Implications of scaling-up cardiovascular disease treatment in South Africa: a microsimulation and cost-effectiveness analysis

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Abstract

Background
Cardiovascular diseases and their risk factors—particularly hypertension, dyslipidemia, and diabetes—have become an increasing concern for middle-income countries. Here, using newly-available, nationally-representative data, we addressed how cardiovascular risk factors are distributed across sub-populations within South Africa, and identified which cardiovascular treatments should be prioritized.

Methods
We analyzed data from a recent, nationally representative South African National Health and Nutrition Examination Survey (SANHANES, 2012, N = 17,743 individuals aged 15 and older), and created a microsimulation model to estimate the health and economic implications of different two globally recognized treatment recommendations: the World Health Organization’s Package of Essential Non-communicable disease interventions (PEN), and South Africa’s Primary Care 101 Guidelines, which are adopted in various other countries.

Findings
South Africans aged 15 years and older had a high prevalence of hypertension (24.8%), dyslipidemia (17.5%), and diabetes (15.3%), but few were treated for dyslipidemia (treatment rates of 71.4%, 3.4%, and 58.4%, respectively). Prevalence was disproportionately high and treatment low among males, black, and poor populations. South Africans in our simulated population experienced a loss of 40.0 DALYs per 1,000 persons per year (95% CI: 29.5, 52.0) from cardiovascular disease or type 2 diabetes complications at current treatment levels, which lowered to 32.9 (95% CI: 24.4, 44.7) under WHO PEN implementation, and to 32.5 (95% CI: 24.4, 44.8) under SA PC 101 implementation, with between a 4.2 (WHO) and 12.6 (SA) percentage increase in blood pressure treatment, 16.0 (WHO) and 14.9 (SA) percentage increase in lipid treatment, and 1.2 (WHO) and 0.6 (SA) percentage increase in glucose control medications. The incremental cost-effectiveness of implementing SA PC 101 over current treatment would
be a saving of $24,902 per DALY averted (95% CI: $14,666, $62,579); compared to a
saving of $17,587 per DALY averted for implementing WHO PEN instead of current
treatment (95% CI: $1,840, $42,589). The cost savings were driven primarily by blood
pressure and lipid therapies, despite the latter being less commonly prescribed than
glucose therapies currently. Under WHO PEN, male, black African, and poor populations
benefited most; under SA primary care 101 guidelines, males benefitted more than
females. Implementing either of these guidelines at 70% coverage would lead reduce
premature mortality due to cardiovascular diseases by over 40% by 2030.

Interpretation
Cardiovascular risk factors are common and disproportionate among disadvantaged
populations in South Africa. Treatment with blood pressure agents and statins may need
greater prioritization than blood glucose therapies, which contrasts with observed
treatment levels despite a lower monthly cost of blood pressure or statin treatment than of
sulfonylurea or insulin treatment.

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Introduction

Cardiovascular diseases and their risk factors—particularly hypertension, dyslipidemia, and diabetes—have become an increasing concern in middle-income countries. While overall prevalence and mortality statistics for cardiovascular disease have been estimated through imputation methods providing a broad sense of the rising burden of disease at country-level and the expected economic consequences of NCDs, only recently have detailed, nationally-representative surveys of cardiovascular disease risk factors been completed. These surveys provide data to answer critical questions such as whether lower-income populations are affected, or only higher-income populations who may be less in need of public health-sector intervention; which strategies and interventions (e.g., blood pressure, lipid management, or diabetes glucose management) are highest priorities given the distribution of disease and avertable complications; and what level of healthcare system budgeting may be necessary and cost-effective for scaling-up management? Despite these questions being posed, few studies have aimed to assess the implications of interventions for countries using real-population survey data rather than imputed aggregate country-wide averages.

NCD management questions are of particular interest to policymakers in South Africa, a country with severe levels of poverty and inequality as a result of its apartheid history. South Africa notably continues to experience a high burden of HIV and tuberculosis, such that dual epidemics of infectious diseases and cardiovascular diseases co-occur in the population, with dire implications on limited healthcare resources. Population-level chronic disease surveys recently conducted in South Africa now provide a uniquely comprehensive understanding of the variations in cardiovascular disease risk and availability and coverage of important cardiovascular disease risk factor management interventions. South Africa is also representative of many middle-income countries experiencing very large socioeconomic inequalities, a rapidly increasing burden of cardiovascular diseases and risk factors, and with a goal of providing more comprehensive healthcare services by governments faced with a finite healthcare budget.

Here, we address how cardiovascular risk factors are distributed across lower-versus higher-income populations in South Africa, and which cardiovascular treatments should be prioritized. We capture both inequalities in risk factors and treatment access—
including for hypertension, dyslipidemia, and type 2 diabetes mellitus. We examine variations in cardiovascular disease risk factors by urban/rural residence, race/ethnicity, and socioeconomic status. We specifically integrate and use microsimulation to estimate the health and economic implications of scaling-up treatment to meet recommendations in two alternative guidelines: the World Health Organization’s Package of Essential Non-communicable disease interventions (PEN), and South Africa’s Primary Care 101 Guidelines.\textsuperscript{9,10} We additionally investigated whether implementation of either guideline would lead to a reduction in premature mortality due to cardiovascular disease risk factors of 30\% by 2030, which is a key aim of the Sustainable Development Goals (Goal 3.4).\textsuperscript{3,4}
Methods

