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Research Paper

The substantial burden of non-communicable diseases and HIV-comorbidity amongst adults: Screening results from an integrated HIV testing services clinic for adults in Soweto, South Africa

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ABSTRACT

Background: South Africa is disproportionately impacted by non-communicable diseases (NCDs) and HIV/AIDS. We investigated the prevalence of known/unknown NCD risk factors, HIV, and NCD risk factor-HIV comorbidity; and treatment status on known diseases to determine the prevalence of controlled/uncontrolled disease.

Methods: This cross-sectional study (June 2018-March 2019) within an integrated testing centre in Soweto, South Africa, screened adults (aged ≥18 years) for body mass index (BMI), hypertension (HT), rapid glucose and cholesterol, and HIV. Results were stratified by age group, sex, HIV-status, and self-reported ART use. Analysis included Fisher's exact, chi-squared, Kruskal Wallis, and Student's T-tests.

Findings: Of 780 enrolled participants, 19.2% were HIV-positive, 37.5% were overweight/obese, 18.0% hypertensive, 10.8% hyperglycaemic, and 8.1% had hypercholesterolaemia. Significantly more women had overweight/obese BMI than men (46.8% vs 19.7%; $p<0.0001$), and women aged 25–34 years had significantly more hypercholesterolaemia than same-aged men (18.2% vs 5.6%; $p = 0.02$). HIV-positive participants had significantly more hyperglycaemia than HIV-negative participants (16.1% vs 9.6%; $p = 0.02$), and those on ART (63.9%) had significantly more hypercholesterolaemia than those not on ART (21.7% vs. 4.9%; $p = 0.002$). Of participants with HT, hyperglycaemia, and hypercholesterolaemia; 72.4%, 96.1%, and 93.3% were newly diagnosed. All participants with previously diagnosed NCDs remained with uncontrolled disease.

Interpretation: There is a high burden of HIV, NCD risk factors, and comorbidity in Soweto, and amongst young adults (18–34 years), especially women. Lowering age requirements for glucose/cholesterol screening to 18+ years, regardless of BMI, HIV-status, or ART use, may yield timely NCD diagnosis/management.

Research in context

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Evidence before this study

Prior to June 2018, the investigators searched PubMed for studies implementing integrated care, specifically for NCDs, amongst people living with HIV, to identify the burden of HIV, NCDs and comorbidity in South Africa. We used the search terms 'integrated care', 'point-of-care', 'HIV', 'non-communicable diseases', 'diabetes mellitus', 'hypertension', and 'hypercholesterolemia' without language restrictions, and did not identify observational or implementation science studies integrating point-of-care testing for both blood glucose (both random and average HbA1c) and cholesterol into a facility-based standard of care HIV testing centre in South Africa.

Added value of this study

This study provides an updated prevalence of HIV, NCD risk factor, and comorbidity amongst adults in Soweto, South Africa, reporting patterns of disease by age, sex and ART-use; and adds to previous work investigating the proportions of previously known and unknown disease and controlled and uncontrolled, previously known disease. This study highlights the large proportion of individuals with chronic disease and comorbidity; amongst relatively young adults (18–34 years); and women presented with chronic diseases at an earlier age than men. The majority of these health conditions were newly diagnosed; and all previously diagnosed participants with HT, high blood glucose and/or cholesterol who had already initiated treatment remained with uncontrolled disease.

Implications of all the available evidence

Implications of all the available evidence. Lowering age requirements for screening to 18+ years for rapid blood glucose and cholesterol screening, regardless of weight classification, HIV-status or ART use, may assist with timely diagnosis and management of NCDs. Guidelines could be reviewed to investigate replacing random plasma glucose with HbA1c for routine testing. More research within the public healthcare sector is needed to expand the generalizability of these findings. Integrative management of NCDs amongst both the general and HIV-infected populations and may improve screening and health-related outcomes in LMICs.

1. Introduction

The main cause of death and disability worldwide are chronic non-communicable diseases (NCDs) (e.g.; cardiovascular disease [CVD] and diabetes mellitus [DM]), attributing to more than three-in-five deaths [1]. Low and middle-income countries (LMICs), such as South Africa, are disproportionately impacted [2], with 90% of NCD-related mortality amongst persons <60 years of age from LMICs [1]. South Africa is also the epicentre of the HIV/AIDS epidemic, carrying over 20% of the world's burden of HIV-1 (7.9 million people living with HIV [PLHIV]) [3,4].

HIV-infection and antiretroviral therapy (ART) use are risk factors for NCDs. The virus causes a persistent inflammatory state and immune dysfunction, which are linked to metabolic syndrome diseases such as DM or dyslipidaemia [5,6]. HIV-positive individuals stable on ART are at higher-risk of NCD comorbidities due to metabolic consequences, such as cardio-metabolic abnormalities associated with treatment [5]. Scale-up of ART has enabled HIV to become a chronic disease with PLHIV reaching nearly the same life expectancy as healthy individuals, and subsequently becoming increasingly at-risk for non-HIV-related chronic conditions of ageing similar to the general population [7].

Studies report the two main NCDs affecting PLHIV residing within LMICs are CVD and DM [8]. CVD has multiple precursors, which if routinely monitored could prevent the onset of disease, reduce costs of hospitalisation, long-term medication and rehabilitation [9]. Hypertension (HT) and dyslipidaemia (elevated blood cholesterol) are chief CVD risk factors (CVDRF) [8]. Obesity is a risk factor for both CVD and DM [7,10], and LMICs are exhibiting greater increases in overweight/obesity relative to high-income countries [11,12]. A meta-analysis of 57 studies in both high-income and LMICs reported the prevalence of HIV comorbidity with the following CVDRFs: HT (21.2%), dyslipidaemia (22.2%), obesity (7.8%), and metabolic syndrome (16.0–31.0%, depending on criteria used) [6].

Screening for HT and checking a patient's weight are the only routine standard of care monitoring for NCDs within South Africas public healthcare sector, including within HIV testing services (HTS) [13,14]. Screening protocols for DM and CVD are currently based on having risk factors largely associated with increased age and obesity [13,14]. Only overweight individuals – of any age - are screened for DM if also exhibiting another risk factor for hyperglycaemia or metabolic decompensation [15]. For adults of normal weight, screening for DM only starts at ≥45 years [15]. Criteria for cholesterol screening and initiation of lipid-lowering therapy centres around being of older age and having DM [15]. Screening for blood glucose and lipids amongst PLHIV is recommended prior to and three months post-ART initiation, or three months after initiating highly active ART and annually thereafter [16]. PLHIV on treatment who are pre-diabetic should be monitored every three to six months [16]. Criteria for blood glucose and lipid-lowering treatment initiation for PLHIV is the same as for HIV-negative patients [16]. Given the impact of NCDs on both the general population and amongst PLHIV, it may be helpful to integrate routine services for management of NCDs.

