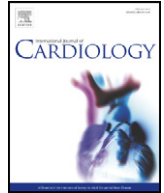




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Elevated risk factors but low burden of heart disease in urban African primary care patients: A fundamental role for primary prevention

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ABSTRACT

Background: Few data describe the case burden of heart disease and cardiovascular risk factors relative to other conditions in urban Africans seeking primary health care.**Methods:** A clinical registry captured data on 1311 consecutive primary care patients (99% African) from two primary care clinics in Soweto, South Africa. Those with suspected sub-clinical heart disease had more advanced cardiologic assessment.**Results:** Overall, 862 women (66%, 41 ± 16 years) and 449 men (38 ± 14 years) were studied. Whilst more men were smokers (47% vs. 14%; OR 5.23, 95% CI 4.01–6.82), more women were obese (42% vs. 14%; OR 4.54, 95% CI 3.33–5.88); blood glucose levels doubling with age in obese women. Although 33% were hypertensive, only 4.9% had type 2 diabetes (n = 45), heart disease (n = 10) and/or cerebrovascular disease (n = 12). Overall, 16% (n = 205) had an abnormal 12-lead ECG with more men than women showing a major abnormality (24% vs. 11%; OR 2.63, 95% CI 1.89–3.46). Of 99 cases (7.6%) subject to advanced cardiologic assessment, 29 (2.2%) had newly diagnosed heart disease: including hypertensive heart failure (13 women vs. 2 men, OR 4.51 95% CI 1.00–21.2), coronary artery disease (n = 3), valve disease (n = 3), dilated cardiomyopathy (n = 3) and 2 cases of acute myocarditis.**Conclusions:** These data demonstrate a relatively low burden of heart disease in urban African patients seeking primary health care. Alternatively, high antecedent risk, particularly among obese women, highlights a key role for enhanced primary prevention.

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1. Introduction

The *Heart of Soweto Study* previously described the impact of epidemiological transition in broadening the spectrum of heart disease [1]. This study included over 5000 *de novo* presentations of heart disease to a tertiary referral hospital servicing one of sub-Saharan Africa's largest urban concentrations of Africans. A key related finding was the clear differential in the nature of heart disease according to the origin of presenting patients; women born in Soweto were more likely to present for tertiary health care with non-communicable forms of disease at an older age. Alternatively, migrants were more likely to present with historically prevalent disease (e.g. rheumatic heart disease) [1]. Community screening programs appear to support observed patterns

of elevations in modifiable risk factors for heart disease [2–4]. However, it is unclear if apparently high levels of risk factors and advanced forms of heart disease are reflected in the case-mix seen in primary care. In the *Heart of Soweto* clinical registry, only 6.8% of confirmed cases of heart disease were directly referred from local clinics [1].

Recognising the central importance of primary health care [5] to assess cardiovascular risk and implement proactive prevention and treatment programs to reduce non-communicable forms of disease in urban communities like Soweto [6], we extended our research into the primary care setting. Using the annual number of incident and prevalent cases managed by the Chris Hani Baragwanath Hospital, we estimated that the case-load of heart disease in each of the 12 primary care clinics in Soweto would be ~350 cases per annum (equivalent to 1 in 200 patient contacts given a typical annual case-load of >15,000). We also postulated that hypertension, as a highly prevalent risk factor [4], would be responsible for many primary care encounters. We further hypothesised that a systematic approach to risk factor profiling and referral for advanced investigation in primary care would reveal a previously hidden burden of sub-clinical heart disease.

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2. Methods

2.1. Study setting

Consistent with the *Heart of Soweto* clinical registry [7] we systematically collected data on consecutive patients attending two pre-selected primary care clinics from a total of 12 in Soweto (644 and 667 patients from Mandela Sissulu and Pimville primary care clinics, respectively). Both of these practices are located in diverse socio-economic locations within the combined townships of Soweto near Johannesburg. The study was undertaken over a 6 month period and involving 50 discrete days of screening (commencing June 2009) and approved by the University of the Witwatersrand Ethical Committee. It conforms to the principles outlined in the Declaration of Helsinki.

