



Assessment of cardiovascular disease risks using Framingham risk scores (FRS) in HIV-positive and HIV-negative older adults in South Africa

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ABSTRACT

The relationship between HIV and cardiovascular diseases (CVDs) remains complex. The aim of this study was to estimate the 10-year CVD risk among HIV-positive and HIV-negative people. The validated Framingham Risk Score (FRS) based on the Framingham Heart study was used to predict the CVD risk. Data for this analysis came from a 2016 cross-sectional study of South African community-dwelling older adults (≥ 50 years). Logistic regression models were constructed to assess the association between CVD risk and HIV. 403 respondents with a mean age 60 (SD = 6.7) years were enrolled, of whom 70% were female, 75% black African, 21.9% smokers, 77.2% never did any vigorous physical activity, and 17% were HIV-positive. The average 10-year CVD risk was 17%; significantly higher in men than women (23.2 vs 14.3%, $p < 0.001$). Overall, 33% had low CVD risk (FRS $< 10\%$), 39% intermediate (FRS 10–19%) and 28% high risk (FRS $\geq 20\%$). Furthermore, participants who were HIV-positive were less likely than HIV-negative participants to have high CVD risk (aOR 0.27, 95% CI 0.11–0.66, $p = 0.004$). These findings of HIV-positive respondents having lower CVD risk than HIV-negative respondents could be due to three issues i) HIV-positive people having lesser cardio-metabolic disease risk factors; ii) possibly higher health care utilization by HIV-positive people; and/or iii) the neglect of HIV-negative people in HIV focused health systems. Periodic cardiovascular disease monitoring using tools like the Framingham Risk Scores is needed. Furthermore, studies with more robust designs are needed to further elucidate the relationship between HIV and CVD risks in HIV endemic sub-Saharan Africa.

1. Background

Globally, the leading causes of death are cardiovascular diseases (CVDs) (Danaei, 2014; Mensah et al., 2014). In 2016, CVDs^b accounted for approximately a third of the global deaths or 18 million lives, of whom over three quarters were among people in low- and middle-income countries (LMICs) (WHO, 2020). As the global population continues to age, more so in LMICs, the risk of CVDs will continue to grow (Giannarelli et al., 2011). In South Africa, CVDs such as atherosclerotic disease and heart failure are increasing in particular among the black African population (Lloyd-Sherlock et al., 2014; van Heerden et al., 2017). South Africa as a country with a rapidly ageing population and a large proportion of people living with HIV, is experiencing a quadruple burden of disease (Econex, 2009; Nojilana et al., 2016; Mayosi et al.,

2009; Msemburi et al., 2019). The more people live longer with HIV due to successful treatment, the greater the risk of HIV infected people developing cardio-metabolic conditions (Bor et al., 2013; Clark et al., 2015). Studies assessing the risk of cardio-metabolic diseases in HIV infected people suggest that longer duration since HIV diagnosis and time since uptake of ART are associated with a higher likelihood of CVD morbidity and mortality (Todowede et al., 2019; Melo et al., 2020; Esser et al., 2013). This has been attributed to among other reasons, HIV induced dyslipidemia and inflammation (Esser et al., 2013; de Gaetano et al., 2010; Rasheed et al., 2008). Some antiretroviral regimens have also been shown to increase the risk of CVD in HIV infected persons. For example, protease inhibitors (PIs) compared to non-nucleoside reverse transcriptase inhibitors (NNRTI) have been found to induce an increase in total cholesterol, low density lipoprotein cholesterol, triglycerides, as

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^b CVDs consist of disorders relating to the heart and blood vessels including: coronary, rheumatic and congenital heart diseases; cerebrovascular disease; peripheral disease; deep vein thrombosis and pulmonary embolism. WHO. Cardiovascular diseases (CVDs). World Health Organization. Accessed 29 July 2020, <https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-cvds>.

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well as an increase in insulin resistance, and hence a reduced glucose tolerance (Oh and Hegele, 2007; Pinto and da Silva, 2018). However, as noted in a review article, the relationship between HIV and CVD risk remains complex (de Gaetano et al., 2010).

Further, many of the studies suggesting an association between HIV infected people and increased risk of cardio-metabolic diseases were conducted in health facility-based HIV-positive patients (de Gaetano et al., 2010). These studies are thus limited by a lack of a suitable HIV-negative comparison group as well as not being population-based. Thus, there is still a lot of uncertainty on the effect of HIV and HIV treatment on the CVD risks of older adults in sub-Saharan countries. Furthermore, in an HIV focused health system significant amounts of resources are directed towards the care and management of individuals with known or current diseases (Benatar et al., 2018). With limited use of community health workers and a large segment of the population only visiting health facilities when they get very sick or their pain worsens (Benatar et al., 2018; Puoane et al., 2017), HIV uninfected people may tend to be left behind which is believed to have contributed to inequalities in health status between HIV infected and uninfected adults in South Africa (Negin et al., 2013).