An HTS centre in Soweto, South Africa, expanded its standard of care services for walk-in adults to include NCD risk factor screenings: body mass index (BMI) calculations, and rapid blood glucose (both random and average [HbA1c]) and cholesterol screenings. This study investigated the prevalence of known and unknown NCD risk factors of HT, hyperglycaemia, dyslipidaemia and obesity; HIV; and NCD risk factor comorbidity amongst HIV-infected adults; as well as treatment status on known diseases to determine the prevalence of controlled and uncontrolled diseases. We investigated disease prevalence by age group and sex.

2. Methods

2.1. Study design, setting and sample

This was a cross-sectional study conducted at an integrated NCD-HTS centre for walk-in adults within the Perinatal HIV Research Unit (PHRU) in Soweto, South Africa. PHRU is a research centre on the grounds of the Chris Hani Baragwanath Academic (Bara) Hospital. The centre offers free wellness services not regularly offered in the public healthcare sector to any walk-in adult and referred patient with Tuberculosis (TB) from the PHRU TB clinic.

A convenience sample of all eligible and consenting walk-in participants between 18 June 2018 and 28 March 2019 were included in the study. If participants made multiple clinic visits within the timeframe, only data from the first visit were analysed.

Study participants consented for both the health screening programme and for their data to be used in research. Participants who did not consent for the use of their data were still able to undergo health screening. All patients with abnormal screening results were

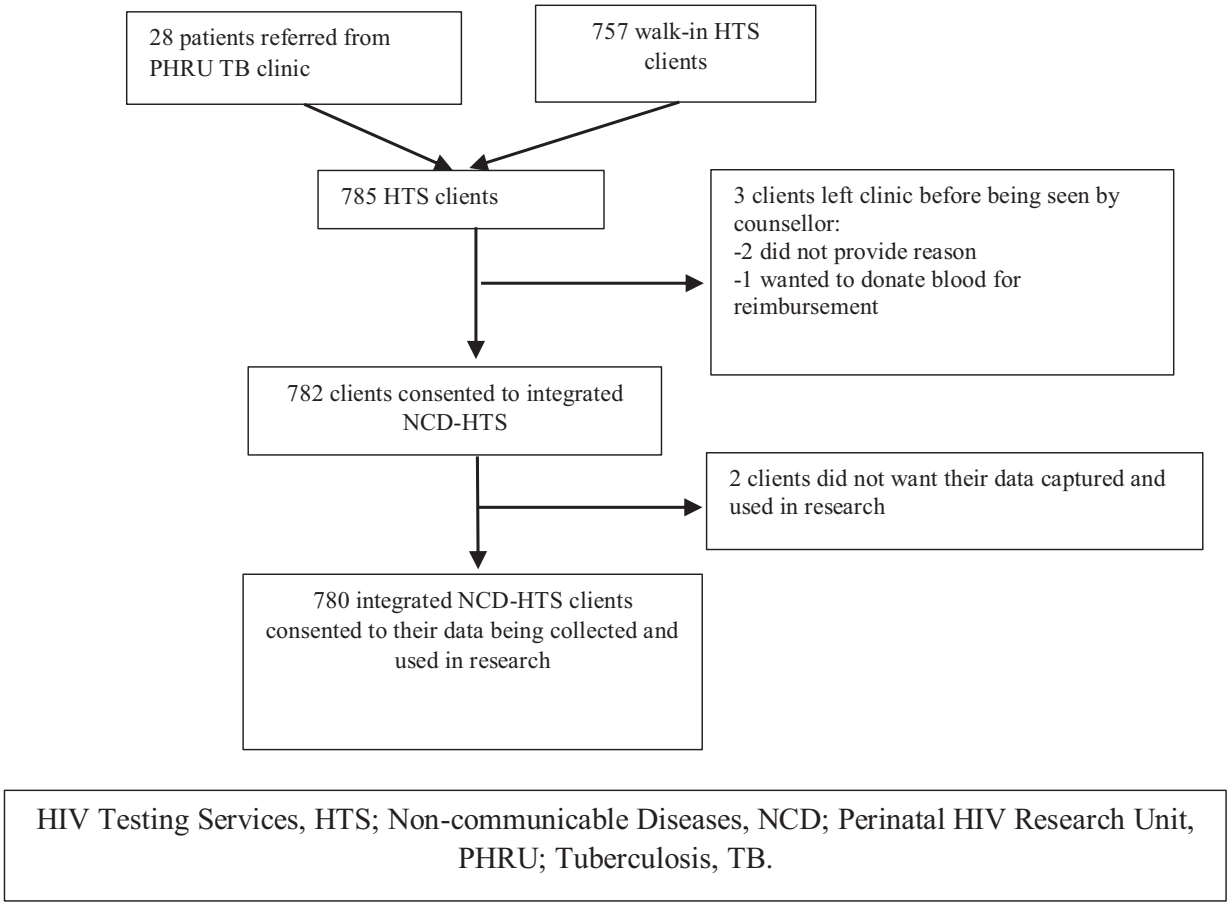

Fig. 1. Integrated non-communicable diseases-HIV testing services participant flow; Soweto, South Africa.

referred out to other public primary healthcare clinics for further management and treatment. Fig. 1 depicts the participant flow for this study.

Eligible participants were adults (≥18 years); fluent in English, isiZulu, and/or Sesotho; and provided written informed consent (with an impartial witness, if needed) for screening procedures.

2.2. Data collection and management

Participant demographics were either self-collected by literate participants or with help of study staff for illiterate participants. Vital signs, health screening results, and other clinical data were collected by the study counsellors and/or nurse. Data were recorded directly onto paper forms comprising the PHRU HTS participant file, which also included the CD4 count pathology reports, as printed from the electronic National Health Laboratory Services laboratory platform and filed by the nurse. All data were assigned participant numeric codes, cleaned and verified prior to entry into the study database (REDCap). Hardcopies of participant files were stored in a locked filing cabinet. PHRU-affiliated authors/study investigators had access to the data.