Model overview

The modeling proceeded in three steps (Figure 1). First, a demographically-representative simulated population for South Africa was constructed based on the most recent Census data and population projections, incorporating estimated population sizes by age, sex, race/ethnicity, and socioeconomic status (as measured by the Multi-dimensional Poverty Index). Second, by repeated sampling from data from the South African National Health and Nutrition Examination Survey (SANHANES, 2012, specifically N = 17,743 individuals aged 15 and older for whom we had data on cardiovascular risk factors), each person in the simulated population was assigned systolic and diastolic blood pressure, total and high-density lipoprotein cholesterol, hemoglobin A1c, and history of cardiovascular disease (myocardial infarction, stroke, and/or congestive heart failure), type 2 diabetes mellitus, and treatment (with blood pressure medications, statins, and/or diabetes medications). SANHANES was a stratified, community-based survey, physical exam, and laboratory study of South Africans across urban and rural areas of all provinces, which had the most comprehensive data available to us on measured cardiovascular disease risk factors. Monte Carlo sampling was performed to capture the co-variations between biomarkers and disease history in the survey, following multiple imputation of missing data with chained equations, and adjustment with survey sample weights to construct population-representative estimates. The Monte Carlo sample was equal to the South African population, and used the complete census survey data, incorporating the SANHANES survey sample weights, and performing repeated sampling (10,000 times) to generate the uncertainty in projecting from the stratified survey sample population to the full national population. Prespecified subgroup analyses of the SANHANES data were performed by sex, black African or non-black African (which includes ‘White’, ‘Colored’, ‘Indian/Asian’, and ‘other’), and poor or non-poor (as defined by South Africa’s multi-dimensional poverty index with a composite score cut-point of >0.33 to be considered poor), to identify variations in risk factors and treatment relations among key societal divisions in the population. Third, cost-effectiveness analysis was performed comparing the WHO PEN
and South African Primary Care 101 (SA PC 101) guidelines.\textsuperscript{9,10} Following current cost-effectiveness analysis guidelines,\textsuperscript{14} the disability-adjusted life-years (DALYs) averted due to treatment of hypertension, dyslipidemia, and type 2 diabetes mellitus, and associated costs of treatment, were computed for each simulated individual, adopting a life-course approach to calculate the DALYs averted and costs accumulated over the remainder of the anticipated lifetime of each person alive or entering the population aged 16 years or older during a simulated 10-year policy planning horizon. Following current modeling guidelines,\textsuperscript{15} the policy planning horizon is the period over which the population of interest is determined, such that 10 years means that all persons already above age 15 years or newly entering the 15+ year old age group over the next 10 years are simulated; the cohort is then followed over their full life-course, meaning that the actual simulation period is typically longer than 10 years, subject to the individual’s simulated life course over each stochastic iteration subject to the age and sex-specific mortality rate. All parameters and equations are detailed in the \textbf{Appendix}, with a link to program code for replication.

\textbf{Treatment simulations}

Three treatment scenarios were simulated.

First, in the \textit{base case simulation}, existing levels of treatment were continued based on the rate of self-reported treatment for elevated blood pressure, dyslipidemia, and type 2 diabetes mellitus, given measured levels of blood pressure (systolic and diastolic), lipids (total and high-density lipoprotein cholesterol), and hemoglobin A1c in the SANHANES.

Second, in the \textit{WHO PEN simulation}, treatments were added to achieve the blood pressure, lipid, and diabetes glucose control guidelines pictured in \textbf{Figure 2A}.

Alternatively, in the third and final simulation, the \textit{SA PC 101 simulation}, treatments were added to achieve the alternative blood pressure, lipid, and diabetes glucose control guidelines pictured in \textbf{Figure 2B}.

In all three simulations, we compared outcomes at the aspirational level of achieving access to treatment among 70\% of the population (varied from 60\% to 80\% in sensitivity analyses), with 70\% of the population with access to treatment subsequently
adhering to the therapy and receiving DALY benefits while the other 30% with access produced costs from receiving therapy but not DALY benefits; these estimates are based on the best-case scenarios observed in European countries,\textsuperscript{16–19} and were applied equally between the two guideline simulations for fair comparison.

*Primary and secondary outcome measures*

The primary outcome was total DALYs averted through treatment from all cardiovascular disease or microvascular type 2 diabetes complications, per 1,000 population. Secondary component outcomes included in the total were DALYs averted from each of: atherosclerotic cardiovascular disease (nonfatal myocardial infarctions or coronary heart disease deaths, or fatal or nonfatal stroke); congestive heart failure exacerbations; renal failure/end-stage renal disease (ESRD) due to hypertensive or diabetic nephropathy; severe vision loss attributable to diabetic retinopathy; and pressure sensation loss or further severe diabetic neuropathy. DALY disutility weights for all outcomes were taken from previously-published primary surveys,\textsuperscript{20} and incorporated into a total DALY loss calculation for each simulated individual by calculating their individualized baseline annual risk of each outcome, subject to competing risks from cardiovascular and non-cardiovascular all-cause mortality for their age and sex, and adjusted for the disability weight for each condition.\textsuperscript{21–23} As per each guidelines’ recommendation, the baseline risk of myocardial infarctions and strokes was estimated using the WHO-ISH equations calibrated to the South African population for the WHO PEN guidelines by calibrating the baseline hazard rate in the equations to the myocardial infarction and stroke rate in the population,\textsuperscript{24} and using the Harvard/NHANES equations for the SA PC 101 guidelines,\textsuperscript{25} with twice the baseline risk of recurrence estimated for those with a prior history of myocardial infarction or stroke.\textsuperscript{26} The baseline risk of all other outcomes was based on the RECODe equations calibrated to the South African population,\textsuperscript{27,28} for the portion of the population without previous self-reported history of the pertinent outcome; the baseline hazard rate was calibrated for each outcome to match the Global Burden of Disease incidence estimates.\textsuperscript{29} We note there are no cardiovascular risk equations developed using longitudinal data from South Africa, so we deferred to the risk equations specified in each guideline to estimate that guidelines’ impact, for
unbiased comparison (the estimated outcomes were not substantially different between calculators, as discussed in Results).