It is imperative to have an accurate estimation of CVD risks not only in HIV infected but in HIV uninfected people also because now that HIV has turned into a chronic and manageable condition, the risks for CVDs may be similar in the two populations (de Gaetano et al., 2010). Individualized CVD risk prediction tools are essential for developing appropriate plans to better manage the growing number of people at risk of CVDs such as older people in HIV endemic settings (Melo et al., 2020; Rosolova and Nussbaumerova, 2011). The Framingham Risk Score (FRS) is one such prediction tool widely used that can be applied to relatively healthy individuals to estimate their probability of fatal or non-fatal cardiovascular events within the next ten years (de Ruijter et al., 2009; D'Agostino et al., 2008).

Therefore, the aim of this study was to estimate the 10-year risk of cardiovascular diseases using the Framingham risk scores in a sample of community-dwelling HIV-positive and HIV-negative older adults from South Africa. We further assessed the relationship between high CVD risk and HIV, adjusting for known confounding factors. This study will contribute to the dearth of information on CVD risks in HIV infected compared to HIV uninfected older adults from an African setting.

2. Methods

2.1. Study setting and design

Data for this analysis came from a cross-sectional study titled: The Sexual health, HIV infection and comorbidity with non-communicable diseases among Older Persons (SHIOP) conducted in 2016. In the SHIOP, 435 older men and women aged 50 years and older were recruited (median age 61, interquartile range 12) from semi-urban (Botha's Hill) and urban (Chatsworth) communities of Durban, KwaZulu-Natal, South Africa. Details about the study design and methods have been published elsewhere (Abbai et al., 2018; Nyirenda et al., 2018). Briefly, well-trained and experienced community engagement officers and field recruiters went to the households within the Botha's Hill and Chatsworth areas where they identified households with members aged ≥ 50 years. These individuals were then invited to the research sites located within the respective areas for further screening and enrolment into the study. A standardized case record form was used to collect socio-demographic information (age, sex, marital status, population group), self-reported lifestyle factors (smoking, alcohol consumption, physical activity), self-reported health status (diagnosis and treatment for hypertension, heart disease, stroke, diabetes, arthritis), sexual behaviour (current sexual activity, lifetime partners, condom use), and knowledge and attitudes towards HIV. In addition, anthropometrical (weight, height) and clinical measurements (blood pressure, glycated haemoglobin (HbA1c), total cholesterol (TC),

low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and HIV testing) were done for each participant.

Written informed consent was obtained from all participants and participant privacy was observed throughout the study. The study was approved by the South African Medical Research Council Ethics committee (EC030-9-2015).

2.2. Clinical measurements

Blood pressure was measured using a European Society of Hypertension (ESH) validated HealthEase digital blood pressure (BP) instrument. Three readings of systolic and diastolic blood pressure were taken with a participant in a sitting position and at least two minutes rest interval between each reading. The average of the three readings was used to classify participants as *normal* (systolic BP < 120 mm Hg or diastolic BP < 80 mm Hg), *pre-hypertensive* (systolic BP 120–139 mm Hg or diastolic BP 80–89 mm Hg), or *hypertensive* (systolic BP ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg).

HIV testing: All participants in the study provided a venous collected blood specimen which was used for HIV testing using two parallel HIV kits - Unigold™ Recombigen® and Determine HIV-1/2 (Abbott Laboratories, Japan) as per manufacturer instructions. All HIV discordant results were to be checked using an ELISA test, but none were recorded in this study.

Glycated haemoglobin (HbA1c): HbA1c was measured using standard laboratory approach from the venous blood specimen. **Lipid profile** for each participant was also measured from the venous blood specimen.

Body mass index (BMI) for each participant was calculated from the weight and height measurements as weight in kilograms divided by height in square meters. In the variable 'obesity', BMI was then categorised as: Normal (BMI ≤ 24.9), overweight (BMI 25–29.9), and obese (BMI ≥ 30). Further details on the clinical measurements and how they were tested have been published elsewhere (Abbai et al., 2018).