2.3. Study measures

2.3.1. Demographics

Data were collected on sex, age, race, nationality, ethnic group, marital status, highest level of education, source of income, and details regarding home residence, as previously described [17]. Participants were asked about their self-perceived alcohol and tobacco use; the questions modelled from the validated 2003 South African Demographic and Health Survey (SADHS) [18].

2.3.2. Health screening results

Participants could opt-out of any health screening. Phlebotomy for CD4 count was only offered to those HIV-positive participants who had not yet initiated ART.

Health screening results included height and weight to calculate BMI, which was then categorised into four classifications (*underweight* < 18.5 kg/m^2; 18.5 kg/m$^2 \leq$ *normal* ≤ 24.9 kg/m^2; 25.0 kg/m$^2 \leq$ *overweight* ≤ 30.0 kg/m^2; and *obese* ≥ 30 kg/m^2); blood pressure (BP) readings (high BP >140/90 mmHG; 90/60 mmHG ≤ normal BP ≤ 140/90 mmHG; low BP <90/60 mmHG); HIV results and CD4 count. These parameters have been previously described in more detail [17].

Additional screening results included:

Average blood glucose (HbA1c) and *random blood glucose*. Measured by using two point of care machines - the *Hemocue HbA1c 501 analyser* and the *Multicare IN*, respectively. The results from both machines classified as high (≥ 6.5 mmol/L and ≥ 11 mmol/L, respectively), normal (all readings outside of those high or low), or low (if either machine read *'low'*).

Total cholesterol (TC). Measured using the point of care *LUX Multiparameter Device*. Results classified as high (≥5 mmol/L) or low, if the machine read '*low*'. Otherwise, TC was classified as normal.

For HIV-positive participants, all self-reported ART use ('on ART' or 'not on ART') was documented.

2.3.3. Health screening history

Health screening history questions included: have you ever been diagnosed with high BP/HT, high blood sugar/diabetes, or high cholesterol; and if yes, have you ever been on treatment for any of those conditions? From these data and the health screening results, the following categories of participants were defined per condition:

Newly diagnosed: HTS participants who did not self-report having a previous condition, but were screened with abnormal results.

Previously diagnosed: HTS participants who self-reported as having a previous condition and were re-screened with abnormal results.

Controlled: HTS participants who were classified as previously diagnosed and self-reported they had ever taken treatment and were re-screened with normal results.

Uncontrolled: HTS participants who were classified as previously diagnosed and self-reported they had ever taken treatment and were re-screened with abnormal results.

2.4. Ethical considerations

The health programme was approved by the University of Witwatersrand, Human Research Ethics Committee (Wits HREC), and approved by the Associate Director for Science, centre for Global Health, Centres for Disease Control and Prevention.

2.5. Data analysis

Frequencies and percentages were determined for categorical variables that were stratified by age group (18–24, 25–34, 35–44 and ≥45 years), sex, HIV status, and ART use.

To test statistical significance for categorical measures stratified by HIV status and sex, chi-squared analysis or Fisher's exact test was used, as appropriate. Descriptive statistics including medians with interquartile ranges (IQR) were determined for continuous measures stratified by sex and HIV status, and compared parametrically and non-parametrically using both the two-group Student's *T*-test and Kruskal-Wallis tests.

A wealth quintile was developed using the socio-economic measures and the Principal Component Analysis (PCA) variable reduction, as previously described [17]. The socio-economic measures included the following variables: type of house, source of water, type of toilet facility, type of fuel used for cooking, type of fuel used for lighting, possession of household items and other ownership items [17]. Five wealth quintiles with 20 percentile intervals were determined.

All statistical analysis was conducted in SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC).

2.6. Role of the funding source

The funder had no role in the study design, data collection or data interpretation. The co-authors affiliated with PHRU had full access to all study data, and the corresponding author had final responsibility for the decision to submit for publication. There were funder co-authors, and the manuscript was approved by the funder prior to submission.

3. Results

3.1. Demographics by age group

There were 780 enrolled participants, of which the largest proportions were women (65.8%, n = 513/780), black African (98.3%, n = 767/780) and of single relationship status (70.7%, n = 551/779) with median age of 32.0 years (IQR: 25.0–42.0). Just over half of participants had either completed high school (matriculated) or had some tertiary education (64.0%, n = 499/780). Only 33.4% were formally employed (n = 259/776), of which 92.3% (n = 239/259) were aged 25 years or older. The majority of participants reported drinking alcohol (65.1%, n = 507/779), with 10.3% drinking excessively (n = 52/507) and 25.5% ever having smoked cigarettes (n = 191/748) (Table 1).

3.2. Screening results by age group and sex

HIV and NCD risk factor screening results are found within Table 2 and Supplementary Table 1.

Of the 775 participants screened for HIV, 19.2% (n = 149/775) were HIV-positive; and of those, the majority were female (72.5%, n = 108/149) (Supplementary Table 1). Of those HIV-positive participants previously diagnosed (48.3%, n = 72/149), 63.9% (n = 46) were on ART. Overall, 86 HIV-positive participants had a median CD4 count of 341 cells/mm^3 (IQR: 246–500). Of those with CD4 count below 200 cells/mm^3, 60% (n = 9/15) were females (with 53.3% being 18–34 years old [n = 8/15]).

HIV prevalence peaked amongst 35–44 year olds (27.5%, n = 50/182) for both sexes (32.7% [n = 36/110] and 19.4% [n = 14/72] for women and men, respectively). Amongst 18–24 year olds, 60.0% (n = 6/10) of the HIV-infections were amongst women. Only one of the HIV-positive 18–24 year olds were previously diagnosed, and he was not on ART; and 18–24 year old men had the lowest median CD4 count (279, IQR: 116–524).

Regarding BMI, 37.5% (n = 289/770) of participants were overweight/obese, with BMI increasing by age group for both sexes. Overall and by age group, significantly more women were classified as overweight/obese than men (46.8% [n = 237/506] vs 19.7% [n = 52/264]; $p < 0.0001$). Over one-third of women in the younger age groups were overweight/obese – 34.6% (n = 44/127) of 18–24 year olds and 43.2% (n = 83/192) of 25–34 year olds. Inversely, significantly more men were classified as underweight in comparison to women (29.2% [n = 77/264] vs 11.7% [n = 59/506]; $p < 0.0001$), and this trend remained by age group. Younger males (18–24 and 25–34 year olds) had the highest proportion of being underweight (38.5% [n = 10/26] and 35.6% [n = 31/87], respectively).