2.2. Participants

Each primary care clinic typically managed more than 300 patients per day with wide-ranging health issues. A study team comprising an experienced cardiac nurse, ECG technician and co-ordinator invited consecutive consenting patients aged over 16 years who presented to the primary care clinic to be screened. All patients were reviewed by a primary health care nurse prior to assessment. A target of assessing approximately 25 consecutive patients each screening day (to study a minimum of 1000 patients) was maintained during the study period. Refusal was rare with no systematic bias in case presentation evident.

2.3. Study data

Each participant was subject to a standardised program of assessment as follows:

- Self-reported cultural and socio-demographic profile; including ethnic origin, duration of residence in Soweto and education status.
- Risk factor profiling; including family history of diabetes or any heart disease and smoking status. Random blood glucose levels (fasting in most cases) were obtained using the Accu-Chek Active (Roche Diagnostics).
- Anthropometric profile; including height and weight with calculation of body mass index (BMI, kg/m²).
- Clinical assessment; including average seated systolic and diastolic blood pressure (BP, mm Hg) and heart rate (beats per minute) using a calibrated Dynamap (Critikon) monitor and physical examination for assessment of any signs and symptoms indicative of potential heart disease (e.g. angina pectoris, exercise intolerance, palpitations, raised jugular venous pressure and audible cardiac murmurs).
- Medical history and management; including prior or current diagnoses and pharmacological therapy related to the prevention or treatment of cardiovascular disease (CVD).
- 12-lead ECG; all ECGs were subject to blinded and standardised coding (by SS) according to Minnesota criteria [8] to document any clinical abnormalities.

Based on all data at the point of primary care assessment, KS and SS categorised all cases into the same CVD categories [9] used in previous *Heart of Soweto* Study reports in addition to broad disease categories using the International Classification of Disease descriptors.

2.4. Advanced cardiac profiling

Any participant with a confirmed diagnosis or high suspicion of underlying heart disease was referred to the Cardiology Unit of the Chris Hani Baragwanath Hospital for further investigation. The same standardised protocol of assessment (including echocardiography using gold-standard guidelines [10]) and classification, as described in previous reports [11,12], were applied.

2.5. Statistical analyses

Data were documented on standardised forms and entered into a database (Microsoft Access) in Soweto and then verified and transferred to SPSS Statistics 17.0 for independent analyses at Baker IDI. Normally distributed continuous data are presented as the mean \pm standard deviation and non-Gaussian distributed variables as the median plus interquartile range. Categorical data are presented as percentages with 95% confidence intervals (CI) shown where appropriate. For patient group comparisons, we initially used Chi Square (χ^2) analysis with calculation of odds ratios (OR) and 95% CIs (where appropriate) for discrete variables. Student's *t*-test and analysis of variance were applied for normally distributed continuous variables. Multiple logistic regression analyses (entry model) were performed on demographic and baseline risk factor profiles to derive adjusted ORs for the risk of recording elevated BP and blood glucose levels (including an interaction term for sex and weight status) and being diagnosed with heart disease. Wherever possible, we have applied the STROBE guidelines [13].

3. Results

3.1. Clinical and socio-demographic profile

In total, 1311 primary care patients were studied. The clinical and socio-demographic profile of the study cohort are summarised in Table 1 according to sex. Overall, there were more women (66%) than men and nearly all (99%) were of African descent and/or originated from Soweto (92%). Women were on average three years older than their male counterparts, were more likely to be unemployed and be long term residents of Soweto.

3.2. Case presentation

Fig. 1 shows that from a broad range of documented conditions (1597 for women and 764 in men), CVD was evident in 4.9% of cases. Primary forms of atherosclerotic disease, including stroke (0.9%) and coronary artery disease (CAD, 0.2%) were extremely rare. In total, 48 cases had a combination of hypertension and an established form of CVD. Other than hypertension, the most common conditions seen were respiratory disease (21% – predominantly pulmonary complications secondary to tuberculosis and other chronic lung diseases), musculoskeletal disorders (17% – predominantly back pain), systemic infectious disease (16% – including HIV/AIDS), neurological disorders (16% – mainly headaches), gastro-intestinal disorders (15% – predominantly diarrhoea) and skin disorders (predominantly fungal

Table 1
Initial clinical and socio-demographic profile (n = 1311).

