



BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Cardiovascular risk factors and markers of myocardial injury and inflammation in people living with HIV in Kenya

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-062352
Article Type:	Original research
Date Submitted by the Author:	28-Feb-2022
Complete List of Authors:	<p>Ahmed, Hassan; The Aga Khan University Hospital Nairobi Mohamed, Jeilan; Aga Khan University - Kenya, Medicine Akuku, Isaiah G; University of Nairobi, Institute of Tropical and Infectious Diseases Lee, K; University of Edinburgh, BHF Centre for Cardiovascular Science Alam, Shirjel R; London School of Hygiene & Tropical Medicine, Department of Non-communicable Disease Epidemiology Perel, Pablo; London School of Hygiene & Tropical Medicine, EPH Shah, Jasmit; Aga Khan University Hospital, Internal Medicine Ali, Mohammed; Emory University, Hubert Department of Global Health Eskander, Sherry; Coptic Hospital and Coptic Hope Center for Infectious Diseases Chung, Michael H; Emory University Shah, Anoop ; London School of Hygiene and Tropical Medicine Department of Non-communicable Disease Epidemiology, Department of Non-Communicable Disease Epidemiology; Imperial College Healthcare NHS Trust</p>
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Adult cardiology < CARDIOLOGY, EPIDEMIOLOGY

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

ORIGINAL ARTICLE

Cardiovascular risk factors and markers of myocardial injury and inflammation in people living with HIV in Kenya

Hassan A Ahmed, MD¹; Jeilan Mohammed, MD¹; Isaiah G Akuku, MSc²; Kuan Ken Lee, MD³; Shirjel R Alam, MD⁴; Pablo Perel, MD⁴; Jasmit Shah, PhD¹; Mohammed K. Ali, MD⁵; Sherry Eskander, MD⁶; Michael H Chung, MD^{5*} and Anoop S V Shah, MD^{4,7*}

*Contributed equally

¹ Department of Medicine, Aga Khan University

² Institute of Tropical and Infectious Diseases, University of Nairobi

³ BHF Centre for Cardiovascular Sciences, University of Edinburgh

⁴ Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

⁵ Emory University, Atlanta, Georgia, USA

⁶ Coptic Mission Hospital, Nairobi, Kenya, UK

⁷ Imperial College Hospital NHS Trust, London, UK

Correspondence and requests for reprints:

Dr Anoop Shah,

Room 249,

Department of Non-communicable Disease Epidemiology,

London School of Hygiene and Tropical Medicine,

Keppel Street,

London,

UK

WC1E 7HT

Mobile: +(44) 7766 544 156

E-mail: Anoop.Shah@lshtm.ac.uk

Abstract: 278

Table: 4

Word count: 2842 (excluding references and tables)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Objectives: To determine the prevalence of cardiovascular disease (CVD) risk factors and explore associations with high-sensitivity cardiac troponin (hscTnI) and high-sensitivity C-reactive protein (hsCRP) in people living with HIV (PLHIV) in Kenya.

Design: Cross-sectional study

Settings: Community HIV clinics across two sites in Nairobi, Kenya

Participants: 200 PLHIV (≥ 30 years with no prior history of CVD)

Primary and secondary outcome measure: Prevalence of cardiovascular risk factors and its association with hscTnI and hsCRP levels.

Results: Across 200 PLHIV (median age 46 years, IQR 38-53; 61% females), the prevalence of hypercholesterolemia (>6.1 mmol/L) and hypertension were 19% ($n=30/199$) and 30% ($n=60/200$), respectively. Smoking and diabetes prevalence was 3% ($n=5/200$) and 4% ($n=7/200$). HscTnI was below the limit of quantification (<2.5 ng/L) in 65% ($n=109/169$). 38% ($n=75/198$), 33% ($n=65/198$) and 29% ($n=58/198$) had high (>3 mg/L), intermediate (1-3mg/L) and low (<1 mg/L) hsCRP levels, respectively. Framingham laboratory-based risk scores classified 83% of PLHIV at low risk with 12% and 5% at intermediate and high risk. Older age (adjusted odds ratio [aOR] per year increase 1.05, 95% confidence interval [CI] 1.01–1.08) and systolic blood pressure (140–159mmHg [aOR 2.96; 95%CI 1.09–7.90] and >160 mmHg [aOR 4.68, 95%CI 1.55–14] compared to <140 mmHg) were associated with hscTnI levels. No associations were observed between hsCRP and CVD risk factors.

Conclusion: The majority of PLHIV - using traditional risk estimation systems - have a low estimated CVD risk likely reflecting a younger aged population predominantly consisting of women. Hypertension and hypercholesterolemia were common whilst smoking and diabetes rates remained low. Whilst hscTnI values were associated with increasing age and raised blood pressure, no associations between hsCRP levels and traditional cardiovascular risk factors were observed.

Introduction

More than 35 million people are infected with the human immunodeficiency virus (HIV) with two-thirds being resident in sub-Saharan Africa.¹ Although the global incidence for HIV has stabilised, the wide availability of combined antiretroviral therapy (ART) has dramatically improved survival, resulting in a steady increase in prevalence over the last two decades.^{2 3} This improvement in survival has been primarily attributed to a reduction in opportunistic infections especially in low- and lower-middle-income nations. Conversely, mortality due to non-communicable illnesses especially cardiovascular disease has been rising and now account for the majority of deaths in people living with HIV (PLHIV).^{1 4-7}

People living with HIV - based on studies in high-income countries - have a higher risk of cardiovascular disease.^{8 9} Despite this higher risk, previous studies have indicated that PLHIV in sub-Saharan Africa have a lower prevalence of traditional cardiovascular risk factors in comparison to uninfected individuals.^{8,10} Strategies to risk stratify and mitigate cardiovascular disease in this population is now urgently required but is challenging in resource limited nations¹¹ and it remains unclear on optimal approaches with recommendations differing across regions globally.¹²

In a cross-sectional study of PLHIV in Kenya, we evaluate the prevalence of traditional cardiovascular risk factors and the distribution of estimated cardiovascular risk using traditional risk scores. We further explore the distribution of markers of myocardial injury and inflammation in this population.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Methods

Study Setting and population

This was a cross sectional study that conveniently sampled PLHIV ≥ 30 years of age receiving care at the Aga Khan University Hospital and Coptic Hope Center for Infectious Diseases in Nairobi, Kenya from July 2019 to May 2020. Aga Khan University Hospital is a fee-for-service tertiary care centre generally serving a more affluent population whilst the Coptic Hope Center for Infectious Diseases is a Centre of Disease Control President's Emergency Plan For AIDS Relief funded institution to provide free antiretroviral therapy to Kenyans who are unable to afford HIV care and treatment.¹³ Participants with known cardiovascular disease (previous myocardial infarction or stroke) were excluded.

Study procedures and blood sampling

All participants completed a standardized questionnaire to capture data on demographics, including self-reported cardiovascular risk factors, past medical history, current medication and HIV factors including time since diagnosis. Data were captured on handheld devices electronically. Anthropometric and hemodynamic data including office blood pressure, height, weight and heart rate were captured.

Blood sampling

Blood samples were obtained from participants through standard venepuncture. Basic clinical chemistry and haematology was performed. This included assessment of renal function, glycaemic control, non-fasted lipid profiles, high-sensitivity cardiac troponin I (hscTnI) and high-sensitivity C-reactive protein (hsCRP). Given laboratory constraints, HbA1c and haematology was only measured in the Aga Khan University Hopsital population.

High-sensitivity troponin I: The Siemens Atellica IM High Sensitivity Troponin I assay (Siemens Healthineers) is a three-site sandwich immunoassay with a limit of detection of 1.6 ng/L and limit of quantification of 2.5 ng/L. The upper reference limit 99th centile was determined in 2007 samples from healthy individuals as 34 ng/L in women, and 53 ng/L in men, with a single threshold of 45 ng/L. In the reference range population, 75% of patients had values greater than the limit of detection. The level where the inter-assay coefficient of variation is <10% is 6 ng/L.¹⁴

High-sensitivity C-reactive protein: The Siemens Atellica High Sensitivity C-Reactive protein assay was used to measure hsCRP levels in stored serum. The assay range is from 0.1 to 50 mg/L with a coefficient of variation of 6.8% at 1.16 mg/L.¹⁵

Study definitions

Traditional cardiovascular risk factors were defined as those routinely measured in cardiovascular risk estimation systems and include basic anthropometry, diabetes and smoking status, lipid profile, and arterial blood pressure assessment. Body mass index (BMI) was calculated from measured height and weight and classified as normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (equal to or greater than 30 kg/m²). Current or past smoking history was self-reported by participants. Hypertension was defined as self-reported hypertension or measured SBP \geq 140 mmHg or DBP \geq 90 mmHg, or physician-prescribed blood pressure-lowering medications.¹⁶ Dyslipidemia was defined as a self-reported history. Hypercholesterolaemia was defined as a total cholesterol \geq 6.21 mmol/L. A high low-density lipoprotein (LDL) was defined as levels $>$ 4.1 mmol/L.¹⁷ Diabetes mellitus was defined as self-reported type 1 or 2 diabetes mellitus. Patients, in whom HbA1c was measured, were classified as those with high (\geq 6.5%), intermediate (5.7–6.4%) and low levels ($<$ 5.7%).¹⁸

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The hsCRP was categorized as low (<1 mg/L), intermediate (1–3 mg/L), or high (>3 mg/L).¹⁹ High-sensitivity cardiac troponin levels were categorised as below the limit of quantification (2.5 ng/L), above the limit of quantification but below the 99th centile upper reference limit and above the 99th centile upper reference limit (45 ng/L).²⁰

Statistical Analysis

Baseline demographics, clinical and lifestyle variables, laboratory biomarkers including markers of myocardial injury, inflammation, glycaemic control, and lipid profiles were summarised overall and stratified by gender. Continuous variables were reported as median and interquartile range, while the categorical variables were summarized as frequencies and percentages. Statistical differences between groups were assessed using Pearson’s chi-square test or Fisher’s exact test and unpaired two-samples Wilcoxon test or Student’s t-test as indicated. Sex-specific framingham laboratory-based risk equations were used to quantify the estimated 10-year CVD risk for each study participant. The equation used age, gender, smoking status, use of anti-hypertensive medications, prevalent diabetes, and systolic blood pressure. The risk estimations were computed according to algorithms accessed at <https://framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/>. Predicted cardiovascular event risk percentage over the next 10 years was classified as low (< 10%), intermediate (10–20%), and high risk (> 20%).

In further analysis, we evaluated the relationship between baseline markers of myocardial injury and inflammation and traditional cardiovascular risk factors. We calculated the 25th and 75th percentiles of observed hscTnI data and ordinally scaled it as <2.50 ng/L (undetectable), 2.50-3.02 ng/L, 3.02-7.12 ng/L, ≥7.12 ng/L given the skewness of the variable.²¹ Three multivariable ordinal (Cumulative logit) models and linear regression models with hscTnI and

hsCRP as the response variable, respectively, were fitted. The independent variables were age, sex and cardiovascular risk factors. Model I adjusted for age per year increase, sex, study site as a surrogate for socioeconomic status and creatinine. Model II additionally adjusted for hypertension, diabetes, and smoking status (never smoker, former smoker, current smoker). Model III adjusted for variables in Model I plus systolic blood pressure (SBP < 130 mmHg, SBP 130 -139 mmHg, SBP 140-159 mmHg, SBP >160 mmHg) and hsCRP or hscTnI. Models were constructed on complete cases with no imputation. All analysis was carried out in R (Version 4.1.2).

Ethics statement

Patients were enrolled only after providing written informed consent prior to participation. After receiving site approval from the Coptic Hope Center for Infectious Diseases in Nairobi, we obtained ethics approval for data analysis from The Aga Khan University Hospital, Nairobi Research Ethics Committee (approval letter reference: 2018/REC-84). The research was carried out in accordance with the Helsinki Declaration's principles.

Patient and Public Involvement

This was a small pilot study and patients and the public were not involved in the study

Results

Two hundred patients (median age 46 years [IQR 38 to 53 years], 61% females) were recruited in this cross-sectional study consisting (*Figure S1*). Prevalence of smoking was 2.5% across the cohort and higher in males compared to females. Hypertension was the most common cardiovascular risk factor at 30% with rates higher in males (33%) compared to females (28%). Self-reported dyslipidemia was low at 0.5% but much higher when classified according to a total cholesterol concentration >6.1 mmol/L (19%). The prevalence of elevated LDL \geq 4.2 mmol/L was 14%. Seventeen percent of the population had a systolic blood pressure \geq 140 mmHg and 15% of the population had a diastolic blood pressure \geq 90 mmHg. Obesity rates were high with 29% considered obese and 36% overweight. Obesity rates were higher in women at 34% compared to males (22%). Past history of malaria and tuberculosis remained high at 32% and 18% respectively. Over 90% of participants were receiving antiretroviral therapy and median duration of diagnosis to study recruitment was 12 years (*Table 1 and Table 2*). Given differences in the population served at Aga Khan University and Coptic hospitals, we observed important differences in baseline characteristics. Patient treated at Coptic hospital has lower income levels and higher rates of elevated blood pressure (*Table S1*).