Relative risk reductions through treatment

To estimate the DALYs averted by treatment, the baseline DALYs associated with each individual for each condition were adjusted by the relative risk reduction attributable to each treatment (see detailed tables and equations in Appendix). For blood pressure treatment, the relative risk reduction for myocardial infarctions and strokes were estimated using the Smith-Spangler equation calculating relative risk as a function of age and change in systolic blood pressure; the equations were previously validated against data from a meta-analysis of 61 randomized trials. Anticipated change in systolic blood pressure was estimated from the mean reduction in systolic blood pressure estimated for each medication in a prospective meta-analysis of 354 randomized trials, given the typical drug choice and dosing recommended by each guideline (Figure 2). The relative risk reduction from blood pressure (specifically angiotensin-converting-enzyme inhibitor) therapy for congestive heart failure exacerbations was estimated from the SOLVD trial, and for renal failure was estimated by a prior systematic review estimating relative risk reduction by systolic blood pressure reduction. For dyslipidemia treatment, the relative risk reduction for myocardial infarction and stroke from statin treatment (given the South African guideline’s recommendation of simvastatin 10mg daily, Figure 2) was obtained from a meta-analysis of 27 randomized trials. Finally, for glycemic treatment of type 2 diabetes, the relative risk reductions for each of the nephropathy, neuropathy and retinopathy outcomes from glucose control were each taken from a prior systematic review and meta-analysis of randomized trials estimating relative risk reduction by hemoglobin A1c achieved, where the estimated hemoglobin A1c reduction typically produced by each therapy in the guidelines (Figure 2) was taken from an evidence-based review incorporating the dosing guidelines detailed in the Appendix.

Cost-effectiveness analyses

Concordant with recent updates to cost-effectiveness analysis guidelines, we performed cost-effectiveness analysis over the life-courses of individuals in the simulated
population. DALYs and costs were calculated from a health care sector perspective, in
the absence of reliable and consistent data on time costs, unpaid caregiver costs,
transportation costs, labor market earnings lost, and social service costs for a societal
perspective. An impact inventory specifying each set of costs and their sources is
specified in the Appendix, along with the CHEERS guideline checklist for cost-
effectiveness analysis reporting. In short, to calculate costs, we extracted information on
the costs of care for each risk factor and outcome from the 2012 South Africa Department
of Health Uniform Patient Fee Schedule for externally funded patients, as these most
closely align with the costs to the health care services of providing care. For the costs of
blood tests, 2012 data were not available, so we used fees from the South Africa National
Health Laboratory Services for 2013. Where there were two or more cost-options for the
treatment components of a given risk factor or outcome, we chose the most conservative
one. All costs were updated for inflation to 2018 U.S. Dollars for global comparison, and
both costs and DALYs were discounted at a standard 3% annual rate. Two incremental
cost-effectiveness ratios (ICERs) were computed: (i) the ICER of expanding from
existing levels of treatment reflected in SANHANES to the WHO PEN guidelines; and
(ii) the ICER of expanding from existing levels of treatment reflected in SANHANES to
the South Africa Primary Care 101 guidelines.

Uncertainty analyses
Simulations were repeated 10,000 times while sampling with replacement from
the distribution of all input parameter values (see Appendix), to compute 95%
confidence intervals around the primary and secondary outcome metrics, as well as
around the ICER calculations.

Analyses were performed in R (v. 3.4.3., The R Foundation for Statistical
Computing, Vienna). The study was deemed exempt from human subjects review by the
Stanford University Institutional Review Board (e-Protocol #39274).

Role of the funding source
The funders had no role in the design, conduct, analysis, or writing up of the
study. The corresponding author had full access to the data and took the decision to
submit for publication.
Results

Demographic distribution of current risk and treatment

The SANHANES input data (2012, N = 17,743)\(^8\) revealed high levels of hypertension, dyslipidemia, and type 2 diabetes mellitus among the South African population aged 15 years and older, yet most of the population reported being untreated for these conditions (Table 1). Based on the SANHANES study sample weights, 24.8% of the South African population aged 15 years and older would have hypertension (BP \(\geq 140/90\) mmHg per South African definitions, or on treatment), 17.5% would have dyslipidemia (total cholesterol \(\geq 6.21\) mmol/L, low-density lipoprotein cholesterol \(\geq 4.14\) mmol/L, high-density lipoprotein cholesterol \(< 1.03\) mmol/L, triglycerides \(\geq 2.25\) mmol/L, or on treatment\(^37\)), and 15.3% would have diabetes mellitus or diabetes mellitus (hemoglobin A1c \(\geq 6.5\%\) [48 mmol/mol] or on treatment\(^38\)).

The SANHANES data revealed low levels of treatment among male, African, and poor populations (as defined by South Africa’s multi-dimensional poverty index \(^{11,12}\)), with lipid-lowering therapy being particularly uncommon (Table 1). SANHANES self-reported treatment survey questions suggested that 71.4% of people with hypertension received treatment, of whom 70.7% achieved a blood pressure \(\leq 140/90\) mmHg; by contrast, only 3.4% of those with dyslipidemia received statin treatment, among whom 11.3% achieved LDL \(\leq 2.5\) mmol/L, but 58.4% of those with diabetes received glucose-lowering treatment, among whom 8.9% achieved hemoglobin A1c \(\leq 7\%\).

Base case simulation

In the base case simulation in which the existing levels of treatment were continued, our microsimulation—accounting for competing mortality risks over the life-course—suggested that the simulated population would experience a loss of 40.0 DALYs from cardiovascular disease or type 2 diabetes microvascular complications (95% CI: 29.5, 52.0), per 1,000 population per year.\(^{39}\) Of the 40.0 DALYs lost per 1,000 population per year, 42% were from years of life lost (YLLs based on WHO life expectancy estimates\(^{40}\)), while the remaining 58% were from years of life lived with disability (YLDs). The total 40.0 DALYs lost per 1,000 per year were also 73% attributable to cardiovascular disease, versus 27% attributable to type 2 diabetes microvascular...
complications. The base case simulation suggested that the majority of estimated DALYs lost were attributable to atherosclerotic cardiovascular disease (myocardial infarctions and strokes; 18.7 per 1,000 per year), followed by congestive heart failure (10.7 per 1,000 per year), renal failure/ESRD (9.2 per 1,000 per year), diabetic retinopathy (0.8 per 1,000 per year), and diabetic neuropathy (0.6 per 1,000 per year; Table 2).

In the base case simulation, the overall premature mortality rate (death rate for those under 70 years old) due to CVD was 39.5 per 1,000 population per year (95% CI: 28.0, 52.0). The populations facing the highest DALY losses from cardiovascular disease and type 2 diabetes complications were male (64.3% of total DALYs lost, with the remaining 35.7% among females), black African (57.6% of total DALYS lost, with the remaining 42.4% being among non-black Africans), and poor (60.3% of total DALYs lost, with the remaining 39.7% being among non-poor populations by the Multi-Dimensional Poverty Index measure\textsuperscript{11,12}).

