Are behavioural risk factors to be blamed for the conversion from optimal blood pressure to hypertensive status in Black South Africans? A 5-year prospective study

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Background Longitudinal cohort studies in sub-Saharan Africa are urgently needed to understand cardiovascular disease development. We, therefore, explored health behaviours and conventional risk factors of African individuals with optimal blood pressure (BP) ($\leqslant$120/80 mm Hg), and their 5-year prediction for the development of hypertension.

Methods The Prospective Urban Rural Epidemiology study in the North West Province, South Africa, started in 2005 and included African volunteers ($n = 1994$; aged > 30 years) from a sample of 6000 randomly selected households in rural and urban areas.

Results At baseline, 48% of the participants were hypertensive ($\geqslant$140/90 mmHg). Those with optimal BP ($n = 478$) were followed at a success rate of 70% for 5 years (213 normotensive, 68 hypertensive, 57 deceased). Africans that became hypertensive smoked more than the normotensive individuals (68.2% vs 49.8%), and they also had a greater waist circumference [ratio of geometric means of 0.94 cm (95% CI: 0.86–0.99)] and greater amount of γ-glutamyltransferase [0.74 U/l (95% CI: 0.62–0.88)] at baseline. The 5-year change in BP was independently explained by baseline γ-glutamyltransferase [$R^2 = 0.23$, $\beta = 0.13$ U/l (95% CI: 0.01–0.19)]. Alcohol intake also predicted central systolic BP and carotid cross-sectional wall area (CSWA) at follow-up. Waist circumference was another predictor of BP changes [$\beta = 0.18$ cm (95% CI: 0.05–0.24)] and CSWA. HIV infection was inversely associated with increased BP.

Conclusions During the 5 years, 24% of Africans with optimal BP developed hypertension. The surge in hypertension in Africa is largely explained by modifiable risk factors. Public health strategies should focus aggressively on lifestyle to prevent a catastrophic burden on the national health system.

Keywords Ethnicity, atherosclerosis, alcohol, γ-glutamyl transferase, obesity

Introduction

A recent systematic global analysis in 5.4 million participants showed that global blood pressure (BP) decreased since 1980. However, region-specific inspection of these data shows that in men and women from Africa, the mean systolic BP (SBP) actually increased. In addition, the highest mean BPs recorded worldwide were in African countries.[1]

Urbanization is most likely the culprit for these BP increases, which can be because of accompanying dietary, lifestyle and behavioural changes.[2] The Heart of Soweto study confirmed that two-thirds of urban South Africans present multiple risk factors for cardiovascular disease. This study highlighted the potentially devastating consequences of advanced forms of hypertensive heart disease in urban Africans in the absence of prevention strategies.[3]

The South African National Demographic and Health Survey,[4] and review articles of other cross-sectional epidemiological studies in sub-Saharan Africa[5–7] highlight the importance of various risk factors for cardiovascular disease in Africans, such as obesity, salt intake and smoking. The severe paucity of longitudinal studies on the development of hypertension in Black South Africans (as expressed by several authors[6,8,9]) has hampered investigations to identify which health behaviours and conventional risk factors are the strongest predictors for the development of hypertension over time.

The present study will use data collected longitudinally from two examinations (2005 and 2010) in a Black South African population, which has a high cardiovascular disease rate. These data provide an excellent opportunity (i) to explore and compare risk factors for the development of hypertension, and (ii) to determine whether a 5-year change in BP is associated with arterial structure and function. This particular study will focus on Africans having optimal BP at baseline.

Methods

Study population

This longitudinal study forms a part of the multinational Prospective Urban and Rural Epidemiology (PURE) study.[10] In 2005, the baseline data collection of the South African leg (North West Province) included 1994 African volunteers (aged >30 years) from a sample of 6000 randomly selected households in rural and urban areas (Figure 1). We performed the first follow-up data collection in 2010 and had a 62% successful follow-up rate.

This particular sub-study focused on participants having optimal BP ($\leqslant$120/80 mmHg) at baseline ($n=478$) and being classified as either normotensive ($n=213$) or hypertensive ($n=68$) after a 5-year follow-up (Figure 1).

Participants were fully informed about the objectives and procedures of the study before their first recruitment. Trained African field workers fluent in English and Tswana assisted and conveyed all information in the participants' home language. All participants gave written informed consent.