Stored serum was available to measure hscTnI concentrations in 169 of the 200 participants. Despite using a hscTnI assay, the majority had concentrations below the limit of quantification at <2.5 ng/L (n=109/169, 65%). Fifty-nine patients (n = 59/169 ,35%) had concentration levels above the limit of quantification but below the 99th centile upper reference limit. Serum hsCRP was measured in 198 of the 200 participants. The median hsCRP was 2 mg/L (IQR 0.8 to 4.2 mg/L). Levels were numerically higher in women compared to men (2.2 mg/L versus 1.5 mg/L). High-sensitivity CRP categorised 75 (38%) patients as having a high level (> 3mg/L)

with 65 (33%) and 58 (29.3) at intermediate (1-3 mg/L) and low (<1 mg/L) levels. Levels of hscTnI and hsCRP did not differ when stratified by site (*Table S2*).

Table 1: Baseline demographics and clinical characteristics¹

Characteristics	All patients (n=200)	Sex		<i>p</i> -value ²
		Females (n= 121)	Males (n = 79)	
Age, median (Q1, Q3), years	45.5 (37.7, 52.6)	44.2 (37.3, 50.5)	47.3 (38.0, 53.1)	0.206
Years of education, median (Q1, Q3)	14.0 (12.0, 16.0)	14.0 (12.0, 16.0)	15.0 (12.0, 16.5)	0.174
Highest level of education attained				
Primary/none/don't know, %	30/200 (15.0)	18/121 (14.9)	12/79 (15.2)	0.825
Secondary, %	45/200 (22.5)	29/121 (24.0)	16/79 (20.3)	
Higher Education/University, %	125/200 (62.5)	74/121 (61.2)	51/79 (64.6)	
Marital status				
Married (monogamous/polygamous) , %	128/200 (64.0)	64/121 (52.9)	64/79 (81.0)	<0.001
Single	26/200 (13.0)	23/121 (19.0)	3/79 (3.8)	
Separated/widowed/divorced/refused/cohabiting/others, %	46/200 (23.0)	34/121 (28.1)	12/79 (15.2)	
Employment status				
Salaried Job or self-employed, %	180/200 (90.0)	105/121 (86.8)	75/79 (94.9)	0.148
Unemployed/housewife/retiree, %	13/200 (6.5)	11/121 (9.1)	2/79 (2.5)	
Casual labourer, %	7/200 (3.5)	5/121 (4.1)	2/79 (2.5)	
Household income per month				
< 15,001 KES ³ , %	34/198 (17.2)	26/119 (21.8)	8/79 (10.1)	0.051
> 15,001 KES, %	164/198 (82.8)	93/119 (78.2)	71/79 (89.9)	
Cardiovascular risk factors				
Smoking				
<i>Current smoker</i> , %	5/200 (2.5)	2/121 (1.7)	3/79 (3.8)	<0.001
<i>Ex-smoker</i> , %	44/200 (22.0)	11/121 (9.1)	33/79 (41.8)	
<i>Never smoker</i> , %	151/200 (75.5)	108/121 (89.3)	43/79 (54.4)	
Diabetes, %	7/200 (3.5)	4/121 (3.3)	3/79 (3.8)	0.661
Self-reported hypertension ⁴ , %	44/200 (22.0)	30/121 (24.8)	14/79 (17.7)	0.315
Cumulative hypertension ⁵ , %	60/200 (30.0)	34/121 (28.1)	26/79 (32.9)	0.570
Self-reported dyslipidemia, %	1/197 (0.5)	1/119 (0.8)	0/78 (0.0)	0.153
Chronic kidney disease, %	2/200 (1.0)	1/121 (0.8)	1/79 (1.3)	0.863
HIV				
Time since (months) HIV ⁶ infection, Median (Q1, Q3)	143.0 (59.0, 191.0)	144.0 (62.0, 191.0)	131.0 (56.5, 191.0)	0.574

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the variable.

² *p*-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon test for continuous variables, two-sided; bold *p*-values indicate statistical significance (*p*<0.05).

³ KES, Kenya shillings currency code

⁴ Self-reported physician-diagnosed hypertension.

⁵ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

⁶ HIV, human immunodeficiency virus,

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Characteristics	All patients (n=200)	Sex		<i>p</i> -value ²
		Females (n= 121)	Males (n = 79)	
Currently on ART ⁷ , %	195/200 (97.5)	119/121 (98.3)	76/79 (96.2)	0.385
Past medical history				
Malaria, %	21/200 (10.5)	10/121 (8.3)	11/79 (13.9)	0.298
Tuberculosis, %	12/200 (6.0)	7/121 (5.8)	5/79 (6.3)	1.000
Clinical characteristics				
Body mass index, BMI (Kg/m ²), median (Q1, Q3)	26.8 (23.4, 30.8)	27.9 (23.8, 32.3)	26.0 (23.2, 29.6)	0.010
<i>BMI <25</i> , %	71/200 (35.5)	37/121 (30.6)	34/79 (43.0)	0.100
<i>BMI 25 to 29</i> , %	71/200 (35.5)	43/121 (35.5)	41/79 (33.9)	
<i>BMI >30</i> , %	58/200 (29.0)	41/121 (33.9)	17/79 (21.5)	
Systolic blood pressure (mmHg), Median (Q1, Q3), n = 200	120.0 (110.0, 133.0)	120.0 (110.0, 130.0)	122.0 (111.5, 133.0)	0.272
<i>SBP < 130 mmHg</i> , %	136/200 (68.0)	86/121 (71.1)	50/79 (63.3)	0.173
<i>SBP 130 -139 mmHg</i> , %	30/200 (15.0)	19/121 (15.7)	11/79 (13.9)	
<i>SBP 140-159 mmHg</i> , %	19/200 (9.5)	7/121 (5.8)	12/79 (15.2)	
<i>SBP >160 mmHg</i> , %	15/200 (7.5)	9/121 (7.4)	6/79 (7.6)	
Diastolic blood pressure (mmHg), Median (Q1, Q3), n = 200	78.0 (71.0, 85.0)	77.0 (71.0, 84.0)	80.0 (72.0, 85.0)	0.301
<i>DBP < 85 mmHg</i> , %	149/200 (74.5)	92/121 (76.0)	57/79 (72.2)	0.417
<i>DBP 85 – 89 mmHg</i> , %	22/200 (11.0)	10/121 (8.3)	12/79 (15.2)	
<i>DBP 90 – 99</i> , %	17/200 (8.5)	12/121 (9.9)	5/79 (6.3)	
<i>DBP > 100</i> , %	12/200 (6.0)	7/121 (5.8)	5/79 (6.3)	
Heart rate (bpm) median (Q1, Q3)	78.0 (74.0, 82.0)	76.5 (74.8, 84.2)	78.0 (72.0, 81.0)	0.474
Current cardiovascular medications				
RAAS modulators, %	16/200 (8.0)	11/121 (9.1)	5/79 (6.3)	0.662
Calcium channel blockers, %	8/200 (4.0)	5/121 (4.1)	3/79 (3.8)	1.000
Beta-blockers, %	8/200 (4.0)	5/121 (4.1)	3/79 (3.8)	1.000
Diuretics, %	10/200 (5.0)	8/121 (6.6)	2/79 (2.5)	0.321
Statins, %	2/200 (1.0)	1/121 (0.8)	1/79 (1.3)	1.000

⁷ ART, antiretroviral therapy.

Table 2 Biochemistry and haematology¹

Characteristics	All patients (n=200)	Sex		p-value ²
		Females (n=121)	Males (n=79)	
Creatinine, median (Q1, Q3), n=197	85.0 (73.0, 101.0)	77.5 (69.0, 89.3)	99.0 (89.0, 113.0)	<0.001
Urea, median (Q1, Q3), n=196	3.7 (3.1, 4.6)	3.6 (3.0, 4.3)	3.8 (3.2, 5.0)	0.013
Hemoglobin, mean (SD) , n=98* ³	14.01 (2.06)	12.90 (1.77)	15.31 (1.55)	<0.001
Glucose, median (Q1, Q3), n=197	4.8 (4.4, 5.3)	4.8 (4.3, 5.3)	4.9 (4.5, 5.3)	0.169
HbA1c, median (Q1, Q3), n=98*	5.6 (5.4, 5.9)	5.6 (5.4, 5.8)	5.8 (5.4, 6.1)	0.013
HbA1c <5.7, %	50/98 (51.0)	34/53 (64.2)	16/45 (35.6)	0.004
HbA1c 5.7 – 6.4, %	45/98 (45.9)	19/53 (35.8)	26/45 (57.8)	
HbA1c >= 6.5, %	3/98 (3.1)	0/53 (0.0)	3/45 (6.7)	
Lipid profiles				
Total cholesterol, median (Q1, Q3), n=196	4.6 (3.9, 5.1)	4.7 (3.9, 5.2)	4.5 (3.9, 5.1)	0.706
TC < 4.7, %	107/196 (54.6)	59/118 (50.0)	48/78 (61.5)	0.393
TC 4.8 – 5.1, %	22/196 (11.2)	15/118 (12.7)	7/78 (9.0)	
TC 5.2 – 6.1, %	30/196 (15.3)	21/118 (17.8)	9/78 (11.5)	
TC >= 6.2, %	37/196 (18.9)	23/118 (19.5)	14/78 (17.9)	
LDL, median (Q1, Q3), n=196	3.0 (2.3, 3.6)	3.0 (2.4, 3.7)	3.0 (2.3, 3.5)	0.747
LDL < 2.6	75/196 (38.3)	46/118 (39.0)	29/78 (37.2)	0.619
LDL 2.6 – 3.3	53/196 (27.0)	30/118 (25.4)	23/78 (29.5)	
LDL 3.4 – 4.1	41/196 (20.9)	23/118 (19.5)	18/78 (23.1)	
LDL >= 4.2	27/196 (13.8)	19/118 (16.1)	8/78 (10.3)	
HDL, median (Q1, Q3), n=196	1.2 (1.0, 1.5)	1.2 (1.1, 1.5)	1.1 (1.0, 1.3)	0.001
Trigylcerides, median (Q1, Q3), n=196	1.4 (0.9, 2.0)	1.2 (0.9, 1.7)	1.7 (1.0, 2.7)	0.0005
Trig < 1.7	123/196 (62.8)	86/118 (72.9)	37/78 (47.4)	<0.0001
Trig 1.7 – 2.2	32/196 (16.3)	19/118 (16.1)	13/78 (16.7)	
Trig >2.3	41/196 (20.9)	13/118 (11.0)	28/78 (35.9)	
Cardiac and inflammatory biomarkers				
High sensitivity troponin I, median (Q1, Q3), n=169	2.5 (2.5, 3.0)	2.5 (2.5, 2.5)	2.7 (2.5, 3.8)	<0.0001
hscTnI < 2.5 ng/L, %	109/169 (64.5)	78/103 (75.7)	31/66 (47.0)	<0.001
hscTnI 2.5 – 45 ng/L	59/169 (34.9)	24/103 (23.3)	35/66 (53.0)	
hscTnI >= 45 ng/L	1/169 (0.6)	1/103 (1.0)	0/66 (0.0)	

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the laboratory marker.

² p-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon test or Student's t-test for continuous variables, two-sided; bold p-values indicate statistical significance (p<0.05).

³ * Hemoglobin and hemoglobin A1c (HbA1c) summaries are from Aga Khan University Hospital only.

Characteristics	All patients (n=200)	Sex		p-value ²
		Females (n=121)	Males (n=79)	
High-sensitivity CRP, median (Q1, Q3), n=198	2.0 (0.8, 4.2)	2.2 (0.9, 4.5)	1.5 (0.8, 3.8)	0.144
hsCRP < 1mg/L	58/198 (29.3)	31/120 (25.8)	27/78 (34.6)	0.300
hsCRP 1 - 3 mg/L	65/198 (32.8)	39/120 (32.5)	26/78 (33.3)	
hsCRP >3 mg/L	75/198 (37.9)	50/120 (41.7)	25/78 (32.1)	

Using the sex stratified Framingham laboratory-based risk score with lipids, the majority of the HIV population was classified at low risk (83%) with 12% at intermediate risk and 5% at high risk. Although sample sizes remained limited when stratified by sex and risk category, the prevalence of hypertension remained higher in women compared to men (*Table 3*) and as expected higher in the intermediate and high-risk groups across the population (*Table S3*).