The base case cost analysis suggested an average cost of $607,820 per 1,000 per year for cardiovascular and type 2 diabetes complications (95% CI: $513,818, $705,805), of which the majority of dollars spent were attributable to medical treatment for atherosclerotic cardiovascular disease ($248,108 per 1,000 per year), followed by type 2 diabetes ($183,006 per 1,000 per year), then end-stage renal disease ($138,195 per 1,000 per year; Table 2).

\textit{WHO PEN simulation}

WHO PEN guideline implementation would be expected to produce a 4.2 percentage point rise in the proportion of the population prescribed blood pressure (BP) medications, 16.0 percentage point rise in the proportion of the population prescribed statins, and a 1.2 percentage point rise in the proportion of the population prescribed glucose-lowering medications. A small portion of people would be removed from medication because they would not be indicated to have treatment under the WHO PEN guidelines despite currently being on treatment (7% of those currently on BP medications, 1% of those currently on statins, and 1% of those currently on glucose-lowering medications). Rather than simply prescribing a higher number of medications, the WHO PEN implementation also increased the targeting of medications towards those
at highest risk for cardiovascular disease and type 2 diabetes complications. Specifically, in the base case simulation, the average atherosclerotic cardiovascular disease risk for those prescribed BP or statin medications was 25.9% over 10 years, and the average risk for any microvascular complication of diabetes for those prescribed glucose-lowering medications was 24.4% over 10 years. By contrast, in the WHO PEN simulation, the average atherosclerotic cardiovascular disease risk for those prescribed BP or statin medications was 31.1% over 10 years, and the average risk for any microvascular complication of diabetes for those prescribed glucose-lowering medications was 26.7% over 10 years.

South Africans in our simulated population experienced a loss of 32.9 DALYs from cardiovascular disease or type 2 diabetes complications (95% CI: 24.4, 44.7), per 1,000 population per year from implementing WHO PEN, down from 40.0 DALYs per 1,000 per year in the base case simulation of current treatment levels. The largest improvements in DALYs lost to cardiovascular disease and type 2 diabetes complications from implementing WHO PEN, versus the current levels of treatment, were from atherosclerotic cardiovascular disease (5.0 DALYs averted per 1,000 population per year), followed by renal failure/ESRD (1.0 DALYs averted per 1,000 population per year), then congestive heart failure (0.8 DALYs averted per 1,000 population per year), diabetic retinopathy (0.2 DALYs averted per 1,000 population per year), and finally diabetic neuropathy (0.1 DALYs averted per 1,000 population per year; Table 2). Male, black African, and poor populations benefited most (Figure 3). The overall premature mortality rate (death rate for those under 70 years old) due to CVD was 23.4 per 1,000 population per year (95% CI: 14.0, 34.0), down from 39.5 in the base case (a 40.8% reduction).

Implementation of the WHO PEN guidelines increased costs from treatment of hypertension, dyslipidemia, and glycemic treatment for type 2 diabetes, while saving costs through averted atherosclerotic cardiovascular disease events, congestive heart failure exacerbations, and microvascular complications of diabetes (Table 2). The net cost estimates for the WHO PEN simulation were negative due to averted cardiovascular and microvascular events, saving on average $124,870 per 1,000 per year compared to the base case (95% CI: $13,435, $217,206). The incremental cost-effectiveness of
implementing WHO PEN rather than the current treatment would be a savings of $17,587 per DALY averted (95% CI: $1,840, $42,589). The total absolute cost, however, would be $482,950 (95% CI: $296,612, $692,370) per 1,000 population per year, as compared to the current South African healthcare budget for primary healthcare services of $374 per 1,000 population per year.41

South Africa Primary Care 101 (SA PC 101) simulation

SA PC 101 guideline implementation produced a 12.6 percentage point rise in the proportion of the population prescribed BP medications (versus a 4.2 percentage point rise under WHO PEN), 14.9 percentage point rise in the proportion of the population prescribed statins (versus a 16.0 percentage point rise under WHO PEN), and a 0.6 percentage point rise in the proportion of the population prescribed glucose-lowering medications (versus a 1.2 percentage point rise under WHO PEN). A small portion of people would be removed from medication because they would not be indicated to have treatment under the SA PC 101 guidelines despite currently being on treatment (7% of those currently on BP medications, 1% of those currently on statins, and 1% of those currently on glucose-lowering medications, nearly fully overlapping with those removed by WHO PEN).

South Africans in our simulated population experienced a loss of 32.5 DALYs from cardiovascular disease or type 2 diabetes complications (95% CI: 24.4, 44.8), per 1,000 population per year when implementing the SA PC 101 guidelines, down from 40.0 DALYs per 1,000 per year in the base case simulation of current treatment levels and 32.9 DALYS per 1,000 per year in the WHO PEN simulation. The slightly higher number of DALYs averted under SA PC 101 than under the WHO PEN guidelines was due to higher BP medication prescription rate and associated reductions in atherosclerotic cardiovascular disease rates; a larger number of people with slightly lower average risk were treated under SA PC 101, versus the smaller number of people with higher average risk treated under WHO PEN. In the SA PC 101 simulation, the average atherosclerotic cardiovascular disease risk for those prescribed BP or statin medications was 23.1% over 10 years (versus 31.1% under WHO PEN), and the average risk for any microvascular complication of diabetes for those prescribed glucose-lowering medications was 27.8%
over 10 years (versus 26.7% under WHO PEN). The largest improvements in DALYs lost were from atherosclerotic cardiovascular disease, followed by renal failure/ESRD, then congestive heart failure (Table 2). Males benefited more than females, but no disproportionate benefits were observed between black Africans and non-black Africans, or between poor and non-poor populations (Figure 3). The overall premature mortality rate (death rate for those under 70 years old) due to CVD was 22.1 per 1,000 population per year (95% CI: 13.0, 32.0), down from 39.5 in the base case (a relative reduction of 44.1%) and 23.4 in the WHO PEN simulation (a relative reduction of 5.5%).