The study complied with all applicable requirements of USA and international regulations, in particular, the Helsinki declaration of 1975 (as revised in 2008) for investigation of human participants. The Ethics Committee of the North-West University (Potchefstroom Campus) approved this study.

Questionnaires

African field workers interviewed participants using structured demographic, socio-economic, lifestyle and physical activity questionnaires that were developed and standardized for the international PURE study.[10] The field workers also used validated quantitative food frequency questionnaires to assess dietary intake. This data was coded by two dieticians in collaboration with the Medical Research Council of South Africa.

Anthropometric measurements

Height, weight and waist circumferences were measured using standardized methods, with calibrated instruments by International Society for the Advancement of Kinanthropometry accredited anthropometrists (Precision Health Scale, A & D Company, Japan; Leicester Height Measure, Seca, Birmingham, UK).

Cardiovascular measurements

After a 10-minute rest period, BP was measured in duplicate (5 minutes apart) on the right upper arm, while the participants were seated upright with the right arm supported at heart level. SBP, diastolic BP (DBP) and heart rate were measured with the validated OMRON HEM-757 (Omron Healthcare, Kyoto, Japan). We used appropriate sized cuffs for obese participants.

At follow-up (2010), we performed the following additional cardiovascular measurements: augmentation index (AI) and estimated central SBP (cSBP) were measured using the Omron 9000AI (Omron HealthCare, Kyoto, Japan) while the participant was in a sitting position.

The carotid intima-media thickness (CIMT) was obtained using a SonoSite Micromax ultrasound system (SonoSite Inc., Bothell, WA) and a 6–13 MHz linear array transducer. Images from at least two optimal angles of the left and right common carotid artery were obtained. A single reader conducted measurements using a semi-automated program, namely the Artery Measurement Systems II v1.139 (Chalmers University of Technology, Gothenburg, Sweden). For the purpose of this study, far wall measurements were used. We also calculated the cross-sectional wall area (CSWA) to confirm that structural and not functional changes in luminal diameter as

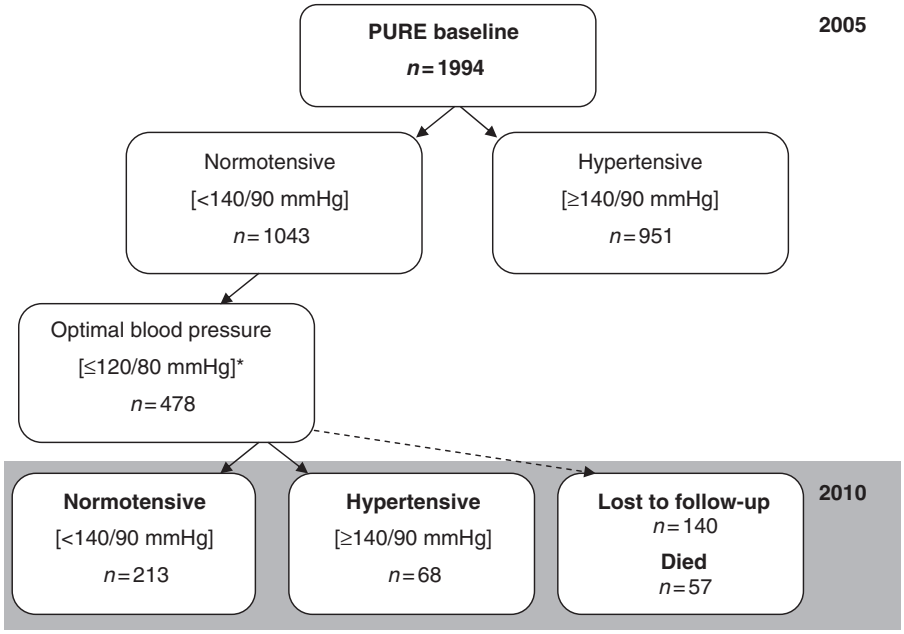

Figure 1 Outline of study population. *Retrospectively, we determined that 82 participants were misclassified as not being in the optimal group, i.e. having optimal BP at follow-up (2010) without using antihypertensive medication

follows: $CSWA = \pi(d/2 + CIMT)^2 - \pi(d/2)^2$, where d denotes luminal diameter.