Association between hscTnI and hsCRP and traditional cardiovascular risk factors were also evaluated (*Table 4*). The findings from cumulative logit models showed that older patients were more likely to have higher hscTnI levels (adjusted odds ratio (aOR) per year: 1.05, 95% confidence interval (CI): 1.01–1.09, p<0.011). Female patients, compared to male patients, were identified as having lower hscTnI levels. Systolic blood pressures (SBP) of 140–159 mmHg and SBP >160 mmHg were associated with higher hscTnI concentrations (aOR 2.96 (95% CI: 1.09–7.90, p=0.030) and 4.68 (95% CI: 1.55–14.1, p=0.006, respectively) compared to those with SBP <130 mmHg. Our study did not find any strong associations between hsCRP and traditional cardiovascular risk factors including age, hypertension, diabetes and smoking. We also did not find any association between SBP levels and hsCRP. Levels of hsCRP were higher for HIV-patients with higher hscTnI levels. Study site - as a surrogate for socioeconomic status – was not associated with hscTnI or hsCRP.

Table 3: Cardiovascular risk factors, markers of myocardial injury and inflammation by cardiovascular risk category¹

Variable	Framingham risk score classification (FRS lipid) ²			p-value for trend ³	
	Low	Intermediate	High	Increasing	Two-sided
Males					
All (%)	58 (73.4)	14 (17.7)	7 (8.9)		
Smoking				–	0.503
Current smoker, %	3/58 (5.2)	0/14 (0.0)	0/7 (0.0)		
Ex-smoker, %	22/58 (37.9)	6/14 (42.9)	5/7 (71.4)		
Never smoker, %	33/58 (56.9)	8/14 (57.1)	2/7 (28.6)		
Diabetes, %	3/58 (5.2)	0/14 (0.0)	0/7 (0.0)	0.163	0.326
Hypertension ⁴ , %	12/58 (20.7)	6/14 (42.9)	7/7 (100.0)	<0.001	<0.001
Hyperlipidemia, %	0/58 (0.0)	0/13 (0.0)	0/7 (0.0)	–	–
Lipid profiles					
Total cholesterol, median (Q1, Q3)	4.3 (3.8, 4.9)	4.5 (4.3, 5.4)	6.2 (5.0, 6.8)	0.005	0.007
TC < 4.7, %	39/57 (68.4)	8/14 (57.1)	1/7 (14.3)	–	<0.001
TC 4.8 – 5.1, %	7/57 (12.3)	0/14 (0.0)	0/7 (0.0)		
TC 5.2 – 6.1, %	5/57 (8.8)	4/14 (28.6)	0/7 (0.0)		
TC ≥ 6.2, %	6/57 (10.5)	2/14 (14.3)	6/7 (85.7)		
LDL, median (Q1, Q3)	3.0 (2.3, 3.4)	3.2 (2.3, 3.5)	3.9 (3.5, 5.2)	0.016	0.039
LDL < 2.6, %	22/57 (38.6)	6/14 (42.9)	1/7 (14.3)	–	0.008
LDL 2.6 – 3.3, %	20/57 (35.1)	3/14 (21.4)	0/7 (0.0)		
LDL 3.4 – 4.1, %	11/57 (19.3)	5/14 (35.7)	2/7 (28.6)		
LDL ≥ 4.2, %	4/57 (7.0)	0/14 (0.0)	0/7 (0.0)		
HDL, median (Q1, Q3)	1.1 (1.0, 1.4)	1.0 (0.8, 1.2)	1.0 (0.9, 1.2)	0.923	0.161
Triglycerides, median (Q1, Q3)	1.6 (1.0, 2.2)	2.3 (1.1, 4.1)	3.2 (2.3, 4.1)	0.008	0.017
Trig < 1.7	30/57 (52.6)	6/14 (42.9)	1/7 (14.3)	–	0.018

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the cardiovascular risk factor/marker.

² Risk categories classified as low (<10%), intermediate (10-19%) and high (≥ 20%)

³ p-values for trend were calculated Jonckheere-Terpstra for continuous variables and Cochran-Armitage, or Cochran-Mantel-Haenszel tests, appropriate, for categorical variables.

⁴ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

Variable	Framingham risk score classification (FRS lipid) ²			p-value for trend ³	
	Low	Intermediate	High	Increasing	Two-sided
Trig 1.7 – 2.2	11/57 (19.3)	1/14 (7.1)	1/7 (14.3)		
Trig >2.3	16/57 (28.1)	7/14 (50.0)	5/7 (71.4)		
Cardiac and inflammatory biomarkers					
High sensitivity troponin I, median (Q1, Q3)	2.5 (2.5, 3.4)	3.4 (2.8, 5.2)	4.1 (2.9, 7.1)	0.013	0.020
hscTnI < 2.5 ng/L, %	26/48 (54.2)	3/11 (27.3)	2/7 (28.6)	–	0.083
hscTnI 2.5 – 45 ng/L	22/48 (45.8)	8/11 (72.7)	5/7 (71.4)		
hscTnI >= 45 ng/L	0/48 (0.0)	0/11 (0.0)	0/7 (0.0)		
High-sensitivity CRP, median (Q1, Q3)	1.5 (0.8, 4.0)	2.3 (0.8, 3.1)	1.0 (0.7, 3.6)	0.523	0.95
hsCRP < 1mg/L	19/57 (33.3)	5/14 (35.7)	3/7 (42.9)	–	0.782
hsCRP 1 - 3 mg/L	20/57 (35.1)	4/14 (28.6)	2/7 (28.6)		
hsCRP >3 mg/L	18/57 (31.6)	5/14 (35.7)	2/7 (28.6)		
Creatinine, median (Q1, Q3)	100.0 (89.5, 113.2)	98.5 (94.8, 115.0)	91.0 (79.0, 104.5)	0.702	0.610
Females					
All (%)	108 (89.3)	9 (7.4)	4 (3.3)		
Smoking					
Current smoker, %	2/108 (1.9)	0/9 (0.0)	0/4 (0.0)	–	0.241
Ex-smoker, %	11/108 (10.2)	0/9 (0.0)	0/4 (0.0)		
Never smoker, %	95/108 (88.0)	9/9 (100.0)	4/4 (100.0)		
Diabetes, %	0/108 (0.0)	2/9 (22.2)	2/4 (50.0)	1.000	<0.0001
Hypertension ⁵ , %	24/108 (22.2)	7/9 (77.8)	3/4 (75.0)	<0.0001	<0.001
Hyperlipidemia, %	0/106 (0.0)	1/9 (11.1)	0/4 (0.0)	0.976	0.048
Lipid profiles					
Total cholesterol, median (Q1, Q3)	4.6 (3.8, 5.1)	5.4 (4.9, 6.1)	4.4 (4.3, 4.7)	0.07	0.031
TC < 4.7, %	54/105 (51.4)	2/9 (22.2)	3/4 (75.0)	–	0.883
TC 4.8 – 5.1, %	13/105 (12.4)	2/9 (22.2)	0/4 (0.0)		
TC 5.2 – 6.1, %	18/105 (17.1)	2/9 (22.2)	1/4 (25.0)		
TC >= 6.2, %	20/105 (19.0)	3/9 (33.3)	0/4 (0.0)		
LDL, median (Q1, Q3)	2.9 (2.4, 3.5)	4.0 (3.3, 4.2)	2.9 (2.6, 3.2)	0.042	0.082
LDL < 2.6, %	43/105 (41.0)	2/9 (22.2)	1/4 (25.0)		0.357

⁵ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

Variable	Framingham risk score classification (FRS lipid) ²			p-value for trend ³	
	Low	Intermediate	High	Increasing	Two-sided
LDL 2.6 – 3.3, %	27/105 (25.7)	1/9 (11.1)	2/4 (50.0)		
LDL 3.4 – 4.1, %	19/105 (18.1)	3/9 (33.3)	1/4 (25.0)		
LDL >= 4.2, %	16/105 (15.2)	3/9 (33.3)	0/4 (0.0)		
HDL, median (Q1, Q3)	1.2 (1.1, 1.5)	1.2 (1.1, 1.7)	1.0 (0.9, 1.2)	0.699	0.620
Triglycerides, median (Q1, Q3)	1.1 (0.9, 1.7)	1.6 (1.4, 2.0)	2.0 (1.8, 2.3)	0.001	0.003
Trig < 1.7	80/105 (76.2)	5/9 (55.6)	1/4 (25.0)	–	0.020
Trig 1.7 – 2.2	15/105 (14.3)	2/9 (22.2)	2/4 (50.0)		
Trig >2.3	10/105 (9.5)	2/9 (22.2)	1/4 (25.0)		
Cardiac and inflammatory biomarkers					
High sensitivity troponin I, median (Q1, Q3)	2.5 (2.5, 2.5)	2.8 (2.5, 4.1)	2.7 (2.6, 5.2)	0.003	0.006
hscTnI < 2.5 ng/L, %	74/92 (80.4)	3/7 (42.9)	1/4 (25.0)	–	0.003
hscTnI 2.5 – 45 ng/L	17/92 (18.5)	4/7 (57.1)	3/4 (75.0)		
hscTnI >= 45 ng/L	1/92 (1.1)	0/7 (0.0)	0/4 (0.0)		
High-sensitivity CRP, median (Q1, Q3)	2.0 (0.9, 4.3)	6.9 (2.2, 10.3)	2.6 (2.5, 4.4)	0.012	0.022
hsCRP < 1mg/L	30/107 (28.0)	1/9 (11.1)	0/4 (0.0)	–	0.128
hsCRP 1 - 3 mg/L	34 (31.8)	2/9 (22.2)	3/4 (75.0)		
hsCRP >3 mg/L	43 (40.2)	6/9 (66.7)	1/4 (25.0)		
Creatinine, median (Q1, Q3)	76.0 (69.0, 85.5)	88.0 (75.0, 94.0)	91.0 (84.2, 99.5)	0.047	0.047

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

Table 4: Relationship between baseline markers of myocardial injury and inflammation and traditional cardiovascular risk factors, displayed as multivariable-adjusted odds ratios¹⁶ for hscTnI and multivariable-adjusted mean differences¹⁷ for hsCRP

	High-sensitivity troponin I			High-sensitivity C-Reactive Protein		
Risk factor	Model I AOR ¹⁸ (95% CI) ¹⁹	Model II AOR (95% CI)	Model III AOR (95% CI)	Model I Adjusted Coef. ²⁰ (95% CI)	Model II Adjusted Coef. (95% CI)	Model III Adjusted Coef. (95% CI)
Age (years)	1.05 (1.02 to 1.09, p= 0.004)	1.05 (1.01 to 1.09, p= 0.021)	1.04 (1.00 to 1.08, p= 0.032)	0.004 (-0.12 to 0.12, p=0.952)	0.01 (-0.11 to 0.14, p=0.860)	0.02 (-0.13 to 0.17, p=0.775)
Sex						
Male	Reference	Reference	Reference	Reference	Reference	Reference
Female	0.32 (0.14 to 0.70, p= 0.004)	0.39 (0.16 to 0.93, p= 0.035)	0.38 (0.17 to 0.84, p= 0.018)	1.66 (-0.85 to 4.18, p=0.194)	1.49 (-1.28 to 4.25, p=0.290)	0.04 (-3.39 to 3.47, p=0.980)
Study Site ²¹						
AKUNH	Reference	Reference	Reference	Reference	Reference	Reference
Coptic	1.08 (0.54 to 2.16, p=0.832)	0.97 (0.48 to 1.99, p=0.941)	0.91 (0.44 to 1.90, p=0.805)	0.78 (-1.70 to 3.27, p=0.536)	0.91 (-1.63 to 3.45, p=0.481)	0.87 (-2.02 to 3.76, p=0.553)
Hypertension	–	2.76 (1.36 to 5.63, p= 0.005)	–	–	1.23 (-3.91 to 6.45, p=0.366)	–
Diabetes	–	0.53 (0.06 to 3.37, p=0.513)	–	–	1.41 (-6.24 to 9.06, p=0.903)	–
Smoking						
Never smoker	Reference	Reference	–	–	Reference	–