2.3. Statistical analysis

Descriptive bivariate analyses were used to describe the data. Data are presented in frequencies and percent for categorical variables, and using means and standard deviations for continuous variables as appropriate. Multiple logistic regression models were constructed to examine the relationship between the binary dependant variable high CVD risk (FRS $\geq 20\%$) and HIV, adjusted for population group, education attainment, physical activity, alcohol use, obesity, and triglycerides (independent variables). These factors are known from the literature to be commonly associated with cardio-metabolic morbidity. All factors that are part of the FRS outcome variable like age, hypertension and total cholesterol were, however, excluded from the models. Where we report p-values, a two-tailed p-value of < 0.05 was used to determine statistical significance. All analyses were conducted in STATA 14.2 (StataCorp LP, 2014).

2.3.1. Description of independent factors

Age was collected in single years as at last birthday from interview date. This was then categorised into 5-year and 10-year age groups. Classification into male or female was based on the assigned sex as per national identity document. Population group was categorised as black African or non-African based on South Africa's population group classifications. The latter group were predominantly South Africans of Asian origin, except for one white participant. Regarding education, participants were asked for their highest level of education attained. This was categorised into: none, primary, and secondary or higher. The variable physical activity was based on the question "Do you do any vigorous sports, fitness or recreational (leisure) activities like running, swimming, bowling, playing football, or cricket for at least 10 min that cause large increases in breathing or heart rate?" Responses were on a Likert scale:

Always, Often, Sometimes/Rarely, Never, Don't Know. The variable alcohol is included in the model as a dichotomous factor (Yes/No), although in the survey participants were asked if they ever consumed alcohol with responses on a Likert scale (Yes, daily; Yes, but not daily; No, quit; Never). Obesity was a categorical variable in the logistic regression model based on the BMI measurements. Likewise, we used the dichotomised triglycerides variable in the logistic regression models (Normal ≤ 2.25 mmol/L vs High > 2.5 mmol/L).

2.3.2. Description of outcome variable

Framingham Risk Score (FRS) predicts a general 10-year risk of developing a cardiovascular event based on a Cox model developed from the Framingham Heart Study (D'Agostino et al., 2008; D'Agostino et al., 2013). We computed the FRS using information on age, sex, smoking, total cholesterol, high density lipoprotein (HDL-c) cholesterol, diabetes, systolic blood pressure and treatment for hypertension based on validated predictors and coefficients developed by Linden (Framingham, 2015). As done by others (Selvarajah et al., 2014; Boateng et al., 2018; Wekesah et al., 2020; Mashinya et al., 2015), FRS was stratified into low, intermediate and high cardiovascular risk. Where low risk was defined as $FRS < 10\%$, $FRS 10\text{--}19\%$ as intermediate risk and $FRS \geq 20\%$ as high risk. Although the survey was among participants aged ≥ 50 years (range 50–94 years), our analysis was restricted to individuals aged 50–75 years as the Framingham Heart Study on which the FRS was developed only enrolled participants between age 30 and 75 years. The model has not been validated in persons beyond age 75 years.

3. Results

3.1. Descriptive characteristics of study respondents

A total of 403 participants with a mean age 60.3 (SD = 6.7) met the age inclusion criterion for the Framingham Risk Score (FRS), of whom 70.0% were female, 74.7% black African, 21.9% smokers, 77.2% never did any vigorous physical activity, and 17.4% were HIV-positive (Table 1). Participants had a high mean BMI of 32.1 (SD 22.5). Participants were also characterised by a high mean systolic (135.4 mmHg, SD 21.1) and diastolic (82.6 mmHg, SD 12.6) blood pressure as well as high mean cholesterol and triglycerides. Over half of the participants self-reported to have hypertension (58.1%), of whom 86.8% self-reported to be on hypertension treatment. About a quarter of participants self-reported being diabetic (24.6%), with 89.9% of them reporting to be on treatment for diabetes. Less than one in ten self-reported ever having had a heart attack event (4.5%), and currently taking aspirin or statins to prevent a heart attack (8.7%).

3.2. Prevalence of cardiovascular disease risk using Framingham risk scores (FRS)

The average 10-year cardiovascular disease event risk in this sample was 17.0%, with the average significantly higher in men than women (23.2 vs 14.3%, $p < 0.001$). Fig. 1 displays the point estimates and 95% confidence intervals for the 10-year cardiovascular disease risk classified as low ($FRS < 10\%$), intermediate ($FRS 10\text{--}19\%$) or high ($FRS \geq 20\%$) stratified by sex. Overall, 33.0% of participants had low 10-year CVD risk; 38.7% intermediate and 28.3% were at high risk. Among women, the highest proportion (41.1%) were at low risk and only 21.3% were at high risk. The opposite was the case among men, where the highest proportion were high risk (44.6%) and only 14.0% were at low risk.