Blood sampling

Participants were requested to be in a fasted state for ~10 hours before sample collection in the mornings. A registered nurse obtained a blood sample with a sterile winged infusion set from the antebrachial vein branches. Samples were prepared according to appropriate methods and were stored at −80°C in the laboratory. In the rural areas, samples were rapidly frozen and stored at −18°C (no longer than 5 days) until they could be transported to the laboratory facility and were then stored at −80°C until analysis.

Biochemical measurements

Fasting sodium fluoride (glucose) and serum samples for total and high-density lipoprotein cholesterol (HDL-C), creatinine, γ-glutamyltransferase, uric acid and high-sensitivity C-reactive protein (CRP) were analysed using two sequential multiple analysers (Konelab 20i, Thermo Scientific, Vantaa, Finland; Cobas Integra 400 Plus, Roche, Switzerland). We calculated the estimated creatinine clearance by using the Cockcroft–Gault formula. Glycosylated haemoglobin (HbA1c) was determined on-site in ethylenediaminetetraacetic acid-treated whole blood using the D-10 Haemoglobin testing system (Bio-Rad Laboratories, Hercules, CA). We determined HIV status according to the protocol of the South African Department of Health by using the First Response rapid HIV card test (PMC Limited, Daman, India). The result was confirmed with the SD Bioline HIV 1/2 3.0 card test (Standard Diagnostics, INC, Korea).

Statistical analyses

We used Statistica version 10 (StatSoft Inc., Tulsa, OK) and SPSS version 18 (PASW Inc., Chicago, IL) for statistical analyses. Variables with a non-Gaussian distribution were logarithmically transformed. We compared the means and proportions by an independent *t*-test and the χ^2 test, respectively. We also investigated independent associations of conventional and behavioural risk factors with percentage change in SBP, DBP or pulse pressure (PP) and also with central SBP, CSWA and AI by using multiple linear regression analyses. We identified covariates by a backward stepwise procedure. Covariates considered for entry in the models were age, gender, rural/urban location, baseline smoking and HIV status (0, no; 1, yes), experience of stress at home, education, baseline and change in body mass index, waist circumference, total cholesterol, HDL-C, HbA1c, γ-glutamyltransferase, uric acid, estimated creatinine clearance and CRP.

Results

Characteristics of participants

Cardiovascular data for 1994 participants were obtained at baseline, with 47.8% being classified as hypertensive (Figure 1). Within the normotensive group ($n = 1043$), a subgroup of 478 participants

with optimal BP ($\leqslant$120/80 mmHg) was identified at baseline.

During 5 years, we were able to follow up 338 of the 478 participants (70.7%) of whom 57 (11.9%) participants passed away. Participants that passed away had lower body mass index [ratio of geometric means of 1.16 kg/m^2 (95% CI: 1.08–1.25)] and higher CRP [ratio of geometric means of 0.28 mg/l (95% CI: 0.17–0.45)] than the follow-up group, likely because of the higher percentage of HIV infection (58 vs 18%). This group also self-reported a higher proportion of alcohol drinkers than the follow-up group (47.4 vs 30.3%), which was confirmed by elevated γ-glutamyltransferase levels [ratio of geometric means of 0.57 U/l (95% CI: 0.47–0.70)].

Participants lost to follow-up ($n = 140$) were younger [difference of 3.42 years (95% CI: 1.74–5.10)] and better educated than those followed up. Apart from these differences, this group was comparable to the follow-up group—also with regard to biochemical measurements, such as HbA1c, γ-glutamyltransferase and CRP, and cardiovascular measurements, such as BP and heart rate [differences in SBP of −0.36 mmHg (95% CI: −2.15–1.43)].

Table 1 Baseline values of participants with optimal BP ($\leqslant$120/80 mmHg) at baseline remaining normotensive (<140/90 mmHg) or becoming hypertensive ($\geqslant$140/90 mmHg) after 5-year follow-up ($n = 281$)