Overall, 18.0% (n = 139/772) of participants had high BP. Relative to females, significantly more males had high BP (23.9% [n = 63/264] vs. 15.0% [n = 76/508]; p = 0.002). The prevalence of high BP increased by age group for both sexes, rising from 3.1% (n = 4/127) and 7.7% (n = 2/26) in 18–24 year-old women and men, respectively; to 31.6% (n = 24/76) and 38.5% (n = 30/78) in 45+ year old women and men, respectively.

About one in ten adults (10.8%, n = 83/766) had high HbA1c, with a similar prevalence by sex. Of the 83 participants with high HbA1c, only four also had high random blood glucose. Of the younger age groups, 7.2% (n = 31/433) had high blood glucose (8.5% [n = 13/153] and 6.4% [n = 8/280] of 18–24 and 25–34 year olds, respectively).

Overall, 62 (8.1%, n = 62/768) participants screened had high TC, of which 54.8% (n = 34/62) were women aged 35 years and older compared to 24.2% (n = 15/62) of their male counterparts. The proportion of women aged 25–34 years with high TC was three times greater than that of men of similar age (18.2% [n = 20/110] vs 5.6% [n = 4/71]; p = 0.02).

The oldest age group (≥45 years) had the highest proportion of overweight/obesity (50.6%, n = 78/154), high BP (35.1%, n = 54/154), high blood glucose (20.3%, n = 31/153) and high TC (16.2%, n = 25/154). Prevalence of comorbidity by sex is within Table 3 and Supplementary Table 2.

Overall, significantly more HIV-negative participants were classified as overweight/obese than HIV-positive participants (39.5%

Table 1
Integrated Non-communicable Diseases-HIV Testing Services Centre Participant Characteristics by Age Group, Soweto, South Africa.

		Age in years			
	Total[a]	18–24	25–34	35–44	≥45
Median age (IQR)	32.0 (25.0–42.0)	22.0 (20.0–23.0)	29.0 (26.0–32.0)	38.0 (37.0–41.0)	52.0 (48.0–58.0)
Sex					
Female (%)	513/780 (65.8)	127/153 (83.0)	198/287 (69.0)	111/185 (60.0)	77/155 (49.7)
Male (%)	267/780 (34.2)	26/153 (17.0)	89/287 (31.0)	74/185 (40.0)	78/155 (50.3)
Race					
Black African (%)	767/780 (98.3)	150/153 (98.0)	282/287 (98.3)	182/185 (98.4)	153/155 (98.7)
Mixed Race/White (%)	13/780 (1.7)	3/153 (2.0)	5/287 (1.7)	3/185 (1.6)	2/155 (1.3)
Nationality					
Other (%)	21/780 (2.7)	3/153 (2.0)	8/287 (2.8)	4/185 (2.2)	6/155 (3.9)
South African (%)	759/780 (97.3)	150/153 (98.0)	279/287 (97.2)	181/185 (97.8)	149/155 (96.1)
Ethnic group					
Other (%)	98/776 (12.6)	17/153 (11.1)	35/285 (12.3)	33/185 (17.8)	13/153 (8.5)
Sotho (%)	127/776 (16.4)	29/153 (19.0)	34/285 (11.9)	33/185 (17.8)	31/153 (20.3)
Tsonga (%)	74/776 (9.5)	12/153 (7.8)	22/285 (7.7)	28/185 (15.1)	12/153 (7.8)
Tswana (%)	60/776 (7.7)	11/153 (7.2)	20/285 (7.0)	14/185 (7.6)	15/153 (9.8)
Xhosa (%)	79/776 (10.2)	16/153 (10.5)	34/285 (11.9)	17/185 (9.2)	12/153 (7.8)
Zulu (%)	338/776 (43.6)	68/153 (44.4)	140/285 (49.1)	60/185 (32.4)	70/153 (45.8)
Marital status					
Divorced\Widowed (%)	35/779 (4.5)	0/153 (0.0)	1/287 (0.3)	10/185 (5.4)	24/154 (15.6)
Living Together\Married (%)	193/779 (24.8)	12/153 (7.8)	54/287 (18.8)	60/185 (32.4)	67/154 (43.5)
Single (%)	551/779 (70.7)	141/153 (92.2)	232/287 (80.8)	115/185 (62.2)	63/154 (40.9)
Highest education					
Some High School (%)	281/780 (36.0)	75/153 (49.0)	108/287 (37.6)	59/185 (31.9)	39/155 (25.2)
Matriculated (%)	163/780 (20.9)	37/153 (24.2)	71/287 (24.7)	39/185 (21.1)	16/155 (10.3)
Tertiary (%)	336/780 (43.1)	41/153 (26.8)	108/287 (37.6)	87/185 (47.0)	100/155 (64.5)
Source of income					
Employed (%)	259/776 (33.4)	20/153 (13.1)	105/286 (36.7)	80/183 (43.7)	54/154 (35.1)
Self-employed (%)	143/776 (18.4)	23/153 (15.0)	48/286 (16.8)	41/183 (22.4)	31/154 (20.1)
Social/Disability grant (%)	110/776 (14.2)	22/153 (14.4)	50/286 (17.5)	25/183 (13.7)	13/154 (8.4)
Parents (%)	153/776 (19.7)	80/153 (52.3)	52/286 (18.2)	15/183 (8.2)	6/154 (3.9)
Pension (%)	23/776 (3.0)	1/153 (0.7)	2/286 (0.7)	2/183 (1.1)	18/154 (11.7)
Unemployed (%)	88/776 (11.3)	7/153 (4.6)	29/286 (10.1)	20/183 (10.9)	32/154 (20.8)
Wealth quintile					
Quintile 1 (%)	208/780 (26.7)	49/153 (32.0)	76/287 (26.5)	48/185 (25.9)	35/155 (22.6)
Quintile 2 (%)	177/780 (22.7)	33/153 (21.6)	63/287 (22.0)	37/185 (20.0)	44/155 (28.4)
Quintile 3 (%)	220/780 (28.2)	42/153 (27.5)	75/287 (26.1)	56/185 (30.3)	47/155 (30.3)
Quintile 4 (%)	152/780 (19.5)	24/153 (15.7)	60/287 (20.9)	41/185 (22.2)	27/155 (17.4)
Quintile 5 (%)	23/780 (2.9)	5/153 (3.3)	13/287 (4.5)	3/185 (1.6)	2/155 (1.3)
Do you drink alcohol?					
No (%)	272/779 (34.9)	39/153 (25.5)	68/286 (23.8)	77/185 (41.6)	88/155 (56.8)
Yes (%)	507/779 (65.1)	114/153 (74.5)	218/286 (76.2)	108/185 (58.4)	67/155 (43.2)
How do you use alcohol?					
Socially	451/507 (89.0)	106/114 (93.0)	188/218 (86.2)	97/108 (89.8)	60/67 (89.5)
Excessively	52/507 (10.3)	7/114 (6.1)	28/218 (12.8)	11/108 (10.2)	6/67 (9.0)
Never	4/507 (0.8)	1/114 (0.9)	2/218 (0.9)	0/108 (0.0)	1/67 (1.5)
Ever smoked cigarettes?					
No (%)	557/748 (74.5)	121/152 (79.6)	184/276 (66.7)	137/178 (77.0)	115/142 (81.0)
Yes (%)	191/748 (25.5)	31/152 (20.4)	92/276 (33.3)	41/178 (23.0)	27/142 (19.0)
Still smoke cigarettes?					
No (%)	3/191 (1.6)	1/31 (3.2)	2/92 (2.2)	0/41 (0.0)	0/27 (0.0)
Yes (%)	188/191 (98.4)	30/31 (96.8)	90/92 (97.8)	41/41 (100.0)	27/27 (100.0)