Implementation of the SA PC 101 guidelines would be expected to increase costs for treatment of BP more than the WHO PEN guidelines, similar costs for dyslipidemia (slightly higher than WHO PEN on average due to a younger group being treated, thus longer time of paying for statins over the life-course), while having lower costs for glycemic treatment for type 2 diabetes than the WHO PEN guidelines (Table 2); in turn, most medical costs from complications through the SA PC 101 implementation were averted from atherosclerotic cardiovascular disease events, but fewer from microvascular complications as compared to the WHO PEN implementation (Table 2). Overall, the SA PC 101 implementation was more cost-saving than the WHO PEN guideline, saving on average $186,765 per 1,000 per year through SA PC 101 compared to the base case (95% CI: $105,597, $319,151; compared to $124,870 for WHO PEN). The total absolute cost, however, of SA PC 101 would be only marginally lower at $421,055 (95% CI: $194,667, $600,208) per 1,000 population per year, as compared to the current South African healthcare budget for primary healthcare services of $374 per 1,000 population per year.41 The incremental cost-effectiveness of implementing SA PC 101 than the current treatment would be a savings of $24,902 per DALY averted (95% CI: $14,666, $62,579; compared to $17,587 for WHO PEN). In sensitivity analyses, ICERs were not substantially changed if access to treatment changed from the base case of 70% to 60% or 80% (Appendix). The incremental cost-effectiveness of blood pressure and lipid therapies become more pronounced at lower levels of baseline treatment, because the incremental impact of treatment was more potent with lower baseline coverage levels. We found that at least 46.7% of the population would need to be diagnosed and treated for hypertension and hyperlipidemia to achieve the 30% mortality reduction goal, which
would not require new blood pressure or lipid screening but would require more treatment initiation and adherence (Appendix).
Discussion

We found high rates of cardiovascular and microvascular risk factors across demographic groups, with low treatment levels (particularly for lipid treatment) among male, black African, and poor populations in South Africa. While treatment subsidization is high among the poor in South Africa, the underlying burden of disease is disproportionately high among the poor, leading to lower treatment levels than desired in this population. Various barriers to access to care – including cultural, trust, and financial barriers to getting to care - conspire with a higher burden of risk factors in poor people to result in this disproportionate burden. Given the distribution of risk factors and treatments at present, our microsimulation suggested a high burden of DALY losses from atherosclerotic cardiovascular disease, followed by congestive heart failure, then diabetes microvascular complications. With implementation of the WHO PEN guidelines, we would anticipate considerably increased treatment rates with statins, followed by increased treatment for hypertension and then glycemic control for diabetes. But we additionally found that implementation of South Africa’s current primary care guidelines had slightly improved overall DALYs averted and better cost-effectiveness than implementation of the WHO PEN guidelines. The key benefits of the South African guidelines in terms of DALYs was a result of more assertive blood pressure treatment, particularly for high-risk patients, while the benefits, in terms of costs, were primarily from less assertive blood glucose control as compared to the WHO PEN guidelines. We found that if either guidelines were implemented with coverage rates similar to a well-performing European health system, SDG target 3.4 (reduction in premature mortality of 30%) would be readily achieved.

Our findings address considerable debate in the literature regarding whether or not cardiovascular diseases and their risk factors affect a sufficient proportion of the population, particularly lower-income groups, to justify widespread treatment. Our microsimulation modeling approach has a key advantage over traditional Markov models of simulating entire distributions of risk, rather than just an average risk level, thus capturing heterogeneities in risk and benefit of treatment. Our results are notable for uniquely assessing inequalities in the disease burden and benefit using nationally-
representative data, which suggest that particularly disadvantaged populations may disproportionately benefit from assertive treatment. Additionally, our results address questions about risk factor prioritization. Our results suggest that treatment with blood pressure agents and statins may need greater prioritization at the population level for people at high cardiovascular risk than blood glucose medications, whilst recognizing the importance of the latter at the individual level. This contrasts with observed treatment levels despite a lower monthly cost of blood pressure or statin treatment than of sulfonylurea or insulin treatment in South Africa, as is the case in many other middle-income countries.\textsuperscript{44} Our findings on prioritization are relevant to many countries implementing WHO PEN or SA PC 101 guidelines (n.b., the South African PC 101 guidelines are now being implemented in Botswana, Nigeria, and Brazil).\textsuperscript{45} The South African guidelines have an explicit focus on population equity.

There are important limitations to our analysis. Simulation studies cannot predict the future and can only anticipate potential outcomes under the premise that the effectiveness observed in randomized trials and meta-analyses will be realized in practice. Achieving European levels of treatment access will undoubtedly require access and adherence initiatives that would increase costs and make the cost-effectiveness less attractive. Improving access to care goes beyond improving availability of treatment and requires overcoming barriers including cultural, trust, and the financial implications of getting to care. These issues are particularly relevant in South Africa related to its apartheid past. Lack of reliable data on costs of successful access and adherence initiatives in South Africa mean that we have not included these in our analysis. However, the costs that we have used do include the costs of infrastructure and personnel to deliver treatment, and are not limited to the costs of medications or equipment. Additionally, improving availability of treatment and hence results of accessing healthcare can engender trust in and usage of those services.\textsuperscript{46} An additional consideration is that randomized trials and meta-analyses that focus on estimating results among mostly North American and European populations may not accurately reflect the effectiveness of therapy among diverse South African populations. We have also calculated cost-effectiveness using broad international guidelines that focus on value per dollar spent; however, Ministries of Finance have numerous competing priorities when
allocating resources, even amongst highly cost-effective interventions that must be considered based on often-fluctuating budgets, as well as the training needs and physical infrastructure of healthcare providers and delivery organizations. The SANHANES data on which our simulations rely have important gaps, particularly the lack of detail concerning access to and pricing of tobacco cessation treatments, and incomplete coverage of all risk factors across the entire sample. However, the data do provide important estimates of how the distributions of other major cardiovascular disease risk factors are prevalent among minority and poor populations, contrary to claims that cardiovascular risk would be isolated to higher-income groups. The data are nevertheless self-reported for key treatment questions, which may lead to over-estimation of treatment levels due to social acceptability bias (e.g., not admitting non-adherence), or under-estimation of treatment if individuals are confused about what medications they are taking and what those medications are for.