	All (n = 1311)	Women (n = 862)	Men (n = 449)	P value
<i>Socio-demographic profile</i>				
Age (years)	40 \pm 16	41 \pm 16	38 \pm 14	<0.001
African descent	1292 (99%)	853 (99%)	439 (98%)	0.089
From Soweto	1207 (92%)	786 (91%)	421 (94%)	0.101
Years in Soweto	29 \pm 19	30 \pm 20	26 \pm 18	<0.001
<6 years education	282 (22%)	193 (22%)	89 (20%)	0.646
Unemployed	744 (57%)	613 (71%)	131 (29%)	<0.0001
<i>Risk profile</i>				
Family history of heart problems	640 (49%)	455 (53%)	185 (41%)	<0.0001
History of smoking	334 (25%)	124 (14%)	210 (47%)	<0.0001
Dyslipidaemia	16 (1.2%)	12 (1.4%)	4 (0.9%)	0.443
Body mass index (kg/m ²)	28.2 \pm 9	29.9 \pm 9.2	24.8 \pm 8.3	<0.0001
Waist circumference (cm)	90 \pm 18	93 \pm 19	85 \pm 15	<0.0001
No regular exercise	1172 (89%)	787 (91%)	385 (86%)	0.004
<i>Pre-existing CVD</i>				
Hypertension	430 (33%)	333 (39%)	97 (22%)	<0.0001
Diabetes	45 (3.4%)	32 (3.7%)	13 (2.9%)	0.441
Stroke	12 (0.9%)	6 (0.7%)	6 (1.4%)	0.248
All forms of CVD	65 (4.9%)	42 (4.9%)	23 (5.1%)	0.751
<i>Clinical presentation</i>				
NYHA Class II or III	215 (16%)	154 (18%)	61 (14%)	0.049
Palpitations	200 (15%)	144 (17%)	56 (12%)	0.045
Chest pain on exertion	220 (17%)	143 (17%)	77 (17%)	0.784
Syncopal episodes	218 (17%)	160 (19%)	58 (13%)	0.009
Peripheral oedema	40 (3.1%)	30 (3.5%)	10 (2.2%)	0.209
Heart rate/minute	72 \pm 12	73 \pm 12	72 \pm 12	0.134
Systolic blood pressure (mm Hg)	132 \pm 22	132 \pm 22	131 \pm 20	0.321
Diastolic blood pressure (mm Hg)	84 \pm 15	85 \pm 16	84 \pm 14	0.119
Blood glucose level (mmol/L)	5.5 \pm 2.0	5.5 \pm 2.0	5.3 \pm 2.0	0.113

CVD = cardiovascular disease; NYHA = New York Heart Association.

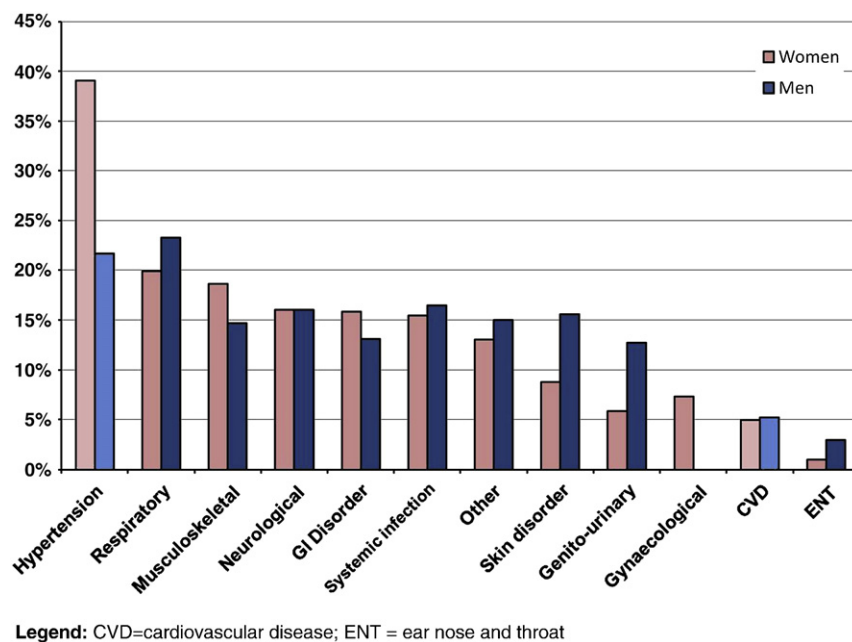


Fig. 1. Major diagnostic groups in male (n = 449) and female (n = 862) case presentations.

disorders). Of the “other” reasons for seeking primary health care, the most common was family planning (e.g. advice on contraception).