Variable	Normotensive at follow-up ($n = 213$)	Hypertensive at follow-up ($n = 68$)	Difference (95% CI)
Socio-demographic profile at baseline			
Age, years	46.4	46.8	0.40 (−1.91–2.71)
Gender, women (%)	139 (65.3)	46 (67.7)	0.02 (−0.12–0.14)
Location, rural (%)	133 (62.4)	39 (57.4)	−0.05 (−0.18–0.07)
No education, *n* (%)	77 (37.0)	28 (43.1)	0.05 (−0.08–0.18)
Employed, *n* (%)	76 (35.7)	23 (33.8)	−0.01 (−0.13–0.11)
Physical activity index	7.56	7.35	−0.21 (−0.72–0.30)
Current/former smoker, *n* (%)	106 (49.8)	45 (68.2)	0.16 (0.03–0.29)
Hypertension medication, *n* (%)	7 (3.3)	7 (10.3)	0.07 (0.01–0.17)
Co-morbidities at baseline			
HIV-positive, *n* (%)	45 (21.1)	6 (8.8)	−0.12 (−0.20–0.02)
Diagnosed diabetes, *n* (%)	1 (0.5)	1 (1.5)	0.01 (−0.01–0.07)
Anthropometric measurements			
Body mass index, kg/m^2[a]	22.6	24.4	0.93 (0.86–0.99)
Waist circumference, cm[a]	74.6	79.0	0.94 (0.91–0.99)
Biochemical measurements			
Total cholesterol, mM/L	4.74	5.04	0.30 (−0.09–0.69)
HDL-cholesterol, mM/L[a]	1.24	1.39	0.89 (0.78–1.01)
Serum glucose, mM/L	4.82	4.94	0.12 (−0.21–0.45)
HbA1c, %[a]	5.56	5.61	0.99 (0.96–1.02)
CRP, mg/L[a]	2.08	2.81	0.74 (0.47–1.16)
Uric acid, mg/L[a]	0.36	0.41	0.87 (0.76–1.02)
γ-Glutamyltransferase, U/L[a]	37.6	50.9	0.74 (0.62–0.88)
Creatinine clearance, ml/min[a,b]	73.9	83.9	0.88 (0.76–1.02)
Cardiovascular measurements			
bSBP, mmHg	107	109	2.00 (−0.30–4.30)
Brachial DBP, mmHg	70.8	72.7	1.90 (0.14–3.66)
Brachial PP, mmHg	36.0	36.4	0.40 (−1.56–2.36)
Heart rate, bpm	72.5	74.4	1.9 (−2.03–5.83)

[a]Values are arithmetic mean, or geometric mean for logarithmically transformed variables, or number of participants (%). Differences between arithmetic means are expressed as absolute values (95% CI) and between geometric means as ratios (95% CI).
[b]Creatinine clearance estimated with the Cockroft–Gault method.
HDL-cholesterol, high-density lipoprotein cholesterol; HbA1c, glycosylated haemoglobin; CRP, C-reactive protein.

We were able to provide data on various conventional and behavioural cardiovascular risk factors of the follow-up group ($n = 281$) (Table 1) of whom 24% became hypertensive during 5 years (Figure 2). The group that became hypertensive smoked more at baseline and had a higher body mass index, waist circumference, serum γ-glutamyltransferase level and tended to have higher HDL-C. A higher proportion of the normotensive group was HIV-infected at baseline (21.1 vs 8.82%).

When comparing the 5-year percentage change of anthropometric, biochemical and cardiovascular variables (Table 2), the only variable that differed between the normotensive and hypertensive groups