Interquartile range, IQR.
[a] Total denominators may vary due to participants choosing not to answer socio-demographic and substance use questions.

[n = 244/618] vs 29.5% [n = 44/149]; p = 0.02), with a significantly higher median BMI (23.5 [IQR: 19.8–27.3] vs. 21.6 [IQR: 18.8–27]; p = 0.03). Both the HIV-negative and positive groups with overweight/obese BMI were comprised mostly of women (80.3% [n = 196/244] vs 90.9% [n = 40/44]). About one-third of both the HIV-negative and HIV-positive groups with high BMI were aged 25–34 years (32.8% [n = 80/244] vs 31.8% [n = 14/44], respectively). Significantly more HIV-positive women had overweight/obese BMIs than HIV-positive men (37.0% [n = 40/108] vs 9.8% [n = 4/41]; p = 0.001), and this was inversely true for underweight BMIs (43.9% [n = 18/41] vs 13.0% [n = 14/108]; $p < 0.0001$).

Of the 139 participants screened with high BP, 16.9% (n = 25) were PLHIV. There was no significant difference in prevalence of high BP by sex amongst PLHIV (females 15.9% [n = 17/107] vs. males 19.5% [n = 8/41]; p = 0.5984).

Significantly more HIV-positive participants had high HbA1c compared to HIV-negative participants (16.1% [n = 24/149] vs 9.6% [n = 59/614]; p = 0.022). The majority proportion of hyperglycaemic HIV-positive participants were female (79.2%, n = 19/24), aged 35–44 years (41.7% [n = 10/24]), and none of them self-reported they were on medication for high blood glucose. Of the 59 hyperglycaemic HIV-negative participants, the majority proportion were female (62.7%, n = 37/59) and aged ≥45 years (42.4%, n = 25/59). Two of the three previously diagnosed hyperglycaemic participants self-reported they had initiated treatment.

There was no significant difference in prevalence of high TC by HIV status; however, the proportion of HIV-positive individuals on ART with high TC was significantly higher than those not on ART (21.7% [n = 10/46] vs. 4.9% [n = 5/103]; p = 0.002).

3.3. Previously diagnosed and controlled disease

Table 4 contains the clinical characteristics of diagnosed participants across conditions. Of the HIV-positive participants, 48.3% (n = 72/149) already knew their HIV-status; and of those, 63.9% (n = 46/72) had already initiated treatment.

Of all participants screened with elevated BP, high HbA1c and high TC, 72.4% (n = 97/134), 96.1% (n = 73/76), and 93.3% (n = 56/60) were newly diagnosed with each condition, respectively. Of the participants who self-reported as previously diagnosed, 83.8% (n = 31/37) of participants with high BP, two (n = 2/3) participants with high HbA1c, and one (n = 1/4) participant with high TC self-reported they had already initiated treatment. All previously diagnosed participants were found to have uncontrolled NCD risk factors after re-screening.

4. Discussion

This study highlights the large proportion of individuals with NCD risk factors, HIV, and comorbidity attending an integrated NCD-HTS centre receiving adult walk-in clients from Soweto, South Africa. Relatively young adults (18–34 years) are also greatly affected. This study shows women are presenting with chronic diseases at an earlier age than men. The majority of these health conditions were newly diagnosed; and all previously diagnosed participants with elevated BP, high blood glucose and/or cholesterol who had already initiated treatment remained with uncontrolled disease.

This study reported over one-third of all participants had overweight/obese BMI, one-fifth had elevated BP, one-in-ten had diabetic-level HbA1c, and eight percent had high TC. Nearly one-in-five adults had HIV-infection. These data support existing research, including national surveys, reporting South Africa has the highest rate of overweight/obese people in sub-Saharan Africa [1], and the prevalence of overweight/obese BMI and elevated BP increase with age [19,20]. While this study's prevalence of high HbA1c was similar to that within formal urban settings as reported by the SADHS [19], it showed over double the prevalence of high TC amongst women than previously reported [19]. Study participants had a higher overall HIV prevalence than reported for black Africans in the Fifth National HIV Prevalence Survey [6]; however, the HIV data were similar to those found within the latest SADHS for Gauteng [19].

The HIV-positive study participants had a high prevalence of comorbidity with each NCD risk factor (elevated BP, hyperglycaemia, dyslipidaemia, and obesity), with significantly more high HbA1c than their HIV-negative counterparts. This finding supports a systematic review which found the prevalence of DM amongst TB pa-

Table 3
Screening results by sex for HIV-infected integrated non-communicable diseases-HIV testing services participants, Soweto, South Africa.