3.3. Cardiovascular risk profile

On presentation, women were more likely to report a family history of any form of heart condition (OR 1.28, 95% CI 1.16–1.46). Women were also more likely to have a personal history of hypertension (OR 1.79, 95% CI 1.47–2.17), far more likely to be obese (42% vs. 14%; OR 4.54, 95% CI 3.33–5.88) and report symptoms suggestive of underlying heart disease (including exercise intolerance, palpitations, chest pain on exertion and syncope). Alternatively, men were far more likely to smoke (OR 5.23, 95% CI 4.01–6.82) and men with hypertension had higher BP than their female counterparts ($151 \pm 22/97 \pm 16$ vs. $146 \pm 22/92 \pm 15$ mm Hg; $p < 0.05$ for both comparisons). Both sexes reported high levels of sedentary behaviour (89%) although 282 individuals (22%) reported having physically active employment. Those undertaking formal exercise (n = 125) typically reported running on a regular basis (38%), attending aerobic programs (11%) and/or playing a team sport (11%). Overall, 3.4% of all patients were diagnosed with type 2 diabetes. However, of 968 random blood glucose levels, 9.8% were >7.0 mmol/L; when accounting for diabetic cases this proportion fell only slightly to 7.9%.

Fig. 2 compares the BP, heart rate and blood glucose and body fatness levels in non-obese (left panels) and obese (right panels) men and women according to age. Regardless of weight status, there was an age gradient in all these parameters. However, the largest gradients were found in obese women, particularly in respect to systolic BP and blood glucose levels; the latter rising from 4.5 ± 1.0 to 6.8 ± 3.2 mmol/L in the youngest vs. oldest age group. This compared to a more modest rise from 5.2 ± 0.6 to 6.2 ± 1.3 mmol/L in obese men. On an adjusted basis, obese women were 2.0-fold (95% CI 1.19 to 3.45) and 2.2-fold (95% CI 1.25 to 4.00) more likely to record a blood glucose level >7.0 mmol/L ($p = 0.01$) and a systolic BP >140 mm Hg ($p = 0.007$), respectively, than obese males.

Consistent with a low-level of diagnosed CVD but a relatively high number of hypertensive cases (102 of which were newly diagnosed and yet to be prescribed treatment), the most commonly prescribed cardiac related medications were thiazide diuretics (n = 302, 23%),

angiotensin converting enzyme inhibitors (n = 147, 11.2%) and calcium antagonists (n = 112, 8.5%). Very few cases were prescribed aspirin (n = 36, 2.7%), beta blockers (n = 23, 1.8%), or a statin (n = 4, 0.3%). There was a positive correlation between the number of prescribed anti-hypertensive agents and elevated BP ($p < 0.001$). For example, in those prescribed single (n = 127), double (n = 138) or triple (n = 63) anti-hypertensive therapy, mean BP were $141 \pm 19/90 \pm 13$, $152 \pm 29/95 \pm 14$ and $161 \pm 28/100 \pm 21$ mm Hg, respectively (all comparisons < 0.05).

3.4. 12-Lead ECG

Table 2 summarises the ECG profile of the study cohort. In total, 1106 cases (84%) had no major abnormality evident. Men were 2.6-fold more likely to have an ECG abnormality (95% CI 1.89–3.46) including evidence of right ventricular hypertrophy (OR 4.65, 95% CI 2.45–8.81), left ventricular hypertrophy (OR 2.94, 95% CI 1.95–4.45) and a tachyarrhythmia (OR 1.97, 95% CI 1.12–3.48). Only two patients had ECG evidence of atrial fibrillation.