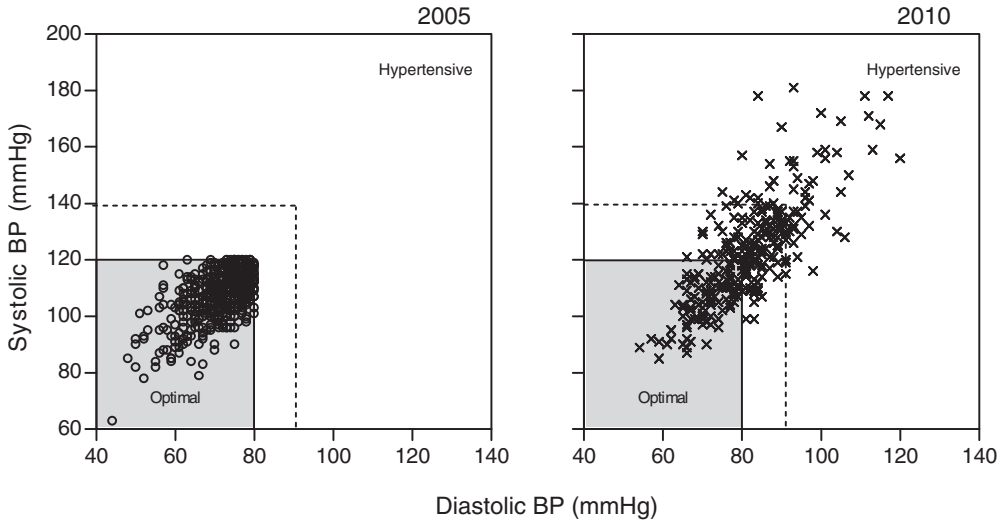

Figure 2 BP distribution of participants with optimal BP ($\leqslant$120/80 mmHg) followed for 5 years ($n = 281$)

Table 2 Percentage change values of participants with optimal blood pressure ($\leqslant$120/80 mmHg) at baseline remaining normotensive ($<$140/90) or becoming hypertensive ($\geqslant$140/90 mmHg) after 5-year follow-up ($n = 281$)

Variable	Normotensive at follow-up ($n = 213$)	Hypertensive at follow-up ($n = 68$)	Difference (95% CI)
Anthropometric measurements			
Body mass index, %	4.77	3.71	−1.06 (−4.56–2.44)
Waist circumference, %	2.91	4.19	1.28 (−1.10–3.66)
Biochemical measurements			
Total cholesterol, %	4.23	0.66	−3.57 (−10.4–3.28)
HDL-cholesterol, %	7.52	17.8	10.3 (−10.7–31.3)
Serum glucose, %	4.69	7.68	2.99 (−3.53–9.51)
HbA1c, %	6.32	7.00	0.68 (−2.51–3.87)
CRP, %	553	65.7	−487 (−1057–82.1)
Uric acid, %	−8.77	−10.9	−2.13 (−11.24–6.98)
γ-Glutamyltransferase, %	3.91	67.9	63.9 (19.8–108)
Creatinine clearance, %[a]	48.3	82.5	34.2 (−3.76–72.2)
Cardiovascular measurements			
bSBP, %	7.50	33.8	26.3 (22.9–29.7)
Brachial DBP, %	8.37	32.8	24.4 (21.2–27.7)
Brachial PP, %	8.69	40.7	32.0 (23.4–40.7)
Heart rate, %	−3.42	−3.93	−0.51 (−4.27–3.25)

Values are arithmetic mean.
[a]Creatinine clearance estimated with the Cockroft–Gault method. Values adjusted for baseline values.
HDL-cholesterol, high-density lipoprotein cholesterol; HbA1c, glycosylated haemoglobin; CRP, C-reactive protein.

Table 3 Cardiovascular measurements taken only at follow-up ($n = 281$)

Variable	Normotensive at follow-up ($n = 213$)	Hypertensive at follow-up ($n = 68$)	Difference (95% CI)
cSBP, mmHg	126	150	24.0 (19.6–28.4)
AI, %[a]	92.1	96.7	4.60 (1.18–8.02)
CIMT far wall, mm	0.68	0.72	0.04 (0.00–0.08)
CSWA, mm^2	13.4	14.4	1.00 (−0.05–2.05)

Values are arithmetic mean.
[a]AI adjusted for heart rate and height.
cSBP, central systolic blood pressure; AI, augmentation index; CIMT, carotid intima media thickness; CSWA, cross-sectional wall area.

Table 4 Forward stepwise regression analyses with 5-year percentage change in bSBP or PP as dependent variable

	SBP, % $R^2 = 0.23$ ($n = 222$)		PP, % $R^2 = 0.29$ ($n = 222$)	
Independent Variable	β	95% CI	β	95% CI
SBP, mmHg	−0.35	(−0.46; −0.29)		
PP, mmHg			−0.47	(−0.58; −0.35)
Age, years			0.14	(0.02; 0.26)
Location, rural/urban	−0.10	(−0.23; −0.04)		
Waist circumference, log cm	0.18	(0.05; 0.24)		
Δ Waist circumference, %	0.09	(−0.03; 0.15)		
Formal school education, no/yes	−0.11	(−0.24; −0.05)	−0.11	(−0.23; 0.01)
HIV infection, no/yes	−0.23	(−0.35; −0.17)	−0.15	(−0.27; −0.04)
γ-Glutamyltransferase, log U/L	0.13	(0.01; 0.19)	0.12	(0.01; 0.23)
Δ γ-glutamyltransferase, %	0.17	(0.05; 0.29)		