16 Cumulative Logit Model with high-sensitivity Troponin-I response as myocardial injury marker. Bold *p*-values indicate statistical significance (*p*<0.05). Model I adjusts for age, sex, creatinine and study site; Model II as for Model I plus history of hypertension, diabetes and smoking status; Model III as for Model I plus systolic blood pressure and hsCRP levels

17 Linear Regression with high-sensitivity C-Reactive Protein (hsCRP) response as inflammation marker. Bold *p*-values indicate statistical significance (*p*<0.05). Model I adjusts for age, sex and creatinine; Model II as for Model I plus history of hypertension, diabetes and smoking status; Model III as for Model I plus systolic blood pressure and hsCRP levels

18 AOR, adjusted odds ratio.

19 CI, confidence interval

20 Coef., coefficient as multivariable mean difference.

21 AKUHN, Aga Khan University Hospital, Nairobi; Coptic, Coptic Hope Center for Infectious Diseases.

	High-sensitivity troponin I			High-sensitivity C-Reactive Protein		
Risk factor	Model I AOR ¹⁸ (95% CI) ¹⁹	Model II AOR (95% CI)	Model III AOR (95% CI)	Model I Adjusted Coef. ²⁰ (95% CI)	Model II Adjusted Coef. (95% CI)	Model III Adjusted Coef. (95% CI)
Former smoker	–	1.19 (0.51 to 2.70, p=0.685)	–	–	0.45 (-3.61 to 4.52, p=0.781)	–
Current smoker	–	1.36 (0.15 to 9.11, p=0.762)	–	–	0.22 (-7.47 to 7.92, p=0.954)	–
Systolic Blood Pressure						
SBP < 130 mmHg	Reference	–	Reference	–	–	Reference
SBP 130 - 139 mmHg	–	–	2.29 (0.87 to 5.87, p=0.087)	–	–	-2.40 (-6.37 to 1.58, p=0.235)
SBP 140- 159 mmHg	–	–	3.08 (1.13 to 8.34, p=0.026)	–	–	-3.47 (-8.13 to 1.19, p=0.143)
SBP > 160 mmHg	–	–	5.40 (1.75 to 16.6, p=0.003)	–	–	-2.09 (-7.45 to 3.26, p=0.441)
High-sensitivity CRP mg/L	–	–	1.05 (1.01 to 1.10, p=0.014)	–	–	–
High-sensitivity troponin-I						
< 2.50 ng/L	Reference	Reference	Reference	Reference	Reference	Reference
2.50–3.02 ng/L	–	–	–	–	–	4.42 (0.78 to 8.07, p=0.018)
3.02–7.12 ng/L	–	–	–	–	–	1.20 (-2.43 to 4.84, p=0.514)
≥ 7.12 ng/L	–	–	–	–	–	0.57 (-3.23 to 4.38, p=0.766)
Creatinine mg/L	1.00 (0.98 to 1.03, p= 0.671)	1.01 (0.99–1.03, p=0.399)	1.01 (0.99 to 1.04, p=0.177)	-0.01 (-0.05 to 0.02, p=0.568)	-0.01 (-0.04 to 0.03, p=0.644)	-0.11 (-0.20 to -0.03, p=0.010)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Discussion

In this small, descriptive, cross-sectional study across two sites in urban Kenya, we evaluated the prevalence of traditional cardiovascular risk factors. We also explored how biochemical markers of inflammation and myocardial injury are associated with traditional cardiovascular risk factors in PLHIV. We make a number of observations. First, in a relatively young population with HIV, some traditional cardiovascular risk factors were common. Smoking and diabetes rates, however, were low. Second, using traditional risk estimation systems, the majority of the young HIV population were categorized as low-risk for future cardiovascular events. Third, across the majority of patients, hsTnI values were below the limit of detection. Fourth, in exploratory analysis we found no associations between hsCRP levels and traditional cardiovascular risk factors but did observe a positive association between hscTnI levels and increasing age and higher systolic blood pressure.

Some traditional cardiovascular risk factors were common in the HIV population studied. Hypertension was self-reported in 1 in 5 individuals and higher, at 1 in 3, when classified by office systolic blood pressure measurement and/or use of anti-hypertensives. Self-reported dyslipidemia was low at 1 in 20 but much higher when based on total cholesterol concentration >6.1 mmol/L (19%). This discordance likely reflects individuals being unaware of their cholesterol status. Smoking and diabetes rates, however, remained relatively low in contrast to PLHIV in high income countries.²⁶ Our prevalence rates of traditional cardiovascular risk factors are in agreement with other studies from the sub-Saharan African region²²⁻²⁴ and discordant to those evaluating PLHIV in high-income settings.^{25 26} Whilst North American / European studies contribute to most of the evidence evaluating cardiovascular disease in HIV,

the region only hosts 6% of the global HIV population compared to 75% for sub-Saharan Africa.^{27 28} PLHIV in sub-Saharan Africa and North America / Europe are different by virtue of the factors associated with HIV acquisition. HIV remains firmly established in the general population in SSA but overwhelmingly affects men who have sex with men and intravenous drug users in North America / Europe.²⁹ These differences probably account for regional discordance in the association between HIV status and prevalence of cardiovascular risk factors that has been observed in the published literature. Positive associations in North America / Europe either become null or even reverse in sub-Saharan Africa.^{22-26 30-33}

Using the sex stratified Framingham laboratory-based risk score, the overwhelming majority of the HIV population was classified at low risk (83%) with 12% at intermediate risk and 5% at high risk. Similar risk categorizations were obtained when using the Framingham non-laboratory-based risk scores. All established cardiovascular risk estimation systems – predominantly developed in high-income countries and not accounting for HIV status are highly influenced by age. As such, our findings likely reflect the younger age distribution in our study.^{12 34} Whether this estimation of low-risk, using generalized risk scores developed predominantly in high-income countries, reflects the observed cardiovascular risk of HIV individuals in sub-Saharan Africa remains uncertain.

Previous studies have shown how biochemical markers, such as hsCRP and hscTnI, may hold promise in improving cardiac risk estimation systems.³⁵ Our study showed that the majority of individuals had undetectable levels of hscTnI with only 1 in 3 patients demonstrating levels above the limit of detection. Previous studies in high-income settings have shown that during acute HIV infection, troponin levels are higher but drop 3-fold once viremic control is achieved.³⁶ A large proportion of our patients were established on antiretroviral therapy and

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

with the duration of diagnosis to study recruitment being nearly 12 years. Two studies showed contrasting results when evaluating the association between troponin levels and presence of coronary plaques, with results primarily applicable to men with HIV in non-endemic regions.³⁷
³⁸ Levels of hsCRP, suggestive of underlying inflammation, were high in this study with women having higher concentrations. Whether higher baseline hsCRP levels relate to increased risk of cardiovascular events in HIV, however, remains uncertain with contrasting data in the published literature.^{39,40} Higher levels of hsCRP in people with HIV is biologically plausible and supported by previous studies^{28 41}, but may not just be reflective of vascular disease.⁴² As such the specificity of hsCRP for cardiovascular disease in PLHIV may be low.

Our study showed, hscTnI levels were higher in males, associated with increasing age, measured systolic blood pressure, and reported history of hypertension. This is similar to what has been observed in the general population.^{43 44} However, surprisingly, in our study, much of the population had troponin concentrations below the limit of quantification despite using a high-sensitivity assay likely reflective of a younger population. Unlike in the general population⁴⁵, We did not show any robust association between hsCRP and traditional cardiovascular risk factors. This may reflect the younger age of our population with previous studies showing higher hsCRP values in the elderly.⁴⁶

This is one of the few studies that has quantified the prevalence of cardiovascular risk factors and explored their association with biochemical markers of inflammation and myocardial injury in HIV populations from two distinct centres in urban Kenya. However, several limitations should be considered. First, our study was cross-sectional and we were unable to evaluate the associations between novel biochemical markers and future cardiovascular events. Second, HIV populations in our study were recruited across two centres in Nairobi,

representing a predominantly urban population. Whether our findings are generalisable to rural populations remains uncertain. Third, given resource limitations, we did not study age- and sex-matched non-HIV populations and were limited to a finite choice of biochemical biomarkers. As such our study is unable to comment on associations between a wider range of biochemical markers and cardiovascular risk factors in the general population and how these may differ to those infected with HIV. For the same reason we were also unable to measure metric if infection control (viral load and CD4 count) at the time of recruitment. Fourth, some of the risk factors such as diabetes status depended on self-reporting – as such, the absence of associations may reflect exposure misclassification. Lastly, we cannot exclude the possibility that associations between biomarkers and outcomes may in part be due to residual confounding or unmeasured confounders.

In conclusion we show that whilst some traditional cardiovascular risk factor prevalences remain high in HIV populations in sub-Saharan Africa, important ones such as smoking are low. This is in contrast to HIV populations in non-endemic regions²⁶. The majority of PLHIV - using traditional risk estimation systems - have a low estimated CVD risk likely reflecting a younger aged population predominantly consisting of women. Whilst hscTnI values were associated with increasing age and higher blood pressure, no associations between hsCRP levels and traditional cardiovascular risk factors were observed.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Contributorship: Dr Shah and Dr Chung conceived the study. Dr Hassan recruited the patients. Dr Shah and Dr Hassan wrote the first draft of the manuscript. All other authors made critical revisions on the paper.

Competing interest: ASVS’s institution has received speaker fees from Abbott Diagnostics. No other comnflcts of interest

Funding: Supported by the Global Challenges Research Fund UKRI and the British Heart Foundation Intermediate Clinical Research Fellowship

Data sharing statement: Data will be available on request to the corresponding author (anoop.shah@lshtm.ac.uk)

Ethical approval information: Ethical approval was obtained from the Aga Khan University Nairobi Research Ethics committee (2018/REC-84). Informed consent was obtained from all subjects participating in the study.

Acknowledgements: None

References

1. Global AIDS update 2016: Joint United Nations Programme on HIV/AIDS, 2016.
Available from: <https://www.unaids.org/en/resources/documents/2016/Global-AIDS-update-2016#:~:text=The%20world%20has%20committed%20to,8%20to%2010%20June%202016.>
2. Mensah GA, Roth GA, Sampson UK, et al. Mortality from cardiovascular diseases in sub-Saharan Africa, 1990-2013: a systematic analysis of data from the Global Burden of Disease Study 2013. *Cardiovasc J Afr* 2015;26(2 Suppl 1):S6-10. doi: 10.5830/CVJA-2015-036
3. Murray CJ, Ortblad KF, Guinovart C, et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014;384(9947):1005-70. doi: 10.1016/S0140-6736(14)60844-8
4. Palella FJ, Jr., Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* 1998;338(13):853-60. doi: 10.1056/NEJM199803263381301
5. Neuhaus J, Angus B, Kowalska JD, et al. Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. *Aids* 2010;24(5):697-706. doi: 10.1097/QAD.0b013e3283365356
6. Mocroft A, Reiss P, Gasirowski J, et al. Serious fatal and nonfatal non-AIDS-defining illnesses in Europe. *Journal of acquired immune deficiency syndromes* 2010;55(2):262-70. doi: 10.1097/QAI.0b013e3181e9be6b [published Online First: 2010/08/12]
7. Antiretroviral Therapy Cohort C. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2010;50(10):1387-96. doi: 10.1086/652283
8. Shah ASV, Stelzle D, Lee KK, et al. Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV. *Circulation* 2018;138(11):1100-12. doi: 10.1161/circulationaha.117.033369 [published Online First: 2018/07/04]
9. Rao SG, Galaviz KI, Gay HC, et al. Factors Associated With Excess Myocardial Infarction Risk in HIV-Infected Adults: A Systematic Review and Meta-analysis. *Journal of acquired immune deficiency syndromes* 2019;81(2):224-30. doi: 10.1097/QAI.0000000000001996 [published Online First: 2019/03/14]
10. Gaziano TA, Abrahams-Gessel S, Gomez-Olive FX, et al. Cardiometabolic risk in a population of older adults with multiple co-morbidities in rural south africa: the HAALSI (Health and Aging in Africa: longitudinal studies of INDEPTH communities) study. *BMC Public Health* 2017;17(1):206. doi: 10.1186/s12889-017-4117-y [published Online First: 2017/02/19]
11. Gaziano TA, Bitton A, Anand S, et al. Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr Probl Cardiol* 2010;35(2):72-115. doi: 10.1016/j.cpcardiol.2009.10.002

12. So-Armah K, Benjamin LA, Bloomfield GS, et al. HIV and cardiovascular disease. *Lancet HIV* 2020;7(4):e279-e93. doi: 10.1016/S2352-3018(20)30036-9 [published Online First: 2020/04/04]

13. Chung MH, Drake AL, Richardson BA, et al. Impact of prior HAART use on clinical outcomes in a large Kenyan HIV treatment program. *Curr HIV Res* 2009;7(4):441-6. doi: 10.2174/157016209788680552 [published Online First: 2009/07/16]

14. Performance Evaluation of the Atellica IM High-Sensitivity Troponin I Assay: Siemens Healthcare Diagnostics Inc. · O; 2020 [Available from: <https://www.siemens-healthineers.com/en-uk/laboratory-diagnostics/assays-by-diseases-conditions/cardiac-assays/cardiac-troponin-assays> accessed 19th March 2021.