Future research efforts should address the question of what key implementation barriers have prevented more assertive statin treatment in the South African population. Additionally, research efforts should identify how to better reach male, black, and poor populations who appear to be disproportionately undertreated for their chronic disease risk—including analysis of the barriers to treatment, such as cultural, social, and economic contexts faced by those underserved populations.

As such research is initiated, our results suggest that the Department of Health in South Africa, and similar nations prepare assertively for increased NCD burdens. Our results suggest that the South African guideline may be more effective in terms of DALYs averted and net overall costs saved, than the current WHO guidelines for management of blood pressure, lipids and diabetes. Particularly assertive treatment with blood pressure and statin medications may help mitigate a high burden of disease, including among historically disadvantaged populations.
Contributors
JD conceived of the study. SB, RGW, and JD conducted the analysis. SB wrote the first draft of the manuscript. All authors contributed to study design, interpretation of results, and editing of the manuscript.

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Conflicts of interest
None.
References


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42 Subramanian S, Corsi DJ, Subramanyam MA, Davey Smith G. Jumping the gun:
the problematic discourse on socioeconomic status and cardiovascular health in India. *Int J Epidemiol* 2013; **42**: 1410–26.


### Tables and Figures

**Table 1**: Characteristics of the studied population, from the South African National Health and Nutrition Examination Survey (SANHANES, 2012, N = 17,743). Results incorporate survey sample weights to adjust for sample selection and provide nationally-representative estimates.

<table>
<thead>
<tr>
<th>Risk factor, mean (95% CI)</th>
<th>Population subgroup</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Poor†</td>
<td>Non-poor</td>
<td>Poor</td>
</tr>
<tr>
<td>N</td>
<td>3,654</td>
<td>1,276</td>
<td>1,222</td>
</tr>
<tr>
<td>Age, yrs (95% CI), N = 17,633</td>
<td>35.2 (16.0, 69.0)</td>
<td>39.8 (16.0, 68.0)</td>
<td>40.0 (16.0, 69.0)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic, mmHg (95% CI), N = 7,048</td>
<td>130.7 (102.0, 173.0)</td>
<td>130.6 (103.0, 172.0)</td>
<td>133.3 (101.0, 171.0)</td>
</tr>
<tr>
<td>Diastolic, mmHg (95% CI), N = 7,039</td>
<td>72.9 (53.0, 98.0)</td>
<td>75.6 (54.0, 99.0)</td>
<td>74.9 (54.0, 96.0)</td>
</tr>
<tr>
<td>Hypertension, % (&gt;140/90 mmHg or taking blood pressure-lowering medications), N =</td>
<td>236/1341 (17.6%)</td>
<td>66/357 (18.5%)</td>
<td>97/394 (24.6%)</td>
</tr>
<tr>
<td></td>
<td>7,099</td>
<td>128/236 (54.2%)</td>
<td>46/66 (69.7%)</td>
</tr>
<tr>
<td>--------------------------</td>
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</tr>
<tr>
<td>Blood pressure treatment, % of hypertensive population, N = 1,761</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure, % treated achieving BP ≤140/90mmHg, N = 1,257</td>
<td></td>
<td>81/128 (63.3%)</td>
<td>36/46 (78.3%)</td>
</tr>
</tbody>
</table>

**Lipids**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>4.1 (2.7, 5.8)</th>
<th>4.1 (2.7, 5.8)</th>
<th>4.5 (2.9, 6.4)</th>
<th>4.7 (3.1, 6.8)</th>
<th>4.4 (2.8, 6.4)</th>
<th>4.5 (3.0, 6.5)</th>
<th>4.8 (3.1, 7.0)</th>
<th>5.0 (3.2, 7.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mmol/L (95% CI), N = 5,419</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-density lipoprotein (HDL) cholesterol, mmol/L (95% CI), N = 5,394</td>
<td></td>
<td>1.2 (0.7, 2.0)</td>
<td>1.2 (0.7, 2.0)</td>
<td>1.3 (0.8, 2.2)</td>
<td>1.2 (0.7, 2.0)</td>
<td>1.3 (0.7, 2.0)</td>
<td>1.3 (0.8, 2.1)</td>
<td>1.3 (0.8, 2.2)</td>
<td>1.3 (0.8, 2.0)</td>
</tr>
<tr>
<td>Low-density lipoprotein (LDL) cholesterol, mmol/L (95% CI), N = 3,308</td>
<td></td>
<td>2.2 (1.2, 3.7)</td>
<td>2.3 (1.2, 3.7)</td>
<td>2.4 (1.1, 4.4)</td>
<td>2.7 (1.3, 4.4)</td>
<td>2.6 (1.3, 4.2)</td>
<td>2.7 (1.2, 4.6)</td>
<td>2.9 (1.4, 4.6)</td>
<td>3.0 (1.4, 5.1)</td>
</tr>
<tr>
<td>Triglycerides, fasting, mmol/L (95% CI), N = 534</td>
<td></td>
<td>1.4 (0.5, 2.7)</td>
<td>1.6 (0.5, 5.0)</td>
<td>1.1 (0.5, 1.9)</td>
<td>2.1 (0.6, 9.3)</td>
<td>1.2 (0.4, 2.9)</td>
<td>1.0 (0.4, 2.2)</td>
<td>1.1 (0.6, 1.9)</td>
<td>1.2 (0.5, 2.7)</td>
</tr>
</tbody>
</table>