Independent variables included in the model: age, gender, rural/urban, waist circumference, Δ waist circumference, education, HIV infection, stress at home, smoking, HDL-cholesterol, Δ HDL-cholesterol, glycosylated haemoglobin, Δ glycosylated haemoglobin, estimated creatinine clearance, Δ estimated creatinine clearance, γ-glutamyltransferase, Δ γ-glutamyltransferase and either baseline systolic BP or PP according to the dependent variable.

was the increase in γ-glutamyltransferase in the hypertensive group. Table 3 presents the cardiovascular measurements that were taken only at follow-up, indicating that central SBP and AI were higher in the group being hypertensive at follow-up.

In an attempt to disregard the cardiovascular effects of antihypertensive medication, we excluded participants who used antihypertensive medication but were classified as normotensive at follow-up ($n = 25$) for all subsequent analyses. Participants in the hypertensive category at follow-up using medication ($n = 19$) were included in the statistical analyses because of the fact that they had elevated BPs.

Adjusted analyses

Independent associations of change in brachial SBP (bSBP), DBP and PP with conventional and behavioural risk factors were determined with forward stepwise regression analyses (Table 4) (results for change in DBP were similar to change in SBP and are, therefore, not shown). Baseline γ-glutamyltransferase contributed to the variance in change of SBP and PP. The 5-year change in γ-glutamyltransferase associated more strongly than baseline values with change in bSBP. Baseline waist circumference related strongly to change in bSBP and DBP, but not with change in PP. Being HIV-infected was inversely associated with changes in SBP and PP during the 5 years.

Independent associations of carotid CSWA, AI or end cSBP with baseline and change in SBP were tested (Table 5). CSWA at follow-up was not associated with baseline and change in SBP. AI at follow-up was independently associated with change in SBP (when SBP was substituted with DBP in these models, similar results were obtained). CSWA was also associated with baseline waist circumference, baseline γ-glutamyltransferase levels and total cholesterol. AI, on the other hand, was inversely associated with baseline waist circumference. The variance in end cSBP was explained by baseline γ-glutamyltransferase.

Table 5 Independent associations with CSWA, AI or cSBP as measured at follow-up

	CSWA, mm^2 $R^2=0.27$ ($n=204$)		AI, %[a] $R^2=0.18$ ($n=204$)		cSBP, mmHg $R^2=0.14$ ($n=219$)	
Independent Variable	β	95% CI	β	95% CI	β	95% CI
Baseline SBP, mmHg					0.16	(0.03; 0.28)
Δ SBP, %			0.25	(0.12–0.37)		
Age, years	0.33	(0.21; 0.45)			0.09	(−0.03; 0.22)
Gender, men/women	−0.27	(−0.39; −0.14)	0.31	(0.18; 0.43)		
Location, rural/urban					−0.19	(−0.31; −0.07)
HIV infection, no/yes	−0.09	(−0.22; 0.03)			−0.16	(−0.29; −0.03)
Waist circ, cm	0.21	(0.08; 0.33)	−0.23	(−0.37; −0.09)		
Δ Waist circ, %			−0.13	(−0.26; −0.01)		
HbA1c, log %			0.10	(−0.03; 0.23)	0.14	(0.02; 0.27)
γ-GT, log U/L	0.12	(0.01; 0.24)			0.16	(0.04; 0.28)
Δ γ-GT, %						
Δ eCcr, %			0.09	(−0.03; 0.21)		
TC, mM/L	0.19	(0.04; 0.33)				
Δ TC, %	0.15	(0.01; 0.29)				

CSWA, carotid cross-sectional wall area; BP, blood pressure; HbA1c, glycosylated haemoglobin; γ-GT, gamma glutamyltransferase; TC, total cholesterol; Waist circ, waist circumference; eCcr, estimated creatinine clearance.

Independent variables included in the model: age, gender, rural/urban, waist circumference, Δ waist circumference, education, HIV infection, stress at home, smoking, total cholesterol, Δ total cholesterol, glycosylated haemoglobin, Δ glycosylated haemoglobin, estimated creatinine clearance, Δ estimated creatinine clearance, γ-glutamyltransferase, Δ γ-glutamyltransferase and baseline and % change in SBP.