Trends in high CVD risk by age and sex are shown in Fig. 2. The 10-year high CVD risk increased with increasing age, with 51.2% of those aged 70–75 at high risk for the overall sample. Although the patterns were similar, there was a huge difference between men and women in the level of CVD risk. The proportion at high CVD risk increased exponentially from around 20% by age 59 to a high of 75% in the age group

Table 1

Baseline characteristics of the included participants aged 50–75 years.

Participants	N = 403
Age in years, mean (SD)	60.3 (6.7)
Female, n (%)	282 (70.0)
African, n (%)	301 (74.7)
Smoking status, n (%)	
Never	281 (69.7)
Current	87 (21.9)
Quit	35 (8.7)
Physical activity, n (%)	
Never	311 (77.2)
Always	31 (7.7)
Rarely	35 (8.7)
Don't know	26 (6.5)
BMI, mean (SD)	32.1 (22.5)
Obesity	
Normal	121 (30.1)
Overweight	99 (24.6)
Obese	182 (45.3)
Blood Pressure	
Systolic blood pressure, mean (SD), mmHg	135.4 (21.1)
Diastolic blood pressure, mean (SD), mmHg	82.6 (12.6)
Cholesterol	
Total Cholesterol, mean (SD), mg/dl	173.5 (37.8)
HDL Cholesterol, mean (SD), mg/dl	50.5 (15.7)
LDL Cholesterol, mean (SD), mg/dl	89.4 (35.3)
Triglycerides, mean (SD), mg/dl	174.0 (112.8)
Self-reported chronic morbidities, n (%)	
Heart disease	22 (5.5)
Arthritis	147 (36.5)
Hypertension	234 (58.1)
Diabetes	99 (24.6)
Self-reported treatment for chronic morbidities[†], n (%)	
Heart disease	16 (72.7)
Arthritis	114 (77.6)
Hypertension	203 (86.8)
Diabetes	89 (89.9)
Heart Attack	
Ever had a heart attack, n (%)	18 (4.5)
Currently taking Aspirin or statins, n (%)	35 (8.7)
HIV, n (%)	
Negative	376 (82.6)
Positive	70 (17.4)

Note: [†] Represents proportion on treatment among those self-reporting the chronic morbidity. For example, for Heart disease ($16/22 \times 100 = 72.7\%$); Arthritis ($114/147 \times 100 = 77.6\%$); Hypertension ($203/234 \times 100 = 86.8\%$); Diabetes ($89/99 \times 100 = 89.9\%$).

70–75 for men compared to 41% for women.

3.3. Factors associated with high risk of cardiovascular disease

Table 2 shows factors associated with a high CVD risk obtained using logistic regression models. HIV, currently drinking or having quit alcohol, and high triglycerides were significantly associated with a high CVD risk in unadjusted and adjusted analyses. Black African relative to non-African participants were significantly less likely to be at high CVD risk only in the unadjusted analysis. Education attainment, physical activity and obesity were all not significantly associated with high CVD risk.

3.4. Effect of HIV on high cardiovascular disease risk

We further explored the risk of high CVD risk by HIV status and sex. Fig. 3 displays the relationship between high CVD risk and HIV for men and women separately, and for the overall sample. Where high CVD risk was defined as Framingham Risk Score ($FRS \geq 20\%$). The relationship between HIV and high CVD risk was adjusted for: population group, educational attainment, alcohol drinking, physical activity, obesity and triglycerides. Model results showed that participants who were HIV-positive were less likely to have high CVD risk among men in