Dyslipidemia, %‡, N = 17,743

<table>
<thead>
<tr>
<th></th>
<th>514/3654 (14.1%)</th>
<th>141/1276 (11.1%)</th>
<th>243/1222 (19.9%)</th>
<th>243/1521 (16.0%)</th>
<th>911/5055 (18.0%)</th>
<th>258/1638 (15.8%)</th>
<th>379/1505 (25.2%)</th>
<th>453/1872 (24.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid-lowering treatment, % of dyslipidemic population, N =</td>
<td>0/514 (0.0%)</td>
<td>3/141 (2.1%)</td>
<td>16/243 (6.6%)</td>
<td>22/243 (9.1%)</td>
<td>6/911 (0.7%)</td>
<td>6/258 (2.3%)</td>
<td>17/279 (4.4%)</td>
<td>36/453 (7.9%)</td>
</tr>
<tr>
<td></td>
<td>Lipid-lowering, % treated achieving LDL≤2.5mmol/L, N = 106</td>
<td>Diabetes mellitus</td>
<td></td>
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<tr>
<td></td>
<td>0/0 (0.0%)</td>
<td>0/3 (0.0)</td>
<td>3/16 (18.8%)</td>
<td>2/22 (9.1%)</td>
<td>0/6 (0.0%)</td>
<td>0/6 (0.0%)</td>
<td>5/17 (29.4%)</td>
<td>2/36 (5.6%)</td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin A1c, % (95% CI), N = 4,710</td>
<td>5.8 (4.9, 6.5)</td>
<td>5.9 (5.0, 7.4)</td>
<td>5.9 (5.0, 6.8)</td>
<td>6.1 (5.1, 8.7)</td>
<td>5.9 (4.9, 7.1)</td>
<td>5.1 (5.0, 9.1)</td>
<td>6.0 (5.0, 8.8)</td>
<td>6.1 (5.1, 8.6)</td>
</tr>
<tr>
<td>Diabetes, %*, N = 4,877</td>
<td>81/873 (9.3%)</td>
<td>36/255 (14.1%)</td>
<td>38/317 (12.0%)</td>
<td>64/312 (20.5%)</td>
<td>227/1603 (14.2%)</td>
<td>87/443 (19.6%)</td>
<td>90/511 (17.6%)</td>
<td>124/563 (22.0%)</td>
</tr>
<tr>
<td>Glucose-lowering treatment, % of population with diabetes, N = 747</td>
<td>47/81 (58.0%)</td>
<td>23/36 (63.9%)</td>
<td>26/38 (68.4%)</td>
<td>40/64 (62.5%)</td>
<td>119/227 (52.4%)</td>
<td>49/87 (56.3%)</td>
<td>57/90 (63.3%)</td>
<td>75/124 (60.5%)</td>
</tr>
<tr>
<td>Glucose-lowering, % treated achieving hemoglobin A1c ≤7%, N = 436</td>
<td>6/47 (12.8%)</td>
<td>1/23 (4.3%)</td>
<td>4/26 (15.4%)</td>
<td>3/40 (7.5%)</td>
<td>10/119 (8.4%)</td>
<td>5/49 (10.2%)</td>
<td>4/57 (7.0%)</td>
<td>6/75 (8.0%)</td>
</tr>
<tr>
<td><strong>Prior cardiovascular history (self-reported)</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, %, N = 15,267</td>
<td>110/3079 (3.6%)</td>
<td>25/1072 (2.3%)</td>
<td>45/1008 (4.5%)</td>
<td>41/1198 (3.4%)</td>
<td>261/4522 (5.8%)</td>
<td>73/1483 (4.9%)</td>
<td>47/1298 (3.6%)</td>
<td>58/1607 (3.6%)</td>
</tr>
<tr>
<td>Congestive heart failure, %, N = 15,232</td>
<td>39/3067 (1.3%)</td>
<td>13/1064 (1.2%)</td>
<td>12/1010 (1.2%)</td>
<td>11/1197 (0.9%)</td>
<td>120/4512 (2.7%)</td>
<td>26/1476 (1.8%)</td>
<td>22/1299 (1.7%)</td>
<td>28/1607 (1.7%)</td>
</tr>
<tr>
<td>Stroke, %, N = 15,282</td>
<td>57/3088 (1.8%)</td>
<td>15/1067 (1.4%)</td>
<td>30/1007 (3.0%)</td>
<td>36/1199 (3.0%)</td>
<td>105/4533 (2.3%)</td>
<td>29/1474 (2.0%)</td>
<td>25/1305 (1.9%)</td>
<td>47/1609 (2.9%)</td>
</tr>
</tbody>
</table>
Poverty was defined by the South African multi-dimensional poverty index, which defines poor versus non-poor status based on health/nutrition assets, educational attainment, and material assets.\textsuperscript{11,12}

Dyslipidemia was defined as measured total cholesterol \( \geq 6.21 \text{ mmol/L} \) [240 mg/dL], low-density lipoprotein cholesterol \( \geq 4.14 \text{ mmol/L} \) [160 mg/dL], high-density lipoprotein cholesterol <1.03 mmol/L [\(<40 \text{ mg/dL}\)], fasting triglycerides \( \geq 2.25 \text{ mmol/L} \) [200 mg/dL], or taking lipid-lowering medications.\textsuperscript{37}

Diabetes mellitus was defined as measured hemoglobin A1c \( \geq 6.5\% \) [48 mmol/mol] or taking glucose-lowering medications.\textsuperscript{38}
Table 2: Disability-adjusted life-years (DALYs), costs, and incremental cost-effectiveness of treating elevated blood pressure, dyslipidemia, and type 2 diabetes mellitus for the South African population, based on current treatment levels (base case), versus with scale-up from currently-observed levels of treatment to 70% population access per the World Health Organization’s Package of Essential Non-communicable disease interventions (WHO PEN), or per the South Africa’s Primary Care 101 Guidelines (SA PC 101).9,10 95% confidence intervals in parentheses are calculated by re-running the model 10,000 times while repeatedly Monte Carlo sampling with replacement from the distributions of all input parameters to estimate uncertainty in the outcome metrics.