[a]AI adjusted for heart rate. Model additionally adjusted for body height.

AI, augmentation index; cSBP, central systolic blood pressure

Sensitivity analyses

We repeated the aforementioned analyses with change in bSBP and end cSBP as dependent variables and substituted baseline and change in γ-glutamyltransferase with baseline self-reported alcohol intake (0, no; 1, yes). By doing so, alcohol intake was similarly associated with change in bSBP ($R^2=0.23$; $\beta=0.21$; 95% CI: 0.09–0.33 mmHg) and end cSBP ($R^2=0.14$; $\beta=0.19$; 95% CI: 0.06–0.31 mmHg). When repeating the aforementioned analyses while excluding HIV-infected participants, the association between change in bSBP and alcohol intake (0, no; 1, yes) or change in γ-glutamyltransferase remained ($R^2=0.22$; $\beta=0.20$; 95% CI: 0.07–0.34 and $R^2=0.197$; $\beta=0.13$; 95% CI: −0.001–0.26 U/l, respectively).

Discussion

Our most prominent finding was that 68 of the 281 Black South Africans (24%) with optimal BP ($\leqslant$120/80 mm Hg) developed hypertension during 5 years. When comparing various conventional and behavioural risk factors, the two strongest contributors toward the development of hypertension were an elevated γ-glutamyltransferase level and abdominal obesity (waist circumference).

γ-Glutamyltransferase was the most consistent predictor for the development of hypertension. This finding was independent of cardiovascular risk factors that were previously associated with hypertension in South African cross-sectional studies, including age, gender,[11] rural and urban location,[5] level of education,[11] employment,[11] smoking,[12] obesity,[13] dietary macronutrient intake,[14] physical activity, cholesterol[3] and HbA1c levels.[15]

Although research has not yet identified an ideal biomarker with sufficient sensitivity and specificity for reliable screening of excessive drinking, a recent study based on the 2005–08 National Health and Nutrition Examination Survey showed that excessive current drinkers had an increased likelihood, of 75–314% for men and 226% for women, of having elevated γ-glutamyltransferase.[16] In their study, the γ-glutamyltransferase level of excessive current drinkers (consuming >5 drinks daily) was 35.3 U/l (31.9–39.0). The participants in our study who became hypertensive had a baseline level of 50.9 U/L (22.5–148), which gives an indication of the severity of alcohol use. Although our group that was in the normotensive range also had a high baseline level of 37.6 U/l (17.4–126), those that became hypertensive showed a greater increase in γ-glutamyltransferase during the 5 years (68% vs 39%). To verify whether γ-glutamyltransferase indeed reflects alcohol intake in

our study, we confirmed our main results by substitution of γ-glutamyltransferase with self-reported alcohol intake (no/yes).

Convincing evidence from >50 prospective population and cross-sectional studies showed the linear dose-response relationship between alcohol misuse and BP,[17] starting at 3–4 drinks/day. The novelty of our result, however, is not the strong link between taking alcohol (γ-glutamyltransferase) and the development of hypertension, but that γ-glutamyltransferase competed shoulder-to-shoulder with an array of other established cardiovascular risk factors and emerged as the strongest predictor for hypertension development.

Within the well-known J-shaped curve of the alcohol–BP relationship,[17] the cardioprotective benefit of moderate alcohol consumption is largely based on increased levels in HDL-C. Most authors agree that HDL-C levels also increase in alcohol misusers.[18–20] Black South Africans are known to have favourable HDL-C levels when compared with the definitions set for Caucasian populations.[2] But this notion may be misleading, as the high prevalence of excessive alcohol consumption in Black South Africans[21] may be the causative factor for the observed elevated HDL-C. It is questionable whether the cardioprotective effect of HDL-C is maintained within this context.[19,20]

Apart from the link between γ-glutamyltransferase and the development of hypertension, we also found that subclinical atherosclerosis (carotid CSWA) after 5 years was independently associated with baseline γ-glutamyltransferase, total cholesterol and waist circumference, independent of changes in SBP and more so in men. Although Black Africans are traditionally less likely to be diagnosed with coronary artery disease,[3] our result suggests that because of the behaviours associated with westernization in both rural and urban areas, this tendency may change in the future.