	Total[a]	Female	Male	*P*-Value[f]
Any ART use?[b]				
No (%)	26/72 (36.1)	18/51 (35.3)	8/21 (38.1)	0.99
Yes (%)	46/72 (63.9)	33/51 (64.7)	13/21 (61.9)	
CD4 Count (Cells/mm3)				
n, Median (IQR)	86, 341 (246–500)	65, 347 (262–507)	21, 315 (182–412)	0.18
BMI (kg/m^2)[c]				
Underweight (%)	32/149 (21.5)	14/108 (13.0)	18/41 (43.9)	<0.0001
Normal (%)	73/149 (49.0)	54/108 (50.0)	19/41 (46.3)	0.69
Overweight/Obese (%)	44/149 (29.5)	40/108 (37.0)	4/41 (9.8)	0.001
n, Median (IQR)	149, 21.6 (18.8–27.0)	108, 23.0 (19.9–29.8)	41, 19.1 (17.2–21.3)	<0.0001
Blood Pressure (mmHg)				
Low (%)	2/148 (1.4)	1/107 (0.9)	1/41 (2.4)	0.50
Normal (%)	121/148 (81.8)	89/107 (83.2)	32/41 (78.1)	
High (%)	25/148 (16.9)	17/107 (15.9)	8/41 (19.5)	
Blood glucose				
Average (HbA1c) (mmol/mol)[d]				
Normal (%)	125/149 (83.9)	89/108 (82.4)	36/41 (87.8)	0.62
High (%)	24/149 (16.1)	19/108 (17.6)	5/41 (12.2)	
Random (mmol/l)[e]				
Normal (%)	147/149 (98.7)	106/108 (98.1)	41/41 (100.0)	–
High (%)	2/149 (1.3)	2/108 (1.9)	0/41 (0.0)	
TC (mmol/l)				
Low (%)	19/149 (12.8)	10/108 (9.3)	9/41 (22.0)	0.04
Normal (%)	115/149 (77.2)	85/108 (78.7)	30/41 (73.1)	0.47
High (%)	15/149 (10.1)	13/108 (12.0)	2/41 (4.9)	0.20
Ever smoked cigarettes?				
No (%)	96/137 (70.1)	80/102 (78.4)	16/35 (45.7)	0.0005
Yes (%)	41/137 (29.9)	22/102 (21.6)	19/35 (54.3)	
Still smoke cigarettes?				
No (%)	–	–	–	–
Yes (%)	41/41 (100.0)	22/22 (100.0)	19/19 (100.0)	

Antiretroviral Therapy, ART; Body Mass Index, BMI; Interquartile Range, IQR; Total Cholesterol, TC.

[a] Total denominators vary due to: (1) participants being allowed to 'opt out' of any health screening, as desired; and (2) participants choosing not to answer questions relating to smoking.

[b] ART use reported only for HIV-infected clients who were previously diagnosed. HIV-positive participants on ART had significantly more high TC than those not on ART (21.7% vs. 4.9%; p = 0.002).

[c] Overall, HIV-uninfected clients had significantly more overweight/obese BMI than HIV-infected clients (39.5% [n = 244/618] vs 29.5% [n = 44/149]; p = 0.024).

[d] HIV-infected clients had significantly more high HbA1c than HIV-uninfected clients (16.1% [n = 24/149] vs 9.6% [n = 59/614]; p = 0.022).

[e] Both participants with high random glucose also had high HbA1c.

[f] Statistical significance was determined using Chi-square or Fisher's exact test, where appropriate. Some p-values are missing due to some small samples sizes reflecting the stratification by age and sex.

tients in sub-Saharan Africa to be significantly high, with an even higher prevalence amongst those co-infected with HIV [21]. Additionally, the participants on ART had significantly higher TC than those treatment naïve HIV-positive participants. This finding is not unique to only dyslipidaemia. Two of the three main classes of ART - protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NRTIs) – are known to increase HIV patients' risk of HT, hyperglycaemia and dyslipidaemia [6,22]. The Southern African Hypertension Society has acknowledged that long-term, highly active ART is associated with a higher prevalence of systolic HT [23], and PIs and NRTIs may affect both calcium channel blockers - the main class of antihypertensive medications – and statins (i.e.; lipid-lowering therapy) through drug interactions affecting drug metabolism [24,25]. This results in either an enhancement or loss of drug efficacy leading to extremely high blood glucose and/or cholesterol levels [17,22].

This study reports high rates of chronic disease precursors amongst younger persons, which differs from previous reports. While national surveys show the prevalence of diabetic-level HbA1c to increase with age [19,20], this study reports 18–24 year olds had higher rates of elevated HbA1c (and elevated TC) than 25–34 year olds. In general, this study reports worrying levels of overweight/obese BMI and diabetic-level HbA1c amongst the 18–24-year olds. About ten percent of 18–35 year olds had elevated BP.

There are patterns of earlier development of chronic diseases for women. As compared to the SADHS, this study reports 18–24 year old females have nine times and four times the reported diabetic-level HbA1c for their age group and same-aged males, respectively [19]. Literature has well documented that women have a higher HIV prevalence across all age groups, and peak HIV-infections occur amongst young women aged 15–24 years [6,19]. This study found significantly more women had HIV-infection - six out of ten HIV-infections amongst 18–24 years olds were amongst women - and overweight/obese BMI than men across all age groups. HIV-positive women had four times the rate of overweight/obese BMI than HIV-positive men.

The majority of participants with elevated BP, high blood glucose and cholesterol were newly diagnosed, supporting literature reporting a significant proportion of South African adults are not aware of their NCD-risk [19]. Of HIV-comorbid participants, one-quarter were newly diagnosed with both HIV and high BP and/or high TC, and half were newly diagnosed with both HIV and high glucose. This study reported greater proportions of undiagnosed disease compared to the SADHS, which shared 29% and 34% of women and men were newly diagnosed with HT; and 64% and 66% of women and men as pre-diabetic [19]. Symptoms of DM are often less severe or absent, with a significant percentage of cases remaining undiagnosed (30–80%) [15,26].

All previously diagnosed participants on NCD-related treatment subsequently re-screened with uncontrolled disease. These proportions are higher than reported by the SADHS (23% and 9% of women and men had uncontrolled BP, and 85% had uncontrolled blood glucose levels) [19]. However, since the study site is a clinical research setting and more likely to attract people with these conditions as opposed to the general setting, this may be why our disease burden is higher than that found within the SADHS. Less than two-thirds of previously diagnosed HIV-positive participants had initiated ART, which excludes all of the 18–24 year olds. Treatment-naïve participants had a low median CD4 count (under 350 cells/mm^3), with the 18–24 year old men having the lowest CD4 count.

More than one-quarter of the 18–25 year olds and one-third of the 18–44 years olds were overweight/obese. Three-fifths of the participants with high cholesterol were under 45 years of age. The majority of HIV-positive participants were previously undiagnosed, had significantly lower median BMI, and were under 45 years of age. HIV-positive participants also had significantly more high HbA1c than HIV-positive individuals. These sub-populations are missed opportunities in the general population screening process for DM and dyslipidaemia. With screening amongst PLHIV based around ART initiation, one-third of the previously diagnosed HIV-positive participants would have been unscreened due to being treatment naive.