<table>
<thead>
<tr>
<th>Outcome metric, mean (95% CI)</th>
<th>Treatment condition</th>
<th>WHO PEN guidelines implemented</th>
<th>SA PC 101 guidelines implemented</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Base case (current levels of treatment)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability-adjusted life-years lost, per 1,000 population per year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All simulated outcomes</td>
<td>40.0 (29.5, 52.0)</td>
<td>32.9 (24.4, 44.7)</td>
<td>32.5 (24.4, 44.8)</td>
</tr>
<tr>
<td>Atherosclerotic cardiovascular disease</td>
<td>18.7 (15.8, 21.8)</td>
<td>13.7 (11.7, 16.3)</td>
<td>13.4 (11.7, 16.2)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>10.7 (7.3, 14.6)</td>
<td>9.9 (6.6, 13.9)</td>
<td>9.8 (6.6, 13.9)</td>
</tr>
<tr>
<td>Renal failure/end-stage renal disease</td>
<td>9.2 (5.5, 13.5)</td>
<td>8.2 (5.2, 12.8)</td>
<td>8.2 (5.2, 13.0)</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>0.8 (0.5, 1.3)</td>
<td>0.6 (0.5, 1.0)</td>
<td>0.6 (0.5, 1.0)</td>
</tr>
<tr>
<td>Diabetic neuropathy</td>
<td>0.6 (0.4, 0.8)</td>
<td>0.5 (0.4, 0.7)</td>
<td>0.5 (0.4, 0.7)</td>
</tr>
<tr>
<td>Healthcare costs, $ per 1,000 population per year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All simulated risk factors and outcomes</td>
<td>607,820 (513,818, 705,805)</td>
<td>482,950 (296,612, 692,370)</td>
<td>421,055 (194,667, 600,208)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>26,429 (26,326, 26,533)</td>
<td>27,019 (23,761, 29,750)</td>
<td>39,165 (35,564, 42,830)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>6,585 (6,308, 6,860)</td>
<td>10,347 (9,575, 10,484)</td>
<td>10,506 (9,743, 11,237)</td>
</tr>
<tr>
<td>Condition</td>
<td>Base Case</td>
<td>Low Case</td>
<td>High Case</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-----------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>183,006 (170,185, 195,023)</td>
<td>139,011 (84,559, 192,761)</td>
<td>77,502 (52,783, 95,728)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>29,243 (21,778, 37,251)</td>
<td>24,533 (11,958, 40,659)</td>
<td>24,451 (11,958, 40,659)</td>
</tr>
<tr>
<td>Renal failure/endo-stage renal disease</td>
<td>138,195 (87,520, 192,544)</td>
<td>117,461 (36,524, 219,146)</td>
<td>118,475 (30,437, 213,058)</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>587 (371, 808)</td>
<td>426 (91, 820)</td>
<td>438 (68, 820)</td>
</tr>
<tr>
<td>Diabetic neuropathy</td>
<td>2,096 (1,486, 2,752)</td>
<td>1,884 (804, 3,100)</td>
<td>1,884 (804, 3,100)</td>
</tr>
<tr>
<td>Incremental cost-effectiveness ratio (Change in $/change in DALYs), versus base case</td>
<td>-</td>
<td>-$17,587 (-42,589, -1,840)</td>
<td>-$24,902 (-62,579, -14,666)</td>
</tr>
</tbody>
</table>
Figure 1: Modeling approach. Legend: SES = socioeconomic status, SANHANES: South African National Health and Nutrition Examination Survey (2012, N = 17,743).
Figure 2: Alternative guidelines for management of elevated blood pressure, dyslipidemia, and type 2 diabetes mellitus for South African providers. Depicted are the (A) World Health Organization’s Package of Essential Non-communicable disease interventions (PEN), and (B) South Africa’s Primary Care 101 Guideline.  

(A)
(B)

**Blood pressure medicines**

- **Non-diabetic w/ CVD, heart failure, or kidney disease, BP ≥130/80**
  - Thiazide, then ACEI, then CCB, then beta-blocker, to BP <130/80

- **Non-diabetic w/o CVD, heart failure, or kidney disease, BP ≥140/90**
  - Thiazide, then ACEI, then CCB, then beta-blocker, to BP <140/90

- **Diabetic, BP ≥140/80**
  - ACEI, then thiazide, then CCB, then beta-blocker, to BP <120-140/70-80

**Statins**

- H/o CVD
  - Or 10-year CVD risk >20%
  - Or diabetic w/ hypertension, obesity, smoking, or age >40
  - Statin (Simvastatin 10mg daily in South Africa)

**Glycemic medications**

- **Diabetic, A1c >7%**
  - Metformin, then Sulfonylurea, Then insulin to target A1c >7%
Figure 3: Variations in disability-adjusted life-years (DALYs) averted from treating elevated blood pressure, dyslipidemia, and type 2 diabetes mellitus for the South African population, by sex, race/ethnicity, and socio-economic status, for the (A) World Health Organization’s Package of Essential Non-communicable disease interventions (PEN), and (B) South Africa’s Primary Care 101 Guidelines\textsuperscript{9,10}.

(A)

<table>
<thead>
<tr>
<th>Sex</th>
<th>DALYs averted, per 1,000 pop per yr (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4.71 [3.98, 5.44]</td>
</tr>
<tr>
<td>Female</td>
<td>2.39 [2.02, 2.76]</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>3.97 [3.35, 4.58]</td>
</tr>
<tr>
<td>Non-Black</td>
<td>3.13 [2.65, 3.62]</td>
</tr>
<tr>
<td>Poverty</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>3.73 [3.16, 4.31]</td>
</tr>
<tr>
<td>Non poor</td>
<td>3.37 [2.84, 3.89]</td>
</tr>
</tbody>
</table>

(B)

<table>
<thead>
<tr>
<th>Sex</th>
<th>DALYs averted, per 1,000 pop per yr (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4.96 [4.07, 5.85]</td>
</tr>
<tr>
<td>Female</td>
<td>2.54 [2.08, 3.00]</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>3.81 [3.12, 4.50]</td>
</tr>
<tr>
<td>Non-Black</td>
<td>3.69 [3.03, 4.35]</td>
</tr>
<tr>
<td>Poverty</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>3.70 [3.03, 4.36]</td>
</tr>
<tr>
<td>Non poor</td>
<td>3.80 [3.12, 4.49]</td>
</tr>
</tbody>
</table>