15. Healthineers S. High Sensitivity C-Reactive Protein (hsCRP) Assay [Available from: <https://www.siemens-healthineers.com/en-uk/cardiac/cardiac-assays/high-sensitivity-c-reactive-protein> accessed 19th March 2021.

16. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):e13-e115. doi: 10.1161/HYP.0000000000000065 [published Online First: 2017/11/15]

17. Roth GA, Fihn SD, Mokdad AH, et al. High total serum cholesterol, medication coverage and therapeutic control: an analysis of national health examination survey data from eight countries. *Bull World Health Organ* 2011;89(2):92-101. doi: 10.2471/BLT.10.079947 [published Online First: 2011/02/25]

18. Kramer CK, Araneta MR, Barrett-Connor E. A1C and diabetes diagnosis: The Rancho Bernardo Study. *Diabetes Care* 2010;33(1):101-3. doi: 10.2337/dc09-1366 [published Online First: 2009/10/20]

19. Zacho J, Tybjaerg-Hansen A, Jensen JS, et al. Genetically elevated C-reactive protein and ischemic vascular disease. *N Engl J Med* 2008;359(18):1897-908. doi: 10.1056/NEJMoa0707402 [published Online First: 2008/10/31]

20. Shah AS, Newby DE, Mills NL. High sensitivity cardiac troponin in patients with chest pain. *Bmj* 2013;347:f4222. doi: 10.1136/bmj.f4222 [published Online First: 2013/07/24]

21. Liu Q, Shepherd BE, Li C, et al. Modeling continuous response variables using ordinal regression. *Statistics in medicine* 2017;36(27):4316-35. doi: 10.1002/sim.7433 [published Online First: 2017/09/06]

22. Clark SJ, Gomez-Olive FX, Houle B, et al. Cardiometabolic disease risk and HIV status in rural South Africa: establishing a baseline. *BMC Public Health* 2015;15:135. doi: 10.1186/s12889-015-1467-1 [published Online First: 2015/04/18]

23. Mugisha JO, Schatz EJ, Randell M, et al. Chronic disease, risk factors and disability in adults aged 50 and above living with and without HIV: findings from the Wellbeing of Older People Study in Uganda. *Glob Health Action* 2016;9:31098. doi: 10.3402/gha.v9.31098 [published Online First: 2016/05/27]

24. Prioreschi A, Munthali RJ, Soepnel L, et al. Incidence and prevalence of type 2 diabetes mellitus with HIV infection in Africa: a systematic review and meta-analysis. *BMJ Open* 2017;7(3):e013953. doi: 10.1136/bmjopen-2016-013953 [published Online First: 2017/04/01]

25. Triant VA, Lee H, Hadigan C, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab* 2007;92(7):2506-12. doi: 10.1210/jc.2006-2190 [published Online First: 2007/04/26]
26. Johnston PI, Wright SW, Orr M, et al. Worldwide relative smoking prevalence among people living with and without HIV. *Aids* 2021;35(6):957-70. doi: 10.1097/QAD.0000000000002815 [published Online First: 2021/01/21]
27. Lawal IO, Ankrah AO, Popoola GO, et al. Arterial inflammation in young patients with human immunodeficiency virus infection: A cross-sectional study using F-18 FDG PET/CT. *J Nucl Cardiol* 2019;26(4):1258-65. doi: 10.1007/s12350-018-1207-x [published Online First: 2018/02/09]
28. Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. *JAMA* 2012;308(4):379-86. doi: 10.1001/jama.2012.6698 [published Online First: 2012/07/24]
29. UNAIDS Data 2020: UNAIDS, 2020.
30. Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. *Arch Intern Med* 2005;165(10):1179-84. doi: 10.1001/archinte.165.10.1179 [published Online First: 2005/05/25]
31. van Zoest RA, Wit FW, Kooij KW, et al. Higher Prevalence of Hypertension in HIV-1-Infected Patients on Combination Antiretroviral Therapy Is Associated With Changes in Body Composition and Prior Stavudine Exposure. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2016;63(2):205-13. doi: 10.1093/cid/ciw285 [published Online First: 2016/05/05]
32. Coetzee L, Bogler L, De Neve JW, et al. HIV, antiretroviral therapy and non-communicable diseases in sub-Saharan Africa: empirical evidence from 44 countries over the period 2000 to 2016. *J Int AIDS Soc* 2019;22(7):e25364. doi: 10.1002/jia2.25364 [published Online First: 2019/07/30]
33. Davis K, Perez-Guzman P, Hoyer A, et al. Association between HIV infection and hypertension: a global systematic review and meta-analysis of cross-sectional studies. *BMC Med* 2021;19(1):105. doi: 10.1186/s12916-021-01978-7 [published Online First: 2021/05/14]
34. Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk: a review for clinicians. *J Am Coll Cardiol* 2009;54(14):1209-27. doi: 10.1016/j.jacc.2009.07.020 [published Online First: 2009/09/26]
35. Gilstrap LG, Wang TJ. Biomarkers and cardiovascular risk assessment for primary prevention: an update. *Clin Chem* 2012;58(1):72-82. doi: 10.1373/clinchem.2011.165712 [published Online First: 2011/11/30]
36. Schuster C, Mayer FJ, Wohlfahrt C, et al. Acute HIV Infection Results in Subclinical Inflammatory Cardiomyopathy. *J Infect Dis* 2018;218(3):466-70. doi: 10.1093/infdis/jiy183 [published Online First: 2018/04/03]
37. Rahman F, Zhang Z, Zhao D, et al. Association of High-Sensitivity Troponin with Cardiac CT Angiography Evidence of Myocardial and Coronary Disease in a Primary

- Prevention Cohort of Men: Results from MACS. *J Appl Lab Med* 2019;4(3):355-69. doi: 10.1373/jalm.2018.028860 [published Online First: 2019/10/30]
38. Fitch KV, DeFilippi C, Christenson R, et al. Subclinical myocyte injury, fibrosis and strain in relationship to coronary plaque in asymptomatic HIV-infected individuals. *Aids* 2016;30(14):2205-14. doi: 10.1097/QAD.0000000000001186 [published Online First: 2016/06/18]
 39. De Luca A, de Gaetano Donati K, Colafigli M, et al. The association of high-sensitivity c-reactive protein and other biomarkers with cardiovascular disease in patients treated for HIV: a nested case-control study. *BMC Infect Dis* 2013;13:414. doi: 10.1186/1471-2334-13-414 [published Online First: 2013/09/06]
 40. Ford ES, Greenwald JH, Richterman AG, et al. Traditional risk factors and D-dimer predict incident cardiovascular disease events in chronic HIV infection. *Aids* 2010;24(10):1509-17. doi: 10.1097/QAD.0b013e32833ad914 [published Online First: 2010/05/28]
 41. Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. *JAMA* 2012;308(4):379—86. doi: 10.1001/jama.2012.6698
 42. Kulkarni M, Bowman E, Gabriel J, et al. Altered Monocyte and Endothelial Cell Adhesion Molecule Expression Is Linked to Vascular Inflammation in Human Immunodeficiency Virus Infection. *Open Forum Infect Dis* 2016;3(4):ofw224. doi: 10.1093/ofid/ofw224 [published Online First: 2016/10/15]
 43. Willeit P, Welsh P, Evans JDW, et al. High-Sensitivity Cardiac Troponin Concentration and Risk of First-Ever Cardiovascular Outcomes in 154,052 Participants. *J Am Coll Cardiol* 2017;70(5):558—68. doi: 10.1016/j.jacc.2017.05.062
 44. Blankenberg S, Salomaa V, Makarova N, et al. Troponin I and cardiovascular risk prediction in the general population: the BiomarCaRE consortium. *Eur Heart J* 2016;37(30):2428-37. doi: 10.1093/eurheartj/ehw172 [published Online First: 2016/05/14]
 45. Saito M, Ishimitsu T, Minami J, et al. Relations of plasma high-sensitivity C-reactive protein to traditional cardiovascular risk factors. *Atherosclerosis* 2003;167(1):73-9. doi: 10.1016/s0021-9150(02)00380-5 [published Online First: 2003/03/06]
 46. Puzianowska-Kuznicka M, Owczarz M, Wiecezowska-Tobis K, et al. Interleukin-6 and C-reactive protein, successful aging, and mortality: the PolSenior study. *Immun Ageing* 2016;13:21. doi: 10.1186/s12979-016-0076-x [published Online First: 2016/06/09]
2. Mensah GA, Roth GA, Sampson UK, et al. Mortality from cardiovascular diseases in sub-Saharan Africa, 1990-2013: a systematic analysis of data from the Global Burden of Disease Study 2013. *Cardiovasc J Afr* 2015;26(2 Suppl 1):S6-10. doi: 10.5830/CVJA-2015-036
 3. Murray CJ, Ortblad KF, Guinovart C, et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014;384(9947):1005-70. doi: 10.1016/S0140-6736(14)60844-8
 4. Palella FJ, Jr., Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient

- Study Investigators. *N Engl J Med* 1998;338(13):853-60. doi: 10.1056/NEJM199803263381301
5. Neuhaus J, Angus B, Kowalska JD, et al. Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. *Aids* 2010;24(5):697-706. doi: 10.1097/QAD.0b013e3283365356
 6. Mocroft A, Reiss P, Gasiorowski J, et al. Serious fatal and nonfatal non-AIDS-defining illnesses in Europe. *Journal of acquired immune deficiency syndromes* 2010;55(2):262-70. doi: 10.1097/QAI.0b013e3181e9be6b [published Online First: 2010/08/12]
 7. Antiretroviral Therapy Cohort C. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2010;50(10):1387-96. doi: 10.1086/652283
 8. Shah ASV, Stelzle D, Lee KK, et al. Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV. *Circulation* 2018;138(11):1100-12. doi: 10.1161/circulationaha.117.033369 [published Online First: 2018/07/04]
 9. Rao SG, Galaviz KI, Gay HC, et al. Factors Associated With Excess Myocardial Infarction Risk in HIV-Infected Adults: A Systematic Review and Meta-analysis. *Journal of acquired immune deficiency syndromes* 2019;81(2):224-30. doi: 10.1097/QAI.0000000000001996 [published Online First: 2019/03/14]
 10. Gaziano TA, Abrahams-Gessel S, Gomez-Olive FX, et al. Cardiometabolic risk in a population of older adults with multiple co-morbidities in rural south africa: the HAALSI (Health and Aging in Africa: longitudinal studies of INDEPTH communities) study. *BMC Public Health* 2017;17(1):206. doi: 10.1186/s12889-017-4117-y [published Online First: 2017/02/19]
 11. Gaziano TA, Bitton A, Anand S, et al. Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr Probl Cardiol* 2010;35(2):72-115. doi: 10.1016/j.cpcardiol.2009.10.002
 12. So-Armah K, Benjamin LA, Bloomfield GS, et al. HIV and cardiovascular disease. *Lancet HIV* 2020;7(4):e279-e93. doi: 10.1016/S2352-3018(20)30036-9 [published Online First: 2020/04/04]
 13. Chung MH, Drake AL, Richardson BA, et al. Impact of prior HAART use on clinical outcomes in a large Kenyan HIV treatment program. *Curr HIV Res* 2009;7(4):441-6. doi: 10.2174/157016209788680552 [published Online First: 2009/07/16]
 14. Performance Evaluation of the Atellica IM High-Sensitivity Troponin I Assay: Siemens Healthcare Diagnostics Inc. · O; 2020 [Available from: <https://www.siemens-healthineers.com/en-uk/laboratory-diagnostics/assays-by-diseases-conditions/cardiac-assays/cardiac-troponin-assays> accessed 19th March 2021.
 15. Healthineers S. High Sensitivity C-Reactive Protein (hsCRP) Assay [Available from: <https://www.siemens-healthineers.com/en-uk/cardiac/cardiac-assays/high-sensitivity-c-reactive-protein> accessed 19th March 2021.
 16. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association

- Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):e13-e115. doi: 10.1161/HYP.0000000000000065 [published Online First: 2017/11/15]
17. Roth GA, Fihn SD, Mokdad AH, et al. High total serum cholesterol, medication coverage and therapeutic control: an analysis of national health examination survey data from eight countries. *Bull World Health Organ* 2011;89(2):92-101. doi: 10.2471/BLT.10.079947 [published Online First: 2011/02/25]
18. Kramer CK, Araneta MR, Barrett-Connor E. A1C and diabetes diagnosis: The Rancho Bernardo Study. *Diabetes Care* 2010;33(1):101-3. doi: 10.2337/dc09-1366 [published Online First: 2009/10/20]
19. Zacho J, Tybjaerg-Hansen A, Jensen JS, et al. Genetically elevated C-reactive protein and ischemic vascular disease. *N Engl J Med* 2008;359(18):1897-908. doi: 10.1056/NEJMoa0707402 [published Online First: 2008/10/31]
20. Shah AS, Newby DE, Mills NL. High sensitivity cardiac troponin in patients with chest pain. *Bmj* 2013;347:f4222. doi: 10.1136/bmj.f4222 [published Online First: 2013/07/24]
21. Liu Q, Shepherd BE, Li C, et al. Modeling continuous response variables using ordinal regression. *Statistics in medicine* 2017;36(27):4316-35. doi: 10.1002/sim.7433 [published Online First: 2017/09/06]
22. Clark SJ, Gomez-Olive FX, Houle B, et al. Cardiometabolic disease risk and HIV status in rural South Africa: establishing a baseline. *BMC Public Health* 2015;15:135. doi: 10.1186/s12889-015-1467-1 [published Online First: 2015/04/18]
23. Mugisha JO, Schatz EJ, Randell M, et al. Chronic disease, risk factors and disability in adults aged 50 and above living with and without HIV: findings from the Wellbeing of Older People Study in Uganda. *Glob Health Action* 2016;9:31098. doi: 10.3402/gha.v9.31098 [published Online First: 2016/05/27]
24. Prioreschi A, Munthali RJ, Soepnel L, et al. Incidence and prevalence of type 2 diabetes mellitus with HIV infection in Africa: a systematic review and meta-analysis. *BMJ Open* 2017;7(3):e013953. doi: 10.1136/bmjopen-2016-013953 [published Online First: 2017/04/01]
25. Triant VA, Lee H, Hadigan C, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab* 2007;92(7):2506-12. doi: 10.1210/jc.2006-2190 [published Online First: 2007/04/26]
26. Johnston PI, Wright SW, Orr M, et al. Worldwide relative smoking prevalence among people living with and without HIV. *Aids* 2021;35(6):957-70. doi: 10.1097/QAD.0000000000002815 [published Online First: 2021/01/21]
27. Lawal IO, Ankrah AO, Popoola GO, et al. Arterial inflammation in young patients with human immunodeficiency virus infection: A cross-sectional study using F-18 FDG PET/CT. *J Nucl Cardiol* 2019;26(4):1258-65. doi: 10.1007/s12350-018-1207-x [published Online First: 2018/02/09]
28. Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. *JAMA* 2012;308(4):379-86. doi: 10.1001/jama.2012.6698 [published Online First: 2012/07/24]
29. UNAIDS Data 2020: UNAIDS, 2020.

30. Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. *Arch Intern Med* 2005;165(10):1179-84. doi: 10.1001/archinte.165.10.1179 [published Online First: 2005/05/25]
31. van Zoest RA, Wit FW, Kooij KW, et al. Higher Prevalence of Hypertension in HIV-1-Infected Patients on Combination Antiretroviral Therapy Is Associated With Changes in Body Composition and Prior Stavudine Exposure. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2016;63(2):205-13. doi: 10.1093/cid/ciw285 [published Online First: 2016/05/05]
32. Coetzee L, Bogler L, De Neve JW, et al. HIV, antiretroviral therapy and non-communicable diseases in sub-Saharan Africa: empirical evidence from 44 countries over the period 2000 to 2016. *J Int AIDS Soc* 2019;22(7):e25364. doi: 10.1002/jia2.25364 [published Online First: 2019/07/30]
33. Davis K, Perez-Guzman P, Hoyer A, et al. Association between HIV infection and hypertension: a global systematic review and meta-analysis of cross-sectional studies. *BMC Med* 2021;19(1):105. doi: 10.1186/s12916-021-01978-7 [published Online First: 2021/05/14]
34. Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk: a review for clinicians. *J Am Coll Cardiol* 2009;54(14):1209-27. doi: 10.1016/j.jacc.2009.07.020 [published Online First: 2009/09/26]
35. Gilstrap LG, Wang TJ. Biomarkers and cardiovascular risk assessment for primary prevention: an update. *Clin Chem* 2012;58(1):72-82. doi: 10.1373/clinchem.2011.165712 [published Online First: 2011/11/30]
36. Schuster C, Mayer FJ, Wohlfahrt C, et al. Acute HIV Infection Results in Subclinical Inflammatory Cardiomyopathy. *J Infect Dis* 2018;218(3):466-70. doi: 10.1093/infdis/jiy183 [published Online First: 2018/04/03]
37. Rahman F, Zhang Z, Zhao D, et al. Association of High-Sensitivity Troponin with Cardiac CT Angiography Evidence of Myocardial and Coronary Disease in a Primary Prevention Cohort of Men: Results from MACS. *J Appl Lab Med* 2019;4(3):355-69. doi: 10.1373/jalm.2018.028860 [published Online First: 2019/10/30]
38. Fitch KV, DeFilippi C, Christenson R, et al. Subclinical myocyte injury, fibrosis and strain in relationship to coronary plaque in asymptomatic HIV-infected individuals. *Aids* 2016;30(14):2205-14. doi: 10.1097/QAD.0000000000001186 [published Online First: 2016/06/18]
39. De Luca A, de Gaetano Donati K, Colafigli M, et al. The association of high-sensitivity c-reactive protein and other biomarkers with cardiovascular disease in patients treated for HIV: a nested case-control study. *BMC Infect Dis* 2013;13:414. doi: 10.1186/1471-2334-13-414 [published Online First: 2013/09/06]
40. Ford ES, Greenwald JH, Richterman AG, et al. Traditional risk factors and D-dimer predict incident cardiovascular disease events in chronic HIV infection. *Aids* 2010;24(10):1509-17. doi: 10.1097/QAD.0b013e32833ad914 [published Online First: 2010/05/28]
41. Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. *JAMA* 2012;308(4):379—86. doi: 10.1001/jama.2012.6698

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

42. Kulkarni M, Bowman E, Gabriel J, et al. Altered Monocyte and Endothelial Cell Adhesion Molecule Expression Is Linked to Vascular Inflammation in Human Immunodeficiency Virus Infection. *Open Forum Infect Dis* 2016;3(4):ofw224. doi: 10.1093/ofid/ofw224 [published Online First: 2016/10/15]

43. Willeit P, Welsh P, Evans JDW, et al. High-Sensitivity Cardiac Troponin Concentration and Risk of First-Ever Cardiovascular Outcomes in 154,052 Participants. *J Am Coll Cardiol* 2017;70(5):558—68. doi: 10.1016/j.jacc.2017.05.062

44. Blankenberg S, Salomaa V, Makarova N, et al. Troponin I and cardiovascular risk prediction in the general population: the BiomarCaRE consortium. *Eur Heart J* 2016;37(30):2428-37. doi: 10.1093/eurheartj/ehw172 [published Online First: 2016/05/14]

45. Saito M, Ishimitsu T, Minami J, et al. Relations of plasma high-sensitivity C-reactive protein to traditional cardiovascular risk factors. *Atherosclerosis* 2003;167(1):73-9. doi: 10.1016/s0021-9150(02)00380-5 [published Online First: 2003/03/06]

46. Puzianowska-Kuznicka M, Owczarz M, Wieczorowska-Tobis K, et al. Interleukin-6 and C-reactive protein, successful aging, and mortality: the PolSenior study. *Immun Ageing* 2016;13:21. doi: 10.1186/s12979-016-0076-x [published Online First: 2016/06/09]

SUPPLEMENT

Cardiovascular risk factors and markers of myocardial injury and inflammation in people living with HIV in Kenya

Hassan A Ahmed, MD¹; Mohammed Jeilan, MD¹; Isaiah G Akuku, MSc²; Kuan Ken Lee, MD³; Shirjel R Alam, MD⁴; Pablo Perel, MD⁴; Jasmit Shah, PhD¹; Mohammed K. Ali, MD;⁵ Sherry Eskander, MD;⁶ Michael H Chung, MD MPH^{5*} and Anoop S V Shah, MD^{4,7*}

*Contributed equally

¹ Department of Medicine, Aga Khan University

² Institute of Tropical and Infectious Diseases, University of Nairobi

³ BHF Centre for Cardiovascular Sciences, University of Edinburgh

⁴ Department of Non-communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

⁵ Emory University, Atlanta, Georgia, USA

⁶ Coptic Hospital, Nairobi, Kenya

⁷ Imperial College Hospital NHS Trust, London, UK

Correspondence and requests for reprints:

Dr Anoop Shah,
Room 249,
Department of Non-communicable Disease Epidemiology ,
London School of Hygiene and Tropical Medicine,
Keppel Street,
London,
UK
WC1E 7HT

Mobile: +(44) 7766 544 156

E-mail: Anoop.Shah@lshtm.ac.uk

Abstract: 299 (300)