3.5. Advanced cardiac assessment (n = 99)

A total of 99 cases, comprising 63 women (7.3% of all women, aged 40 ± 16 years) and 36 men (8.0% of all men, aged 37 ± 14 years), were referred for more advanced cardiologic assessment via the Cardiology Unit of the Chris Hani Baragwanath Hospital (all subsequently attended). This included 68 cases with hypertension, comprising 56 cases without pre-established heart disease, 10 cases of established heart disease and 2 with a prior stroke requiring further investigation. The remainder comprised 31 cases (2.4% of the entire cohort, comprising 16 women and 15 men) with a high index of suspicion for underlying heart disease but without a cardiovascular risk factor. On an adjusted basis, individuals who were older (adjusted OR 1.03, 95% CI 1.02–1.05 per year), male (OR 1.64, 95% CI 1.02–2.64), a smoker (OR 2.43, 95% CI 1.30–4.52) or in NYHA Class II or III (OR 1.74, 95% CI 1.08–2.81) were more likely to be referred for more advanced cardiac assessment.

Mean left ventricular ejection fraction (LVEF) was similar for women ($56 \pm 11\%$) and men ($59 \pm 11\%$). Overall, 17 patients were

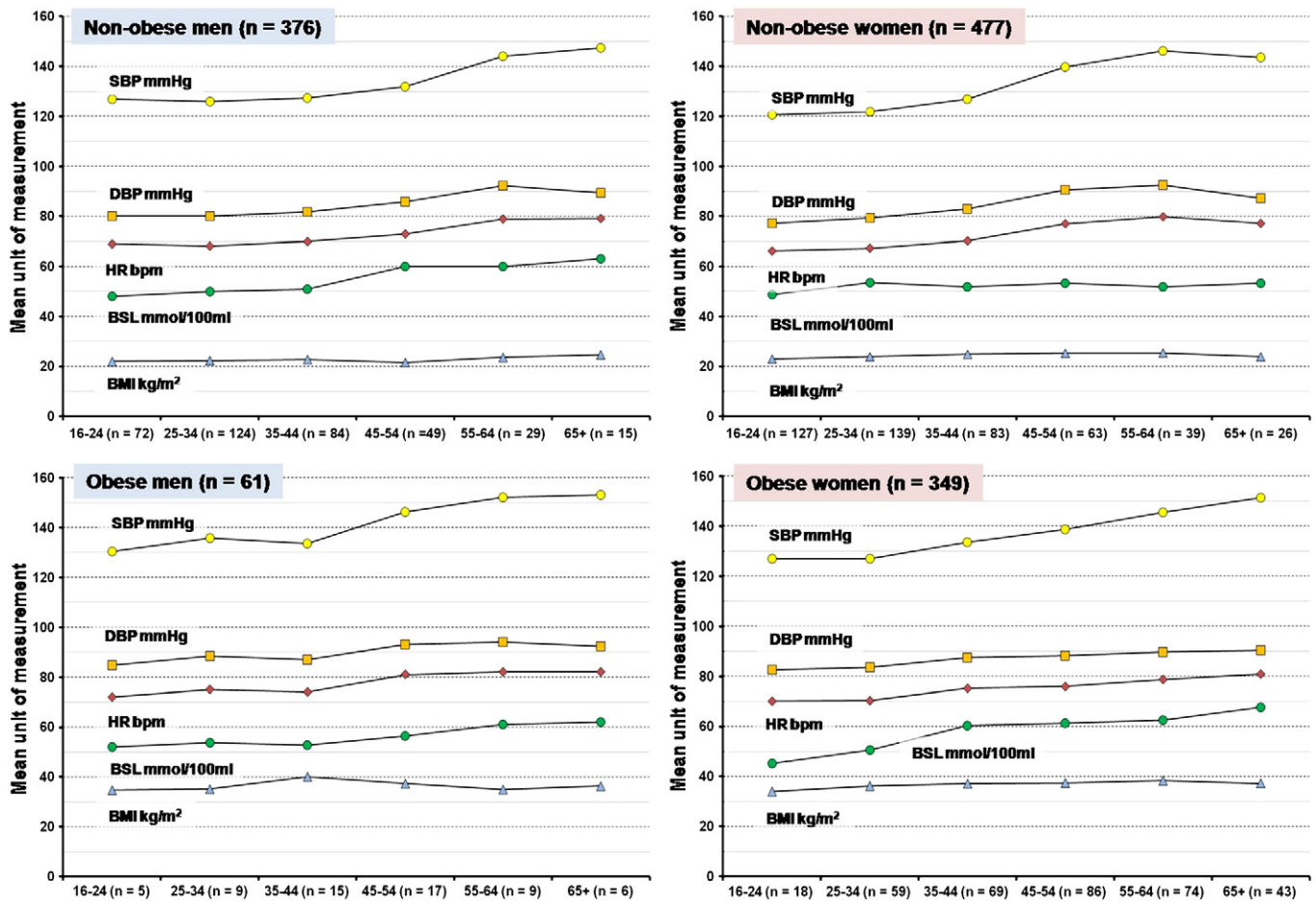


Fig. 2. Key risk factor parameters in non-obese and obese individuals according to age.

found to have left ventricular systolic dysfunction and 12 had evidence of diastolic dysfunction. Of these 29 cases, 5 had normal BP and one individual had no history of CVD. In addition to the 12 cases with pre-established CVD, a further 15 cases were found to have hypertensive heart failure (HF). The majority of these cases were women (n = 13; OR 4.51 95% CI 1.00–21.2 – p = 0.041) and 14 had previously diagnosed hypertension. An additional 3 cases were diagnosed with CAD, 3 cases with degenerative valve disease (a total of 28 cases having some form of valvular dysfunction but none with rheumatic heart

disease), 3 cases with a serious tachyarrhythmia (including the two cases of atrial fibrillation plus one Wolf–Parkinson–White Syndrome), 2 cases with idiopathic cardiomyopathy (CMO), 2 cases with acute myocarditis (post viral infection) and 1 case with post partum CMO. Of these 14 cases, 8 came from the sub-group who had no history of CVD or a cardiovascular risk factor.

4. Discussion