While HbA1c testing is a more sensitive/specific screening method for DM, reflecting the average blood glucose level over the past three months [27,28], random plasma glucose (RPG) screening is conducted in the public health sector [15]. This study's HbA1c and RPG screening results amongst the same participants were poorly correlated. Ten percent of participants had elevated HbA1c, while only four participants also had elevated RPG levels, suggesting the population was not at-risk for DM. Studies have shown that iron deficiency anaemia influences HbA1c levels independent of glycaemia amongst non-diabetic and diabetic patients, alike [29–32], which resolves following iron therapy [33,34]. It is potentially due to the modifications to the structure of haemoglobin and levels of HbA1c in both old and new red blood cells [31,33,34].

Numerous specialist committees on chronic disease management support the earlier screening and treatment of disease, as timely initiation of treatment optimises long-term health outcomes [35]. The American Diabetes Association and the European Association for the Study of Diabetes recommend early pharmacotherapy for the management of hyperglycaemia in type 2 diabetes [36]. Longitudinal, randomised clinical trials, such as the landmark United Kingdom Diabetes Prevention Study, have outlined

Table 4
Diagnosis and treatment initiation participants, Soweto, South Africa.

	Prevalence[a]	Newly diagnosed[b]	Previously diagnosed[c]	Ever been on treatment	Controlled[d]	Uncontrolled[e]
HIV	149/775 (19.2)	77/149 (51.7)	72/149 (48.3)	46/72 (63.9)	46/72 (63.9)	26/72 (36.1)
High Blood Pressure[f]	139/772 (18.0)	97/134 (72.4)	37/134 (27.6)	31/37 (83.8)	–	31/31 (100.0)
High Blood glucose (HbA1c)	83/766 (10.8)	73/76 (96.1)	3/76 (4.0)	2/3 (66.7)	–	2/2 (100.0)
High Total Cholesterol	62/768 (8.1)	56/60 (93.3)	4/60 (6.7)	1/4 (25.0)	–	1/1 (100.0)

[a] Total denominators vary due to participants being allowed to 'opt out' of any health screening, as desired. Additionally, TB patients were not asked questions on history of blood pressure, glucose and cholesterol, which resulted in missing data.
[b] *Newly diagnosed* was defined as HTS client self-reporting normal results at last screening and subsequently screening with abnormal results at the HTS centre.
[c] *Previously diagnosed* was defined as HTS client self-reporting abnormal results at last screening and also screening with abnormal results at the HTS centre.
[d] *Controlled* was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with normal results at the HTS centre. For HIV-infected clients, this simply means, on ART.
[e] *Uncontrolled* was defined as of those HTS clients who were previously diagnosed and had ever been on treatment, who also screened with abnormal results at the HTS centre. Regarding HIV, uncontrolled means ART-naïve.
[f] If the first blood pressure reading was high, then a second reading was taken. The average reading of the two blood pressure readings was then categorised to determine prevalence of high blood pressure. Those HTS clients referred for high blood pressure were clients whose second BP reading was high and who had consented for follow-up.

	149/775 (19.2)	6/127 (4.7)	4/26 (15.4)	0.07	43/197 (21.8)	10/88 (11.4)	0.04	36/110 (32.7)	14/72 (19.4)	0.05	23/77 (29.9)	13/78 (16.7)
	626/775 (80.8)	121/127 (95.3)	22/26 (84.6)		154/197 (78.2)	78/88 (88.6)		74/110 (67.3)	58/72 (80.6)		54/77 (70.1)	65/78 (83.3)
	26/72 (36.1)	–	1/1 (100.0)		7/14 (50.0)	2/3 (66.7)	0.99	6/17 (35.3)	3/6 (50.0)	0.64	5/20 (25.0)	2/11 (18.2)
	46/72 (63.9)	–	–		7/14 (50.0)	1/3 (33.3)		11/17 (64.7)	3/6 (50.0)		15/20 (75.0)	9/11 (81.8)
ls/mm³)												
	86, 341 (246–500)	5, 420 (313–463)	3, 279 (116–524)	0.88	30, 330 (246–500)	7, 338 (156–412)	0.79	24, 363 (240–569)	9, 315 (182–347)	0.27	6, 513 (408–540)	2, 393 (276–510)
)	133/770 (17.3)	22/127 (17.3)	10/26 (38.5)	0.02	27/192 (14.1)	31/87 (35.6)	<0.0001	6/111 (5.4)	19/73 (26.0)	0.0001	4/76 (5.3)	14/78 (17.9)
	348/770 (45.2)	61/127 (48.0)	16/26 (61.5)	0.21	82/192 (42.7)	45/87 (51.7)	0.16	45/111 (40.5)	41/73 (56.2)	0.04	22/76 (28.9)	36/78 (46.2)
se (%)	289/770 (37.5)	44/127 (34.6)	0/26 (0.0)	–	83/192 (43.2)	11/87 (12.6)	<0.0001	60/111 (54.1)	13/73 (17.8)	<0.0001	50/76 (65.8)	28/78 (35.9)
	770, 23.2 (19.4–27.3)	127, 22.7 (19.4–26.5)	26,18.8 (17.6–20.4)	<0.0001	192, 24.0 (21.2–28.7)	87,19.4 (17.0–22.5)	<0.0001	111,25.6 (22.1–31.5)	73,20.4 (18.3–24.1)	<0.0001	76,27.5 (23.0–31.5)	78,23.0 (19.4–27.0
(mmHg)[d]												
	139/772 (18.0)	4/127 (3.1)	2/26 (7.7)	0.50	22/195 (11.3)	11/88 (12.5)	0.81	26/110 (23.6)	20/72 (27.8)	0.53	24/76 (31.6)	30/78 (38.5)
	7/772 (0.9)	3/127 (2.4)	1/26 (3.8)		1/195 (0.5)	1/88 (1.1)		–	–		1/76 (1.3)	0/78 (0.0)
	626/772 (81.1)	120/127 (94.5)	23/26 (88.5)		172/195 (88.2)	76/88 (86.4)		84/110 (76.4)	52/72 (72.2)		51/76 (67.1)	48/78 (61.5)
) (mmol/mol)												
	83/766 (10.8)	11/127 (8.7)	2/26 (7.7)	0.99	16/193 (8.3)	2/87 (2.3)	0.07	15/109 (13.8)	6/71 (8.5)	0.28	14/76 (18.4)	17/77 (22.1)
	683/766 (89.2)	116/127 (91.3)	24/26 (92.3)		177/193 (91.7)	85/87 (97.7)		94/109 (86.2)	65/71 (91.5)		62/76 (81.6)	60/77 (77.9)
/l)[e]												
	4/769 (0.5)	1/127 (0.8)	0/26 (0.0)	–	1/193 (0.5)	0/88 (0.0)	–	2/110 (1.8)	0/71 (0.0)	–	0/76 (0.0)	0/78 (0.0)
	765/769 (99.5)	126/127 (99.2)	26/26 (100.0)		192/193 (99.5)	88/88 (100.0)		108/110 (98.2)	71/71 (100.0)		76/76 (100.0)	78/78 (100.0)
	62/768 (8.1)	5/127 (3.9)	0/26 (0.0)	0.57	6/192 (3.1)	2/88 (2.3)	0.69	20/110 (18.2)	4/71 (5.6)	0.02	14/76 (18.4)	11/78 (14.1)
	88/768 (11.5)	21/127 (16.5)	4/26 (15.4)	–	20/192 (10.4)	19/88 (21.6)	0.01	6/110 (5.5)	5/71 (7.0)	0.66	6/76 (7.9)	7/78 (9.0)
	618/768 (80.5)	101/127 (79.5)	22/26 (84.6)	–	166/192 (86.5)	67/88 (76.1)	0.03	84/110 (76.4)	62/71 (87.3)	0.07	56/76 (73.7)	60/78 (76.9)
garettes?												
	557/748 (74.5)	104/127 (81.9)	17/25 (68.0)	0.12	146/197 (74.1)	38/79 (48.1)	<0.0001	94/109 (86.2)	43/69 (62.3)	0.0002	65/72 (90.3)	50/70 (71.4)
	191/748 (25.5)	23/127 (18.1)	8/25 (32.0)		51/197 (25.9)	41/79 (51.9)		15/109 (13.8)	26/69 (37.7)		7/72 (9.7)	20/70 (28.6)
arettes?												
	3/191 (1.6)	1/23 (4.4)	0/8 (0.0)	–	0/51 (0.0)	2/41 (4.9)	–	–	–	–	–	–
	188/191 (98.4)	22/23 (95.7)	8/8 (100.0)		51/51 (100.0)	39/41 (95.1)		15/15 (100.0)	26/26 (100.0)		7/7 (100.0)	20/20 (100.0)

