated with an increased cardiovascular risk,[36] mediated by mechanisms very similar to those postulated in diabesity.

South Africa is in the middle of an HIV epidemic which is predicted to increase, and as HAART has now become more readily available, we can expect an increase in this peculiar insulin resistance syndrome and the associated increased risk for IHD in patients with AIDS on antiretroviral treatment.

A limitation of this study is that it is not based on TC data from recent national representative surveys, but estimated from a number of smaller surveys conducted in localised areas. Some of these were conducted more than 2 decades ago, and may not reflect current TC levels in these populations since national awareness campaigns have influenced lifestyle and diet, particularly in the white population.[19]

Conclusions

High TC is found in more South Africans than anticipated, and is an important cardiovascular risk factor in all population groups in South Africa. The data also suggest that TC levels are increasing in the black African population, particularly in the younger and more urbanised sector. This trend will continue unless the necessary population-based interventions are initiated. This will require promotion of a prudent diet for all South Africans by the National Department of Health, the Heart and Stroke Foundation of South Africa and the food industry.

The AIDS epidemic and the treatment of large numbers of patients on antiretroviral agents will also affect the pattern of dyslipidaemia in the country; the use of HAART results in insulin resistance, diabesity and abnormal lipid profiles.

To accurately assess the lipid-related risk for IHD in black African people, it is necessary to avoid TC measurement and to focus on measuring LDLC levels or ApoB lipoprotein levels if cost-effective ways of identifying people at risk for IHD are to be found.

The data presented here emphasise that dyslipidaemia in South Africa is mostly an unrecognised – and consequently undiagnosed and poorly treated – condition. This will have to be addressed if IHD and stroke rates are to be contained in the country.

The other members of the Burden of Disease Research Unit of the South African Medical Research Council: Pam Groenewald, Nadine Nannan, Michelle Schneider, Desireé Pieterse, Jané Joubert, Beatrice Nojilana, Karin Barnard and Elize de Kock are thanked for their valuable contribution to the South African Comparative Risk Assessment Project. Ms Leverne Gething is gratefully acknowledged for editing the manuscript. Ms Ria Laubscher and Dr Lize van der Merwe of the MRC Biostatistics Unit made contributions via their statistical expertise and assistance. Our sincere gratitude is also expressed for the valuable contribution of Associate Professor Theo Vos of the School of Population Health, University of Queensland. We thank him not only for providing technical expertise and assistance, but also for his enthusiasm and support from the initial planning stages of this project. We also acknowledge the important contributions of Carlene Lawes, Anthony Rodgers and Stephen Vander Hoorn from the Clinical Trials Research Unit of the University of Auckland.

References

1. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285: 2486-2497.