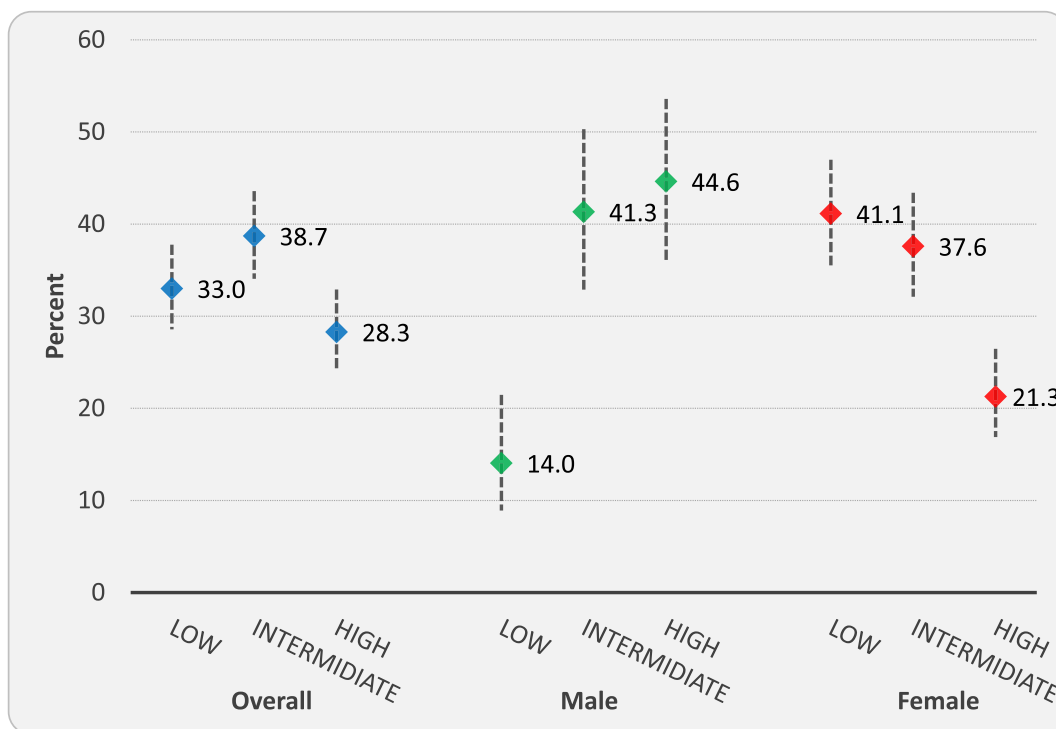


Fig. 1. displays the point estimate and its 95% confidence interval for the proportion of participants classified as low (FRS < 10%), intermediate (FRS 10–19%) or high (FRS ≥ 20%) CVD risk stratified by sex.

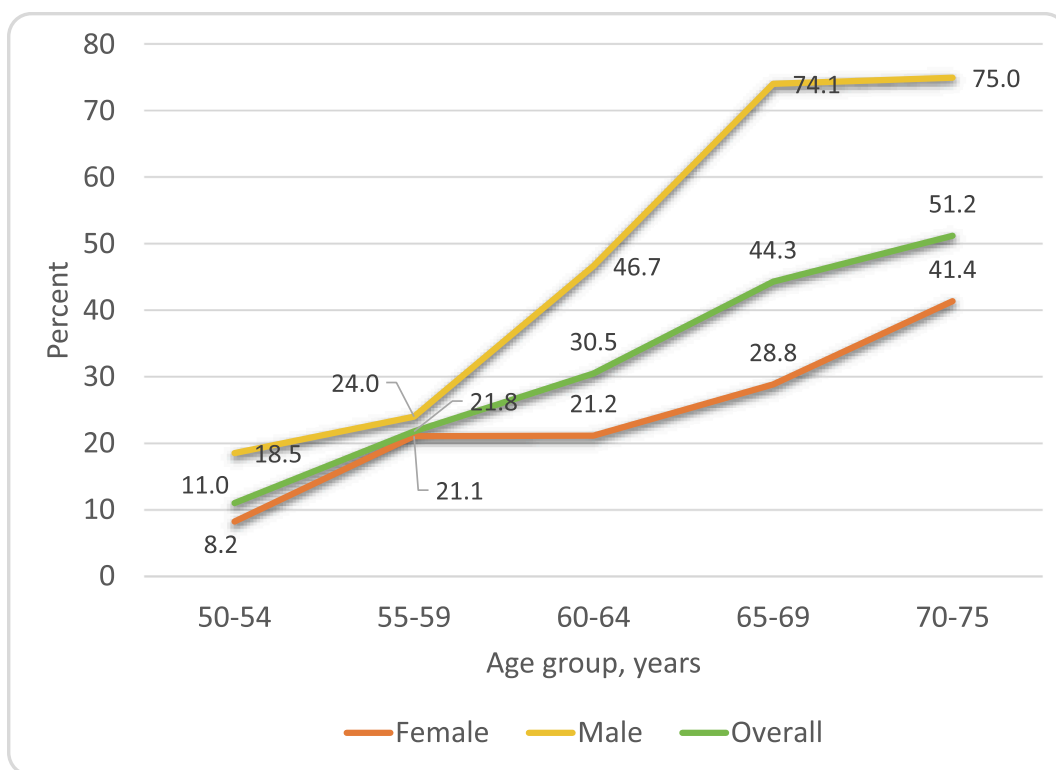


Fig. 2. Percentage of participants with estimated high cardiovascular disease risk by age group and sex Note: OR = Unadjusted odds ratios; aOR = Adjusted odds ratios; adjusted for: HIV, population group, educational attainment, alcohol drinking, physical exercise, obesity and triglycerides.