Antiretroviral, ART; Body Mass Index, BMI; Interquartile range, IQR; Total Cholesterol, TC.

[a] Total denominators vary due to: 1) participants being allowed to opt out of any health screening, as desired; and 2) participants choosing not to answer questions relating to smoking.

[b] ART use reported only for HIV-infected clients who were previously diagnosed. HIV-positive participants on ART had significantly more high TC than those not on ART (23.7% vs. 4.3%; $p = 0.002$).

[c] Overall, men have significantly more underweight BMI as compared to women (28.0% [$n = 74/264$] vs. 11.7% [$n = 59/508$]; $p < 0.0001$), and women have significantly more overweight/obese BMI than men (46.8% [$n = 237/508$] vs. 19.7% [$n = 52/264$]; $p < 0.0001$).

[d] Overall, women have significantly more low BP than men (1.0% [$n = 5/508$] vs 9.8% [$n = 26/264$]; $p = 0.0004$), and significantly more normal BP than men (85.1% [$n = 427/508$] vs. 75.4% [$n = 199/264$]; $p = 0.003$).

[e] All four participants with high random glucose also had high HbA1c.

[f] Statistical significance was determined using chi-square or Fisher's exact test, where appropriate. Some p-values are missing due to some small sample sizes reflecting the stratification by age and sex.

the benefits of earlier rather than delayed glycaemic control with pharmacotherapy. Patients with incident DM who received intensive pharmacotherapy had significantly larger decreases in HbA1c and reduced risk of diabetes-related complications as compared to patients who received conventional dietary management [37,38]. Other studies utilising predictive modelling also support earlier treatment to combat diabetes-related morbidity, especially for the prevention of microvascular disease [39]. Compared to no treatment, a treatment target of HbA1c < 7% (<53 mmol/mol) within six months of diagnosis with DM may reduce the risk of end-stage renal disease by 44% and blindness by 73% compared with no treatment [40,41]. Screening for high TC early on in life could help prevent chronic inflammation, especially amongst PLHIV. Therefore, earlier universal screening and initiation of treatment is cost-effective in the long-term, saving on future costs relating to chronic disease-related morbidity and mortality.

The study site, while the only HTS centre within Bara Hospital and not receiving hospital in-patients, is a research site, impacting generalisability to public health clinics and the general population of Soweto, stratified by sex and age. Due to being a clinical research site offering free wellness services that are not regularly offered in the public healthcare sector, the study site has a higher likelihood of seeing more people with the health conditions of interest. This study included a convenience sample of walk-in participants self-selecting to attend a single HTS clinic in Soweto. The study sample was not randomly sampled from multiple facilities, which may have affected screening results (i.e.; larger or smaller prevalence of disease). Some of the sub-group sample sizes for comparison were small which may have affected statistical precision. ART and other chronic medication initiation/use, as well as health screening history/diagnoses, were self-reported, and not able to be verified through clinic records at the point of initiation. This could have over- or underestimated the proportion of participants on treatment and therefore the proportion of participants with controlled/uncontrolled disease.

This study highlights the substantial burden of HIV, NCDs and comorbidity amongst individuals attending an NCD-HTS centre and from the general adult population of Soweto, South Africa, and amongst relatively young adults (18–34 years), especially women. There are high rates of previously unknown disease and previously diagnosed, uncontrolled disease. Lowering the age requirements for screening to 18+ years for rapid blood glucose and cholesterol screening, regardless of BMI classification, HIV-status or ART use, may assist with timely diagnosis and management of NCDs. There may also be some merit in replacing RPG with HbA1c for routine testing [41]. More research within the public healthcare sector is needed to expand the generalizability of these findings. Integrative management of NCDs amongst the general population and PLHIV may be considered to improve screening and health outcomes in this setting.

5. Contributors

KLH and GEG conceptualised the study and are the co-principal investigators. KLH, KO, TD, and GEG designed the study. KLH, KH, and KO implemented the study, acquired the data, and conducted the statistical analysis. KLH, KH, KO had access to the dataset. KLH, KH, KO, JD, TD and GEG analysed the study findings. MC, JO, and HVR were technical advisors of the study. All authors critically revised the manuscript and consented to final publication.

Declaration of Competing Interest

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Data sharing statement

Study data are available on request to the authors.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2021.101015.

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