To our knowledge, this represents the first systematic attempt to quantify the contribution of clinically overt and sub-clinical heart disease in a primary care setting in sub-Saharan Africa. Specifically, we compiled a registry of consecutive case presentations to two representative primary care clinics in the urban African community of Soweto, South Africa. This extends upon our approach to uncovering the evolving spectrum and burden of risk factors and heart disease in this community via the *Heart of Soweto* Study during 2006–2008 [1,7]. Consistent with other reports outlining the broad spectrum of disease in the region [14], infectious disease predominated, both in the form of systemic infection such as HIV/AIDS and localised manifestations such as tuberculosis, with respiratory disease and musculo-skeletal disorders common reasons for presentation. Although the contribution of diagnosed forms of heart disease was very small (1 in 100 case presentations), the risk factor burden of the cohort, conversely, was high with around 1 in 3 case presentations being hypertensive. This is consistent with previous estimates of this highly modifiable cardiovascular risk factor [3] and resembles BP levels often seen in high income countries [15]. The disproportionate contribution of obese women was important in this regard.

Table 2
12-Lead ECG profile.

	All (n = 1311)	Women (n = 862)	Men (n = 449)	P value
No major abnormalities detected	1106 (84%)	766 (89%)	340 (76%)	<0.001
<i>Rhythm</i>				
Tachyarrhythmia	50 (3.8%)	25 (2.9%)	25 (5.6%)	0.017
Bigeminy/trigeminy	19 (1.5%)	13 (1.5%)	6 (1.3%)	0.805
<i>Conduction defects</i>				
1st degree heart block	29 (2.2%)	17 (2.0%)	12 (2.7%)	0.413
Bundle branch block	12 (0.9%)	8 (0.9%)	4 (0.9%)	0.946
<i>Other abnormalities</i>				
Right ventricular strain	46 (3.5%)	14 (1.6%)	32 (7.1%)	<0.001
Left ventricular strain	103 (7.9%)	43 (5.0%)	60 (13.4%)	<0.001
Left atrial strain	22 (1.7%)	8 (0.9%)	14 (3.1%)	0.003
P pulmonale	16 (1.2%)	5 (0.6%)	11 (2.5%)	<0.001

Although the prevalence of diagnosed type 2 diabetes was relatively low (3.4%), 7% of patients (mainly obese women) were at risk of metabolic disorders on the basis of their blood glucose profile. Significantly, obesity is associated with other rarely reported forms of CVD in Soweto, with obese women in the *Heart of Soweto* cohort being more likely to present with atrial fibrillation [16]. Therefore, the potential impact of enhanced primary prevention in this context is obvious, particularly in truncating a future rise in hypertensive heart disease [17,18] as life-expectancy and unhealthy lifestyles escalate. However, secondary prevention is also important when considering that a further 2 in 100 case presentations (15 of 29 of whom had hypertensive HF) were subsequently diagnosed and appropriately treated.