unadjusted analyses (odds ratios (OR) 0.19, 95% confidence interval (CI) 0.05–0.68, p-value = 0.011), but not in the adjusted analyses (aOR) 0.21, 95% CI 0.04–1.02, p-value = 0.054). For women the association was significant in both the unadjusted (OR 0.35, 95% CI 0.13–0.92, p-

value = 0.033) and adjusted analyses (aOR 0.30, 95% CI 0.10–0.96, p-value = 0.043). Likewise for the overall sample, being HIV-positive was associated with statistically significant lower odds of high CVD risk in both the unadjusted (OR 0.28, 95% CI 0.13–0.60, p-value = 0.001) and

Table 2
Logistic regression factors associated with high risk of cardiovascular disease – modified.

	OR (95% CI)	P > z	aOR (95% CI)	P > z
HIV status				
HIV Negative (referent)	1.00		1.00	
HIV Positive	0.28 (0.13–0.60)	0.001	0.27 (0.11 – 0.66)	0.004
Population group				
Non-African (referent)	1.00		1.00	
African	0.48 (0.30 – 0.77)	0.002	0.60 (0.34 – 1.07)	0.086
Education attained				
None (referent)	1.00		1.00	
Primary	1.08 (0.57 – 2.04)	0.821	1.07 (0.54 – 2.12)	0.852
Secondary or higher	0.83 (0.42 – 1.64)	0.593	0.64 (0.30 – 1.36)	0.245
Drink alcohol				
No (referent)	1.00		1.00	
Yes	1.49 (0.90 – 2.45)	0.119	1.95 (1.07 – 3.54)	0.029
Quit	1.92 (0.99 – 3.66)	0.054	2.31 (1.12 – 4.76)	0.023
Physical exercise				
Never (referent)	1.00		1.00	
Always	0.73 (0.30 – 1.75)	0.477	0.85 (0.34 – 2.16)	0.734
Rarely	1.14 (0.54 – 2.43)	0.728	1.54 (0.66 – 3.58)	0.313
Don't know	0.92 (0.37 – 2.26)	0.854	1.43 (0.54 – 3.82)	0.470
Obesity^a				
Normal	1.00		1.00	
Overweight (referent)	1.33 (0.75 – 2.38)	0.330	1.06 (0.54 – 2.07)	0.874
Obese	0.93 (0.55 – 1.56)	0.779	0.88 (0.46 – 1.68)	0.705
Triglycerides^b				
Normal (referent)	1.00		1.00	
High	3.13 (1.98 – 4.93)	<0.001	3.21 (1.95 – 5.29)	<0.001

Notes:OR = Odds Ratios; aOR = Adjusted Odds Ratios

^a Body Mass Index (BMI) measurements categorised as: Normal (BMI ≤ 24.9), overweight (25–29.9), & obese (≥30)

^b Triglycerides measurements categorized as: Normal ≤ 2.25 mmol/L or High > 2.5 mmol/L.

adjusted analyses (aOR 0.27, 95% CI 0.11–0.66, p-value = 0.004).

4. Discussion

In this study using the Framingham risk scores (FRS) for cardiovascular (CVD) risk, our main goal was to examine the 10-year CVD risk in HIV-positive relative to HIV-negative older adults aged ≥ 50 years. We identified a high CVD risk in our analysis and found that those who were HIV-negative were associated with greater likelihood of high CVD risk than HIV-positive people. Our findings are consistent with those from a study within a longitudinal surveillance system in South Africa. In that study which enrolled only HIV infected participants they reported a better CVD risk profile compared to previous analyses from the same surveillance population that had included HIV uninfected and ART naïve individuals (Mashinya et al., 2015). Findings that HIV-positive participants had lower 10-year CVD risk than HIV-negative participants could possibly be attributed to HIV-positive participants having lower cardio-metabolic disease risk factors than their HIV-negative counterparts, as shown by Rooyen et al. (2014) who found that in HIV infected Black South Africans, HIV-infected participants had significantly lower total cholesterol and HDL cholesterol levels. This is said to be due to ART which has led to a general decrease in opportunistic

infections associated with HIV and increases in life expectancy (Bor et al., 2013; Melo et al., 2020). In addition, HIV infected people also tend to have higher utilization of health facilities increasing the probability of early detection and proper management of chronic infections (Negin et al., 2013). This is compounded by reports of limited utilisation of community health care workers and a large part of the population only seeking health care when they become very sick or the pain worsens (Benatar et al., 2018; Puoane et al., 2017). As such there may be a neglect of HIV-negative people in HIV focused health systems as such resources tend to be channelled towards HIV care and management (Benatar et al., 2018).