Several longitudinal studies have documented the superiority of central over brachial BP as a predictor of cardiovascular damage and complications.[22] In our study, the variance in cSBP was again explained by baseline γ-glutamyltransferase, but rural location showed the strongest association. This may indicate that the rural setting in our study was not a typical deep-rural area described in studies a century ago, with easy access to unhealthy food, tobacco and alcohol products.

Apart from alcohol use, abdominal obesity was one of the strongest predictors for the development of hypertension in our study. The South African Demographic and Health Survey determined that the prevalence of obesity was most common in African women (56.6%) when compared with other ethnic and gender groups.[13] The negative consequences of abdominal obesity were clearly seen in our study, namely independent relationships with the 5-year change in SBP and subclinical atherosclerosis.

The results found with regards to the 'protective effects' of HIV infection for the development of hypertension in our study cannot be ignored. South Africa continues to be the country housing the largest population of people (an estimated 5.6 million people in 2009) living with HIV worldwide.[23] It is well documented that HIV infection has atherogenic, coagulatory, dyslipidaemic and inflammatory effects,[24] but our group has shown a lower or similar BP in HIV-infected compared with uninfected individuals.[25] However, the long-term metabolic and cardiovascular effects of the virus coupled with anti-retroviral treatment, may have severe consequences for the development of cardiovascular disease.

In addition to the poor HIV-profile of South Africans, our results should be portrayed within the context of severe poverty where 65% of participants were unemployed. This is not an unrealistic portrayal of the situation in South Africa, as an estimated 13 million South Africans are unemployed.[26] Although being plagued by infectious and parasitic diseases and nutritional deficiencies,[9] non-communicable diseases such as hypertension should be considered of great economic importance because of their high frequency in young populations, frequent underdiagnosis, undertreatment and severity of complications.[2] Hence, the promotion of preventive measures from an early age,[9] such as reduced alcohol intake and healthy diets, may be of the utmost importance in South Africa.

Our study has several limitations. Firstly, because of the focus of the PURE-study, participants from specific rural and urban environments were selected. Hence, our results are not generalizable to the rest of the country. Secondly, it is possible that misclassification of optimal BP or hypertension occurred during baseline or follow-up, even though they were measured twice under controlled conditions. We were not able to measure microalbuminuria. Furthermore, our methods for measuring certain risk markers, such as physical activity, dietary intake and experience of stress, may not have been sensitive enough to portray these results reliably. Unfortunately, detailed dietary data on salt intake were not available. Studies with 24-hour urinary sodium and potassium excretion data are, therefore, strongly encouraged.[10] Finally, although our results were consistent after multiple adjustments, we cannot exclude residual confounding.

Apart from an article on the prospective Kenya Luo migration study published >20 years ago,[27] to our knowledge this study presents the first results in a longitudinal cohort on the development of hypertension in South Africa—in reply to the urgent call for such studies.[8,9] Although the study was performed under difficult circumstances, much effort was applied in obtaining scientifically reliable results, such as the use of trained African fieldworkers and ethnically validated questionnaires. In addition, we contribute to the body of knowledge regarding

advanced cardiovascular measurements, such as central SBP, CIMT and AI in African populations.[9]

In conclusion, for the time span of 5 years, 24% of African individuals with optimal BP developed hypertension. Our exploration of conventional and behavioural cardiovascular risk factors show that γ-glutamyltransferase at baseline was the most consistent variable that associated independently with 5-year change in brachial BP and PP and also with follow-up central SBP and subclinical atherosclerosis. Abdominal obesity was also a strong predictor of cardiovascular changes. These results confirm that the surge in hypertension and its consequences in Africa are largely caused by modifiable risk factors; therefore, future public health strategies should focus aggressively on lifestyle. The alternative (according to Poulter[7]) is to 'stand back and watch the dreadful toll of human suffering caused by hypertension, knowing it had been largely preventable'.

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KEY MESSAGES

- The development of hypertension in Black South Africans during 5 years was associated with a history of excess alcohol intake (as suggested by measurements of γ-glutamyltransferase and self-report) and obesity as assessed by waist circumference.
- Initial levels of γ-glutamyltransferase also associated with additional cardiovascular assessments at follow-up, namely, estimated cSBP and CIMT, indicated an association with central haemodynamics and cardiovascular structure after a 5-year period.
- This study provides some of the first results from a longitudinal cohort on the development of hypertension in South Africa, in reply to the urgent call for such studies.

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