These data provide an immediate perspective of the currently small contribution of heart disease to primary care presentations in an urban African community in epidemiological transition. It also signals two clear warnings for its immediate and future health. First, the historically large burden of advanced and complex cases of heart disease at the tertiary care level in Soweto [7] is likely to rise if there is no provision for a systematic screening and linked referral program for more advanced disease. Second, the latent pool of hypertensive individuals in Soweto, which we have now confirmed in all three key public health settings – the broader community [4], the primary care setting (these data), and the tertiary care setting [18], is likely to fuel a sustained burden of neurologic [19] and cardiologic cases in the future if successful cost-effective prevention strategies are not implemented. African women with high levels of obesity, hypertension and potentially latent diabetes are particularly vulnerable and must be targeted accordingly. Determining the most cost-effective treatments in a resource poor environment will be important [20]. For example, although anti-hypertensive treatment (including a thiazide diuretic [21]) was consistent with reports from the region those prescribed combination therapy had systolic and diastolic BP readings approximately 5 and 10 mm Hg higher than those on single therapy.

Unfortunately, beyond broader population studies [22,23] there are few comparable primary care studies reported in the literature. Certainly, the large differential between male and female smoking habits is well documented [24] and an estimated 5% of Africans in the region had diabetes in 2000 [25]. The combination of diagnosed diabetes and elevated blood glucose levels in our cohort suggests that diabetes might affect 5–10% of cases. One notable study worthy of comparison is the Hi Hi Study of 403 Africans being managed by primary care services in Cape Town [26]. Renal impairment was found in around one in four cases whilst ECG evidence of left ventricular hypertrophy and/or ischaemic S-T segment changes were found in 35% and 49% of cases, respectively. Although we did not specifically measure renal function in our cohort, data from the Hi Hi cohort are consistent with data from the *Heart of Soweto* tertiary cohort [7].

Overall, our findings are consistent with our initial estimates that <1 in 100 primary care patients in Soweto have an established form of heart disease. However, this number increases to 3 in 100 cases when a system of cardiac referral that is common to most health systems in high income countries is implemented. Such a “return for effort” needs to be carefully evaluated, particularly in association with other potentially more sophisticated strategies (e.g. cardiac bio-markers and hand-held imaging). In addition, more basic methods such as well-defined clinical assessments for heart disease (e.g. auscultating for cardiac murmurs) and utilisation of the 12-lead ECG should be instigated. Consistent with a global strategy to limit the impact of non-communicable heart disease in South Africa [27], our group is planning a primary care prevention trial in this setting with a strong focus on hypertension and metabolic disorders that will formally evaluate strategies to detect those who have already developed heart disease.

This study has a number of limitations that require comment. Due to the volume of cases managed by the participating primary care

clinics and the nature of their medical record system, we were unable to provide accurate estimates of the proportion of cases captured by our registry. Wherever possible, we studied consecutive patients to avoid selection bias. By relying upon a combination of self-report and primary care clinic records, we were unable to verify each and every diagnosis. All 12-lead ECG data were retrospectively and systematically analysed following the study, however not every patient with an abnormality (e.g. 3.5% had ECG evidence of right ventricular strain and often with accompanying p pulmonale) was referred for more advanced assessment. It is also probable that more individuals with sub-clinical or undiagnosed heart disease would have been identified if all patients were subject to the same level of screening.

In conclusion, we examined the burden of cardiovascular risk factors and heart disease cases in a primary care setting in Soweto, South Africa and found that <1 in 100 case presentations were being managed for pre-existing heart disease. This figure rose to 3 in 100 case presentations when suspicious cases were referred for more definitive assessment. Whilst the overall burden of existing heart disease appears to be currently low in Soweto, the role of enhanced primary care prevention applied on a sex-specific basis to truncate a potential epidemic of disease related to hypertension and metabolic disorders is obvious.

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Disclosures

None.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [28].

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