Generally, there was a high cardiovascular disease risk in this sample. The prevalence of participants with a high and intermediate CVD risk was 28.3% and 44.6%, respectively. Those with low CVD risk was only 21.3%. The prevalence of high CVD risk we report in this study is higher than what has been reported in other studies (Todowede et al., 2019; Mashinya et al., 2015; Policarpo et al., 2019). However, our CVD risk prevalence findings are consistent with studies from similar settings (Wu et al., 2019; Pinto Neto et al., 2017). We further found that the 10-year CVD risk was higher in men than women. Our findings on men being at greater CVD risk are in line with what was recently reported by Melo et al. (2020), in a cross-sectional study that evaluated the CVD risks in persons living with HIV using the FRS. It is not clear from our study why men had higher CVD risks than women but previous studies have attributed it to smoking and alcohol, which tend to be prevalent in men than women, risk factors that have been shown to be significantly associated with CVD events (de Gaetano et al., 2010; Wu et al., 2019). Differences between what we report and what has been found by others, however, could be a result of our sample being much older (mean age 60 compared to around 45 years in other studies), as well as our sample having included HIV negative participants (Todowede et al., 2019; Mashinya et al., 2015; Policarpo et al., 2019).

Contributory traditional risk factors to the rising CVD cases are age, hypertension, diabetes mellitus, smoking and obesity (de Gaetano et al., 2010; Ramsay et al., 2016; Danaei et al., 2013). Of these factors, it was shown in a study among HIV-positive adults in Taiwan that a smoking cessation intervention could potentially result in 20 to 35% reduction in the 10-year risk of CVD (Wu et al., 2019). In South Africa, a key driver of the increasing cardio-metabolic disorders is obesity (Mensah, 2013). However, it is yet to be determined what the effect of an obesity reduction intervention would be on cardiovascular morbidity and mortality in the country. A study to this effect is welcome. HIV has also been identified as contributing to increasing cardio-metabolic conditions (Policarpo et al., 2019). If risk factors are not routinely monitored and well controlled, the risk of CVDs may increase with the ageing process, and HIV-induced CVD risk including the longer duration on treatment. Studies suggest HIV infected people are at increased risk of CVD, especially the longer since HIV diagnosis and longer exposure to antiretroviral treatment (ART) (Todowede et al., 2019; Melo et al., 2020; Aboud et al., 2010). It is understood that some ARVs may trigger hyperlipidaemia and a reduced glucose tolerance, which may increase the risk of CVDs in HIV positive individuals (Esser et al., 2013; de Gaetano et al., 2010). Policarpo et al. (2019) further identified high triglycerides and low HDL cholesterol as key factors in this increased CVD risk among HIV positive individuals. However, a major limitation of the studies that report HIV positive people to be associated with increased CVD risk is the lack of a suitable HIV negative control group (Todowede et al., 2019; de Gaetano et al., 2010).

Data for this analysis came from a cross-sectional study using a convenient sampling approach. As such the study is limited in making causal inferences in our outcomes or extrapolating our findings to the general population. There is also the inherent desirability bias in self-reported measures such as being on treatment for hypertension and diabetes as well as smoking status, which are inputs to the Framingham risk score computation. Hence our results may be biased to the extent to which desirability bias influenced participants in self-reported