2. Yusuf S, Hawken S, Ôunpuu S, *et al*. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; 364: 937-952.
3. World Health Organization. *The World Health Report 2002. Reducing Risks, Promoting Healthy Life*. Geneva: WHO, 2002.
4. Lawes CMM, Vander Hoorn S, Law MR, Rodgers A. High cholesterol. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, eds. *Comparative Quantification of Health Risks, Global and Regional Burden of Disease Attributable to Selected Major Risk Factors*. Geneva: WHO, 2004: 391-496.
5. Ranjith N, Verho NK, Verho M, Winkelmann BR. Acute myocardial infarction in a young South African Indian-based population: patient characteristics on admission and gender-specific risk factor prevalence. *Curr Med Res Opin* 2002; 18: 242-248.
6. Walker AR. Changes in public health in South Africa from 1876. *J R Soc Health* 2001; 121: 85-93.
7. Seedat YK, Mayet FG. Risk factors leading to coronary heart disease among the black, Indian and white peoples of Durban. *J Hum Hypertens* 1996; 10: Suppl 3, S93-S94.
8. Pestana JA, Steyn K, Leiman A, Hartzenberg GM. The direct and indirect costs of cardiovascular disease in South Africa in 1991. *S Afr Med J* 1996; 86: 679-684.
9. Kruger HS, Venter CS, Vorster HH. Physical inactivity as a risk factor for cardiovascular disease in communities undergoing rural to urban transition: the THUSA study. *Cardiovasc J S Afr* 2003; 14: 16-23, quiz 23,28.
10. Mollentze WF, Moore AJ, Steyn AF, *et al*. Coronary heart disease risk factors in a rural and urban Orange Free State black population. *S Afr Med J* 1995; 85: 90-96.
11. Alberts M, Urban P, Steyn K, *et al*. Prevalence of cardiovascular diseases and associated risk factors in a rural black population of South Africa. *Eur J Cardiovascular Prev Rehabil* 2005; 12: 347-354.
12. Oelofse A, Jooste PL, Steyn K, *et al*. The lipid and lipoprotein profile of the urban black South African population of the Cape Peninsula – the BRISK study. *S Afr Med J* 1996; 86: 162-166.
13. Seedat YK, Mayet FGH, Latif GH, Joubert G. Risk factors and coronary heart disease in Durban blacks – the missing links. *S Afr Med J* 1992; 82: 251-256.
14. Steyn K, Jooste PL, Langenhoven ML, *et al*. Coronary risk factors in the coloured population of the Cape Peninsula. *S Afr Med J* 1985; 67: 619-625.
15. Steyn K, Levitt NS, Hoffman M, *et al*. The global cardiovascular disease risk pattern in a peri-urban working-class community in South Africa. The Mamre Study. *Ethn Dis* 2004; 14: 233-241.
16. Seedat YK, Mayet FGH, Khan S, Somers SR, Joubert G. Risk factors for coronary heart disease in the Indians of Durban. *S Afr Med J* 1990; 78: 447-454.
17. Seedat YK, Mayet FGH, Gouws E. Risk factors for coronary heart disease in the white community of Durban. *S Afr Med J* 1994; 84: 257-262.
18. Rossouw JE, Jooste PL, Chalton DO, *et al*. Community-based Intervention: The Coronary Risk Factor Study (CORIS). *Int J Epidemiol* 1993; 22: 428-438.
19. Steyn K, Steyn M, Swanepoel ASP, *et al*. Twelve-year results of the Coronary Risk Factor Study (CORIS). *Int J Epidemiol* 1997; 26: 964-971.
20. Ezzati M, Lopez A, Rodgers A, Vander Hoorn S, Murray C. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; 360: 1347-1360.
21. Norman R, Bradshaw D, Schneider M, Pieterse D, Groenewald P. Revised Burden of Disease Estimates for the Comparative Risk Factor Assessment, South Africa 2000. http://www.mrc.ac.za/bod/bod.htm (last accessed 18 January 2007).
22. Asia-Pacific Cohort Studies Collaboration (APCSC). Determinants of cardiovascular disease in the Asia Pacific region: protocol for a collaborative overview of cohort studies. *Cardiovascular Disease Prevention* 1999; 2: 281-289.
23. World Health Organization. *International Classification of Diseases and Related Health Conditions*. 10th ed. Geneva: WHO, 1992.
24. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360: 1903-1913.
25. MacMahon S, Peto R, Cutler J, *et al*. Blood pressure, stroke, and coronary heart disease. Part 1: Prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution bias. *Lancet* 1990; 335: 765-774.
26. Palisade Corporation. @RISK software version 4.5 for Excel. New York: Palisade Corporation, 2002.
27. Maritz FJ. Dyslipidaemia in South Africa. In: Steyn K, Fourie J, Temple N, eds. *Chronic Disease of Lifestyle in South Africa: 1995-2005*. Technical Report. Cape Town: South African Medical Research Council, 2006.
28. Law MR. Plant sterol and stanol margarines and health. *BMJ* 2000; 320: 861-864.
29. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: Systematic review and meta-analysis. *BMJ* 2003; 326: 1423.
30. Jackson R, Lawes CMM, Bennett DA, Milne RJ, Rodgers A. Treatment with drugs to lower blood pressure and blood cholesterol based on an individual's absolute cardiovascular risk. *Lancet* 2005; 365: 434-441.
31. Rogers A, Lawes CMM, Gaziano T, Vos T. The growing burden of risk from high blood pressure, cholesterol and bodyweight. In: Jamison DT, Breman JG, Measham AR, *et al*., eds. *Disease Control Priorities in Developing Countries*. 2nd ed. Washington, DC: Oxford University Press and The World Bank, 2006.
32. Koutkia P, Grinspoon S. HIV-associated lipodystrophy: pathogenesis, prognosis, treatment, and controversies. *Ann Rev Med* 2004; 55: 303-317.
33. Calza L, Manfredi R, Chiodo F. Dyslipidaemia associated with antiretroviral therapy in HIV-infected patients. *J Antimicrob Chemother* 2004; 53: 10-14.
34. Barbaro G. Highly active antiretroviral therapy and the cardiovascular system: the heart of the matter. *Pharmacology* 2003; 69: 177-179.
35. Tershakovec AM, Frank I, Rader D. HIV-related lipodystrophy and related factors. *Atherosclerosis* 2004; 174: 1-10.
36. Sekhar RV, Jahoor F, Pownall HJ, Ballantyne CM, Balasubramanyam A. Cardiovascular implications of HIV-associated dyslipidemic lipodystrophy. *Curr Atheroscler Rep* 2004; 6: 173-179.