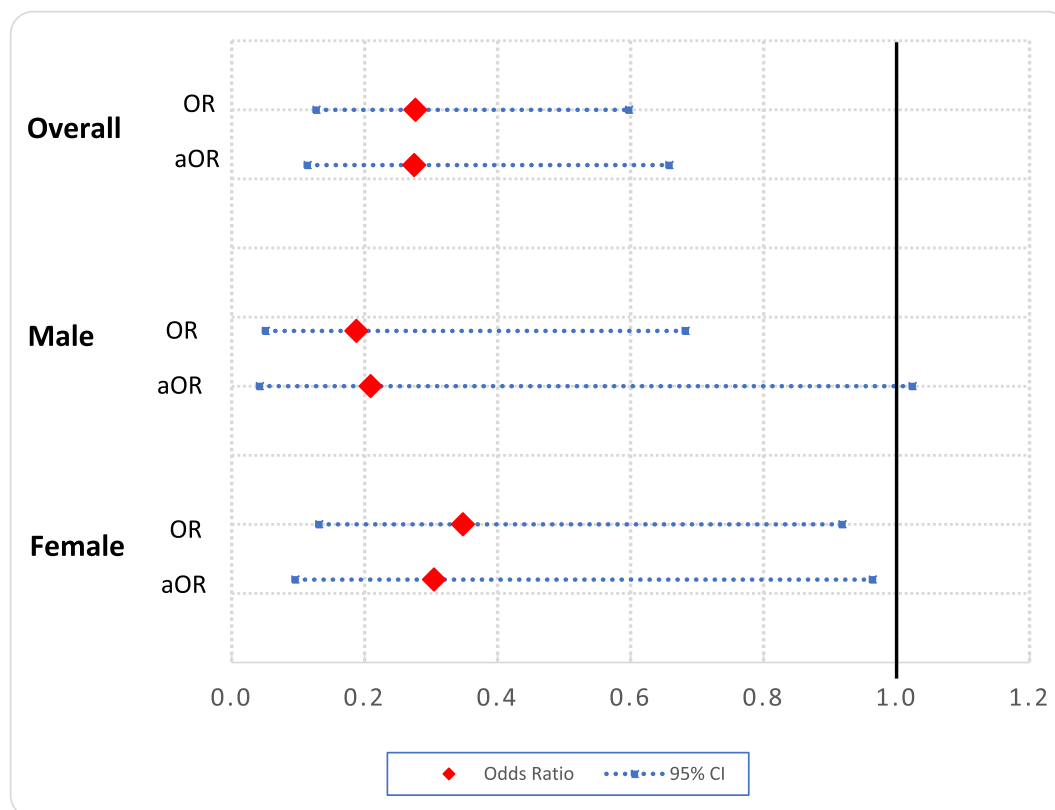


Fig. 3. The chart displays the unadjusted and adjusted odds ratios in HIV-positive relative to HIV-negative participants for high CVD risk. The modelled relationship between high CVD and HIV was adjusted for population group, educational attainment, alcohol drinking, physical exercise, obesity and triglycerides. Where high CVD risk was defined as Framingham Risk Score (FRS) \geq 20%.

responses. Another potential limitation of our study relates to the limitations inherent in the FRS measure. The FRS is among a vast array of CVD-risk estimation tools (Tunstall-Pedoe, 2011; Truett et al., 1967) that one can use. Other estimation tools include: the Pooled Cohort Equations (PCE) (Muntner et al., 2014), QRISK (Hippisley-Cox et al., 2017) and the ACC/AHA (Arnett Donna et al., 2019). Choice of which CVD-risk estimation tool to use is a matter of judgment of robustness and appropriateness for the context at hand (D'Agostino et al., 2008; Tunstall-Pedoe, 2011; Gaziano et al., 2013). There are conflicting results on the performance of the FRS with some studies suggesting the FRS tends to underestimate CVD risk (Boateng et al., 2018; Mashinya et al., 2015), while others report an overestimation of risk by the Framingham (Moreira Guimaraes et al., 2010). It is believed that the inconsistency in findings of underestimation or overestimation in CVD risk by the FRS could be attributed to the score not accounting for HIV and ART associated CVD risk (Wu et al., 2019; Law et al., 2006; Krikke et al., 2016; Triant et al., 2018). We applied the FRS to a sample of HIV-positive and HIV-negative participants despite this uncertainty. Evaluation of the validity of the FRS for this population was beyond the scope of the study. The decision to use the FRS was informed by it being a widely used robust tool in similar settings to ours (Melo et al., 2020; de Ruijter et al., 2009; Wekesah et al., 2020; Mashinya et al., 2015).

In conclusion, our findings are first to suggest HIV-negative older adults may be at higher risk of CVDs than their HIV-positive counterparts. At present it is not clear why this could be so, but can be hypothesized to be related to improved lifestyles, greater health care utilization and recovery of health due to HIV treatment, as previously reported (Bor et al., 2013; Melo et al., 2020; Negin et al., 2013; Mashinya et al., 2015). It could also be indicative of the neglect of the health of HIV-negative people in HIV focused health systems. The prevalence of high CVD risk we report is higher than some previously reported studies but consistent with those from similar settings. This

study therefore suggests that despite the challenges in CVD diagnosis and risk prediction, there is a need for periodic cardiovascular disease monitoring using tools like Framingham scores not only in HIV infected older adults, but in HIV uninfected older adults as well who may be left behind or neglected in HIV dominated health systems. Further studies with more robust designs and possibly prospective follow-up are needed to further elucidate the relationship between HIV and CVD risks in HIV endemic sub-Saharan Africa settings.

CRediT authorship contribution statement

Makandwe Nyirenda: Conceptualization, Methodology, Formal analysis, Data curation, Writing - original draft, Writing - review & editing, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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