Word count: 2,712

Table and Figures: 4

Figure S1: Study flow diagram

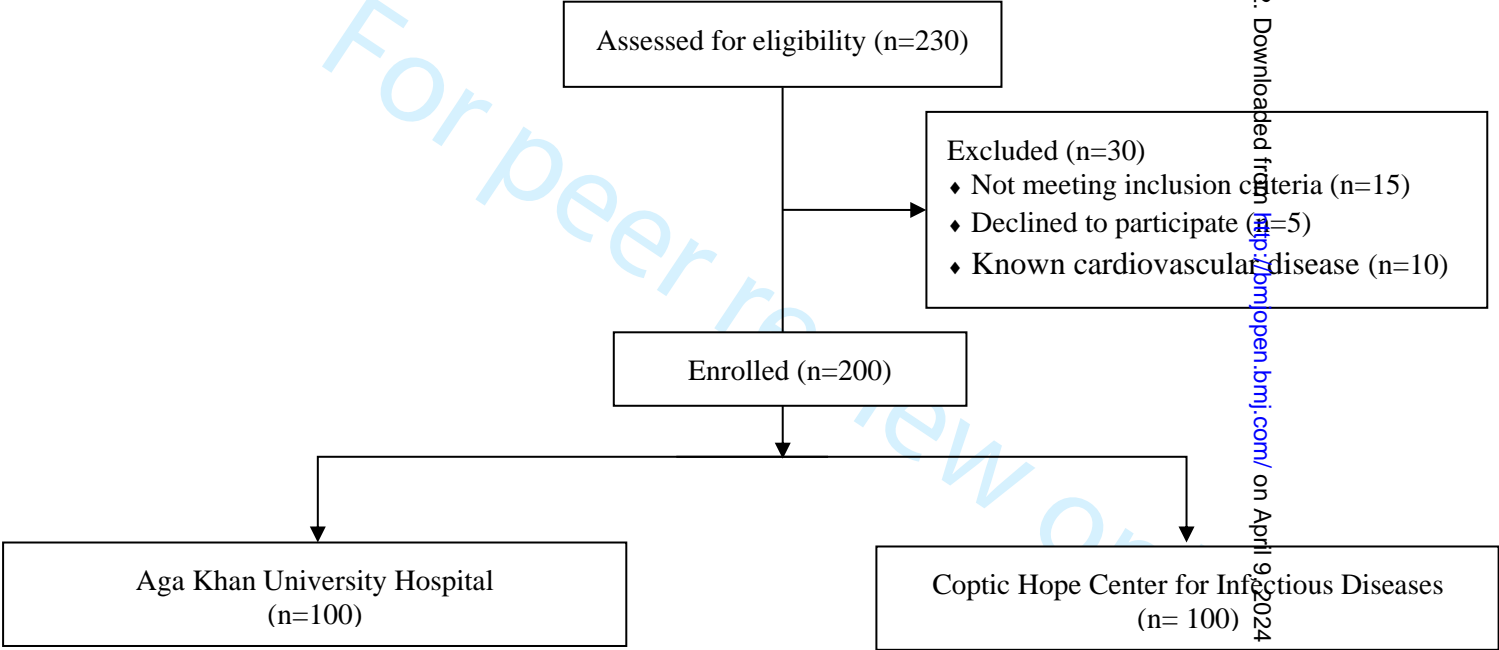


Table S1: Baseline demographics and clinical characteristics by clinical site¹

Characteristics	All patients (n=200)	Site		p-value ²
		Aga Khan University Hospital (n= 100)	Coptic Hope Center for Infectious Diseases (n = 100)	
Age, median (Q1, Q3), years	45.5 (37.7, 52.6)	41.9 (35.3, 49.4)	48.0 (40.5, 54.3)	<0.001
Gender				
Male, %	79/200 (39.5)	46/100 (46.0)	33/100 (33.0)	0.083
Female, %	121/200 (60.5)	54/100 (54.0)	67/100 (67.0)	
Years of education, median (Q1, Q3)	14.0 (12.0, 16.0)	16.0 (13.0, 16.0)	13.5 (10.8, 16.0)	<0.001
Highest level of education attained				
Primary/none/don't know, %	30/200 (15.0)	5/100 (5.0)	25/100 (25.0)	<0.001
Secondary, %	45/200 (22.5)	21/100 (21.0)	24/100 (24.0)	
Higher Education/University, %	125/200 (62.5)	74/100 (74.0)	51/100 (51.0)	
Marital status				
Married (monogamous/polygamous), %	128/200 (64.0)	70/100 (70.0)	58/100 (58.0)	0.119
Single	26/200 (13.0)	13/100 (13.0)	13/100 (13.0)	
Separated/widowed/divorced/refused/cohabiting/others, %	46/200 (23.0)	17/100 (17.0)	29/100 (29.0)	
Employment status				
Salaried Job or self-employed, %	180/200 (90.0)	91/100 (91.0)	89/100 (89.0)	0.117
Unemployed/housewife/retiree, %	13/200 (6.5)	8/100 (8.0)	5/100 (5.0)	
Casual labourer, %	7/200 (3.5)	1/100 (1.0)	6/100 (6.0)	
Household income per month				
< 15,001 KES ³ , %	34/198 (17.2)	6/100 (6.0)	28/98 (28.6)	<0.001
> 15,001 KES, %	164/198 (82.8)	94/100 (94.0)	70/98 (71.4)	
Cardiovascular risk factors				
Smoking				
Current smoker, %	5/200 (2.5)	3/100 (3.0)	2/100 (2.0)	1.000
Ex-smoker, %	44/200 (22.0)	22/100 (22.0)	22/100 (22.0)	
Never smoker, %	151/200 (75.5)	75/100 (75.0)	76/100 (76.0)	
Diabetes, %	7/200 (3.5)	5/100 (5.0)	2/100 (2.0)	0.444
Self-reported hypertension ⁴ , %	44/200 (22.0)	22/100 (22.0)	22/100 (22.0)	1.000
Cumulative hypertension ⁵ , %	60/200 (30.0)	25/100 (25.0)	35/100 (35.0)	0.165
Dyslipidemia, %	1/197 (0.5)	0/100 (0.0)	1/97 (1.0)	0.288
Chronic kidney disease, %	2/200 (1.0)	2/100 (2.0)	0/100 (0.0)	0.036
HIV				
Time since (months) HIV ⁶ infection, Median (Q1, Q3)	143.0 (59.0, 191.0)	106.0 (47.0, 191.0)	159.0 (95.0, 191.0)	0.037
Currently on ART ⁷ , %	195/200 (97.5)	95/100 (95.0)	100/100 (100.0)	0.059
Past medical history				
Malaria, %	21/200 (10.5)	0/100 (0.0)	21/100 (21.0)	<0.001
Tuberculosis, %	12/200 (6.0)	4/100 (4.0)	8/100 (8.0)	0.373
Clinical characteristics				

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the variable.

² p-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon test or Student's t-test for continuous variables, two-sided; bold p-values indicate statistical significance (p<0.05).

³ KES, Kenya shillings currency code

⁴ Self-reported physician-diagnosed hypertension.

⁵ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

⁶ HIV, human immunodeficiency virus,

⁷ ART, antiretroviral therapy.

Table S2 Biochemistry and haematology by clinical site¹

Characteristics	All patients (n=200)	Site ²		p-value ³
		Aga Khan University Hospital (n=100)	Coptic Hope Center for Infectious Diseases (n=100)	
Creatinine, median (Q1, Q3), n=197	85.0 (73.0, 101.0)	89.0 (74.0, 106.0)	83.0 (71.8, 98.2)	0.102
Urea, median (Q1, Q3), n=196	3.7 (3.1, 4.6)	3.8 (3.1, 5.0)	3.5 (3.0, 4.2)	0.011
Hemoglobin, mean (SD), n=98*	—	14.01 (2.06)	—	—
Glucose, median (Q1, Q3), n=197	4.8 (4.4, 5.3)	5.2 (4.9, 5.6)	4.5 (4.1, 4.6)	<0.001
HbA1c, median (Q1, Q3), n=98*	5.6 (5.4, 5.9)	5.6 (5.4, 5.9)	—	—
HbA1c <5.7, %	—	50/98 (51.0)	—	—
HbA1c 5.7 – 6.4, %	—	45/98 (45.9)	—	
HbA1c >= 6.5, %	—	3/98 (3.1)	—	
Lipid profiles				
Total cholesterol, median (Q1, Q3), n=196	4.6 (3.9, 5.1)	4.6 (3.8, 5.3)	4.4 (4.0, 5.1)	0.665
TC < 4.7, %	107/196 (54.6)	52 (53.1)	55 (56.1)	0.955
TC 4.8 – 5.1, %	22/196 (11.2)	11 (11.2)	11 (11.2)	
TC 5.2 – 6.1, %	30/196 (15.3)	15 (15.3)	15 (15.3)	
TC >= 6.2, %	37/196 (18.9)	20 (20.4)	17 (17.3)	
LDL, median (Q1, Q3), n=196	3.0 (2.3, 3.6)	3.1 (2.3, 3.6)	3.0 (2.4, 3.5)	0.858
LDL < 2.6, %	75/196 (38.3)	36 (36.7)	39 (39.8)	0.978
LDL 2.6 – 3.3, %	53/196 (27.0)	27 (27.6)	26 (26.5)	
LDL 3.4 – 4.1, %	41/196 (20.9)	21 (21.4)	20 (20.4)	
LDL >= 4.2, %	27/196 (13.8)	14 (14.3)	13 (13.3)	
HDL, median (Q1, Q3), n=196	1.2 (1.0, 1.5)	1.2 (1.0, 1.4)	1.2 (1.0, 1.5)	0.457
Triglycerides, median (Q1, Q3), n=196	1.4 (0.9, 2.0)	1.5 (1.0, 2.2)	1.3 (0.9, 1.9)	0.196
Trig < 1.7, %	123/196 (62.8)	56 (57.1)	67 (68.4)	0.257
Trig 1.7 – 2.2, %	32/196 (16.3)	19 (19.4)	13 (13.3)	
Trig >2.3, %	41/196 (20.9)	23 (23.5)	18 (18.4)	
Cardiac and inflammatory biomarkers				
High sensitivity troponin I, median (Q1, Q3), n=169	2.5 (2.5, 3.0)	2.5 (2.5, 3.0)	2.5 (2.5, 3.2)	0.654
hscTnI < 2.5 ng/L, %	109/169 (64.5)	46 (66.7)	63 (63.0)	0.848
hscTnI 2.5 – 45 ng/L, %	59/169 (34.9)	23 (33.3)	36 (36.0)	
hscTnI >= 45 ng/L, %	1/169 (0.6)	0 (0.0)	1 (1.0)	
High-sensitivity CRP, median (Q1, Q3), n=198	2.0 (0.8, 4.2)	2.4 (1.1, 4.4)	1.6 (0.7, 4.2)	0.112
hsCRP < 1mg/L, %	58/198 (29.3)	23 (23.5)	35 (35.0)	0.197
hsCRP 1 - 3 mg/L, %	65/198 (32.8)	41 (41.8)	34 (34.0)	
hsCRP >3 mg/L, %	75/198 (37.9)	34 (34.7)	31 (31.0)	

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the laboratory marker.

² *Data for Hemoglobin and hemoglobin A1c (HbA1c) was available for Aga Khan University Hospital only.

³ p-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon test for continuous variables, two-sided; bold p-values indicate statistical significance ($p < 0.05$).

Table S3: Cardiovascular risk factors, markers of myocardial injury and inflammation by Framingham cardiovascular risk category

Variable	Framingham risk score classification (FRS lipid)			<i>p</i> -value for trend ¹
	Low	Intermediate	High	Two-sided
Overall				
All patients (%)	166 (83.0)	23 (11.5)	11 (5.5)	—
Male	58 (34.9)	14 (60.9)	7 (63.6)	0.006
Female	108 (65.1)	9 (39.1)	4 (36.4)	
Smoking				
Current smoker, %	5/166 (3.0%)	0/23 (0.0)	0/11 (0.0)	0.306
Ex-smoker, %	33/166 (19.9)	6/23 (26.1)	5/11 (45.5)	
Never smoker, %	128/166 (77.1)	17/23 (73.9)	6/11 (54.5)	
Diabetes, %	3/166 (1.8)	2/23 (8.7)	2/11 (18.2)	0.999
Hypertension ² , %	36/166 (21.7)	14/23 (60.9)	10/11 (90.9)	<0.001
Hyperlipidemia, %	0/164 (0.0)	1/22 (4.5)	0/11 (0.0)	0.145
Lipid profiles				
Total cholesterol, median (Q1, Q3)	4.5 (3.8, 5.0)	4.9 (4.3, 5.4)	5.1 (4.4, 6.4)	0.001
TC < 4.7, %	93/162 (57.4)	10/23 (43.5)	4/11 (36.4)	0.007
TC 4.8 – 5.1, %	20/162 (12.3)	2/23 (8.7)	0/11 (0.0)	
TC 5.2 – 6.1, %	23/162 (14.2)	6/23 (26.1)	1/11 (9.1)	
TC ≥ 6.2, %	26/162 (16.0)	5/23 (21.7)	6/23 (54.5)	
LDL, median (Q1, Q3)	3.0 (2.3, 3.5)	3.3 (2.4, 3.8)	3.6 (2.9, 4.5)	0.017
LDL < 2.6, %	65/162 (40.1)	8/23 (34.8)	2/11 (18.2)	0.016
LDL 2.6 – 3.3, %	47/162 (29.0)	4/23 (17.4)	2/11 (18.2)	
LDL 3.4 – 4.1, %	30/162 (18.5)	8/23 (34.8)	3/11 (27.3)	
LDL ≥ 4.2, %	12/162 (12.3)	3/23 (13.0)	4/11 (36.4)	
HDL, median (Q1, Q3)	1.2 (1.0, 1.5)	1.1 (0.9, 1.3)	1.0 (0.9, 1.2)	0.043
Triglycerides, median (Q1, Q3)	1.3 (0.9, 1.9)	1.9 (1.2, 3.1)	2.9 (1.8, 3.4)	<0.001
Trig < 1.7	110/162 (67.9)	11s/23 (47.8)	2/11 (18.2)	<0.001
Trig 1.7 – 2.2	26/162 (16.0)	3/23 (13.0)	3/11 (27.3)	
Trig >2.3	26/162 (16.0)	9/23 (39.1)	6/11 (54.5)	
Cardiac and inflammatory biomarkers				
High sensitivity troponin I, median (Q1, Q3)	2.5 (2.5, 2.7)	3.3 (2.5, 4.7)	3.3 (2.5, 7.1)	<0.001
hscTnI < 2.5 ng/L, %	100/140 (71.4)	6/18 (33.3)	3/11 (27.3)	<0.001
hscTnI 2.5 – 45 ng/L	39/140 (27.9)	12/18 (66.7)	8/11 (72.7)	
hscTnI ≥ 45 ng/L	1/140 (0.7)	0/18 (0.0)	0/11 (0.0)	
High-sensitivity CRP, median (Q1, Q3)	1.9 (0.8, 4.1)	2.9 (1.1, 5.3)	2.4 (0.9, 4.2)	0.283
hsCRP < 1mg/L	49/164 (29.9)	6/23 (26.1)	3/11 (27.3)	0.854
hsCRP 1 – 3 mg/L	54/164 (32.9)	6/23 (26.1)	5/11 (45.5)	
hsCRP >3 mg/L	61/164 (37.2)	11/23 (47.8)	3/11 (27.3)	
Creatinine, median (Q1, Q3)	83.0 (72.0, 100.5)	97.0 (87.0, 106.5)	91.0 (79.0, 104.5)	0.009

¹ *p*-values for trend were calculated using Jonckheere-Terpstra for continuous variables and Cochran-Armitage, or Cochran-Mantel-Haenszel tests, as appropriate, for categorical variables.

² Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	Not provided as proof-of-concept study
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	6-7
		(c) Explain how missing data were addressed	7
		(d) If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	supplement

		(c) Consider use of a flow diagram	supplement
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
Outcome data	15*	Report numbers of outcome events or summary measures	Table 1 and 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 4
		(b) Report category boundaries when continuous variables were categorized	Tables 1 - 4
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplement
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Cardiovascular risk factors and markers of myocardial injury and inflammation in people living with HIV in Nairobi, Kenya: a pilot cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-062352.R1
Article Type:	Original research
Date Submitted by the Author:	10-May-2022
Complete List of Authors:	Ahmed, Hassan; The Aga Khan University Hospital Nairobi Mohamed, Jeilan; Aga Khan University - Kenya, Medicine Akuku, Isaiah G; University of Nairobi, Institute of Tropical and Infectious Diseases Lee, K; University of Edinburgh, BHF Centre for Cardiovascular Science Alam, Shirjel R; London School of Hygiene & Tropical Medicine, Department of Non-communicable Disease Epidemiology Perel, Pablo; London School of Hygiene & Tropical Medicine, EPH Shah, Jasmit; Aga Khan University Hospital, Internal Medicine Ali, Mohammed; Emory University, Hubert Department of Global Health Eskander, Sherry; Coptic Hospital and Coptic Hope Center for Infectious Diseases Chung, Michael H; Emory University Shah, Anoop ; London School of Hygiene and Tropical Medicine Department of Non-communicable Disease Epidemiology, Department of Non-Communicable Disease Epidemiology; Imperial College Healthcare NHS Trust
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	HIV/AIDS, Global health, Epidemiology
Keywords:	Adult cardiology < CARDIOLOGY, EPIDEMIOLOGY, HIV & AIDS < INFECTIOUS DISEASES

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Cardiovascular risk factors and markers of myocardial injury and inflammation in people living with HIV in Nairobi, Kenya: a pilot cross-sectional study

Hassan A Ahmed, MD¹; Jeilan Mohammed, MD¹; Isaiah G Akuku, MSc²; Kuan Ken Lee, MD³; Shirjel R Alam, MD⁴; Pablo Perel, MD⁴; Jasmit Shah, PhD¹; Mohammed K. Ali, MD⁵; Sherry Eskander, MD⁶; Michael H Chung, MD^{5*} and Anoop S V Shah, MD^{4,7*}

*Contributed equally

¹ Department of Medicine, Aga Khan University

² Institute of Tropical and Infectious Diseases, University of Nairobi

³ BHF Centre for Cardiovascular Sciences, University of Edinburgh

⁴ Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

⁵ Emory University, Atlanta, Georgia, USA

⁶ Coptic Mission Hospital, Nairobi, Kenya, UK

⁷ Imperial College Hospital NHS Trust, London, UK

Correspondence to:

Dr Anoop Shah,

Room 249,

Department of Non-communicable Disease Epidemiology ,

London School of Hygiene and Tropical Medicine,

Keppel Street,

London,

UK

WC1E 7HT

Mobile: +(44) 7766 544 156

E-mail: Anoop.Shah@lshtm.ac.uk

Abstract: 291

Table: 4

Word count: 2901 (excluding references and tables)

Abstract

Objectives: To determine the prevalence of cardiovascular disease (CVD) risk factors and explore associations with high-sensitivity cardiac troponin (hscTnI) and high-sensitivity C-reactive protein (hsCRP) in people living with HIV (PLHIV) in Kenya.

Design: Pilot cross-sectional study.

Setting: Data were collected from community HIV clinics across two sites in Nairobi, Kenya from July 2019 to May 2020.

Participants: Convenience sample of 200 PLHIV (≥ 30 years with no prior history of CVD).

Outcome measures: Prevalence of cardiovascular risk factors and its association with hscTnI and hsCRP levels.

Results: Across 200 PLHIV (median age 46 years, IQR 38-53; 61% females), the prevalence of hypercholesterolemia (total cholesterol >6.1 mmol/L) and hypertension were 19% (n=30/199) and 30% (n=60/200), respectively. Smoking and diabetes prevalence was 3% (n=5/200) and 4% (n=7/200). HscTnI was below the limit of quantification (<2.5 ng/L) in 65% (n=109/169). 38% (n=75/198), 33% (n=65/198) and 29% (n=58/198) had high (>3 mg/L), intermediate (1-3mg/L) and low (<1 mg/L) hsCRP levels, respectively. Framingham laboratory-based risk scores classified 83% of PLHIV at low risk with 12% and 5% at intermediate and high risk. Older age (adjusted odds ratio [aOR] per year increase 1.05, 95% confidence interval [CI] 1.01–1.08) and systolic blood pressure (140–159mmHg [aOR 2.96; 95%CI 1.09–7.90] and >160 mmHg [aOR 4.68, 95%CI 1.55–14] compared to <140 mmHg) were associated with hscTnI levels. No associations were observed between hsCRP and CVD risk factors.

Conclusion: The majority of PLHIV - using traditional risk estimation systems - have a low estimated CVD risk likely reflecting a younger aged population predominantly consisting of women. Hypertension and hypercholesterolemia were common whilst smoking and diabetes rates remained low. Whilst hscTnI values were associated with increasing age and raised blood pressure, no associations between hsCRP levels and traditional cardiovascular risk factors were observed.

Strengths and limitations of this study

- Involvement of people living with HIV from a low- and middle-income settings and from distinct socioeconomic backgrounds.

- Assessment of relatively novel biochemical markers of cardiovascular risk alongside more traditional cardiovascular risk factors.
- Due to the cross-sectional design, we were unable to evaluate the associations between novel biochemical markers and future cardiovascular events.
- The study population was from an urban setting, so generalizability to rural settings is unknown.
- There was no age- and sex-matched uninfected control group.

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

More than 35 million people are infected with the human immunodeficiency virus (HIV) with two-thirds being resident in sub-Saharan Africa.¹ Although the global incidence for HIV has stabilised, the wide availability of combined antiretroviral therapy (ART) has dramatically improved survival, resulting in a steady increase in prevalence over the last two decades.^{2 3} This improvement in survival has been primarily attributed to a reduction in opportunistic infections especially in low- and lower-middle-income nations. Conversely, mortality due to non-communicable illnesses especially cardiovascular disease has been rising and now account for the majority of deaths in people living with HIV (PLHIV).^{1 4-7}

People living with HIV - based on studies in high-income countries - have a higher risk of cardiovascular disease.^{8 9} Despite this higher risk, previous studies have indicated that PLHIV in sub-Saharan Africa have a lower prevalence of traditional cardiovascular risk factors in comparison to uninfected individuals.^{8,10} Strategies to risk stratify and mitigate cardiovascular disease in this population is now urgently required but is challenging in resource limited nations¹¹ and it remains unclear on optimal approaches with recommendations differing across regions globally.¹²

In this cross-sectional pilot study of PLHIV in Kenya, we evaluate the prevalence of traditional cardiovascular risk factors and the distribution of estimated cardiovascular risk using traditional risk scores. We further explore the distribution of markers of myocardial injury and inflammation in this population. Our additional objectives are to evaluate the logistic feasibility, including recruitment rates, for a full-scale study investigating mechanisms in HIV-associated cardiovascular disease.

Methods

Study setting and population

This was a pilot, prospective, cross-sectional study of PLHIV ≥ 30 years in Nairobi, Kenya. Population sample size was determined based on the fixed recruitment period from July 2019 to May 2020. Patients were recruited based on convenient sampling and invited to participate as long as they received care at the two clinical sites (Aga Khan University Hospital and Coptic Hope Center for Infectious Diseases) where the researchers and their research teams were based. Aga Khan University Hospital is a fee-for-service tertiary care centre generally serving a more affluent population whilst the Coptic Hope Center for Infectious Diseases is a Centre of Disease Control President's Emergency Plan For AIDS Relief funded institution to provide free antiretroviral therapy to Kenyans who are unable to afford HIV care and treatment.¹³ Participants with known cardiovascular disease (previous myocardial infarction or stroke) were excluded.

Study procedures and blood sampling

All participants completed a standardized questionnaire to capture data on demographics, including self-reported cardiovascular risk factors, past medical history, current medication and HIV factors including time since diagnosis. Data were captured on handheld devices electronically. Anthropometric and hemodynamic data including office blood pressure, height, weight and heart rate were captured.

Blood sampling

Blood samples were obtained from participants through standard venepuncture. Basic clinical chemistry and haematology was performed. This included assessment of renal function, glycaemic control, non-fasted lipid profiles, high-sensitivity cardiac troponin I (hs-cTnI) and

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

high-sensitivity C-reactive protein (hsCRP). Given laboratory constraints, HbA1c and haematology was only measured in the Aga Khan University Hopsital population.

High-sensitivity troponin I: The Siemens Atellica IM High Sensitivity Troponin I assay (Siemens Healthineers) is a three-site sandwich immunoassay with a limit of detection of 1.6 ng/L and limit of quantification of 2.5 ng/L. The upper reference limit 99th centile was determined in 2007 samples from healthy individuals as 34 ng/L in women, and 53 ng/L in men, with a single threshold of 45 ng/L. In the reference range population, 75% of patients had values greater than the limit of detection. The level where the inter-assay coefficient of variation is <10% is 6 ng/L.¹⁴

High-sensitivity C-reactive protein: The Siemens Atellica High Sensitivity C-Reactive protein assay was used to measure hsCRP levels in stored serum. The assay range is from 0.1 to 50 mg/L with a coefficient of variation of 6.8% at 1.16 mg/L.¹⁵

Study definitions

Traditional cardiovascular risk factors were defined as those routinely measured in cardiovascular risk estimation systems and include basic anthropometry, diabetes and smoking status, lipid profile, and arterial blood pressure assessment. Body mass index (BMI) was calculated from measured height and weight and classified as normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (equal to or greater than 30 kg/m²). Current or past smoking history was self-reported by participants. Hypertension was defined as self-reported hypertension or measured SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.¹⁶ Dyslipidemia was defined as a self-reported history. Hypercholesterolaemia was defined as a total cholesterol ≥ 6.21 mmol/L. A high low-density lipoprotein (LDL)] was defined as levels > 4.1 mmol/L.¹⁷ Diabetes mellitus was

defined as self-reported type 1 or 2 diabetes mellitus. Patients, in whom HbA1c was measured, were classified as those with high ($\geq 6.5\%$), intermediate (5.7–6.4%) and low levels ($< 5.7\%$).¹⁸ The hsCRP was categorized as low (< 1 mg/L), intermediate (1–3 mg/L), or high (> 3 mg/L).¹⁹ High-sensitivity cardiac troponin levels were categorised as below the limit of quantification (2.5 ng/L), above the limit of quantification but below the 99th centile upper reference limit and above the 99th centile upper reference limit (45 ng/L).²⁰

Statistical analysis

Baseline demographics, clinical and lifestyle variables, laboratory biomarkers including markers of myocardial injury, inflammation, glycaemic control, and lipid profiles were summarised overall and stratified by gender. Continuous variables were reported as median and interquartile range, while the categorical variables were summarized as frequencies and percentages. Statistical differences between groups were assessed using Pearson's chi-square test or Fisher's exact test and unpaired two-samples Wilcoxon test or Student's t-test as indicated. Sex-specific framingham laboratory-based risk equations were used to quantify the estimated 10-year CVD risk for each study participant. The equation used age, gender, smoking status, use of anti-hypertensive medications, prevalent diabetes, and systolic blood pressure. The risk estimations were computed according to algorithms accessed at <https://framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/>. Predicted cardiovascular event risk percentage over the next 10 years was classified as low ($< 10\%$), intermediate (10–20%), and high risk ($> 20\%$).

In further analysis, we evaluated the relationship between baseline markers of myocardial injury and inflammation and traditional cardiovascular risk factors. We calculated the 25th and 75th percentiles of observed hscTnI data and ordinally scaled it as < 2.50 ng/L (undetectable),

2.50-3.02 ng/L, 3.02-7.12 ng/L, ≥ 7.12 ng/L given the skewness of the variable.²¹ Three multivariable ordinal (Cumulative logit) models and linear regression models with hscTnI and hsCRP as the response variable, respectively, were fitted. The independent variables were age, sex and cardiovascular risk factors. Model I adjusted for age per year increase, sex, study site as a surrogate for socioeconomic status and creatinine. Model II additionally adjusted for hypertension, diabetes, and smoking status (never smoker, former smoker, current smoker). Model III adjusted for variables in Model I plus systolic blood pressure (SBP < 130 mmHg, SBP 130 -139 mmHg, SBP 140-159 mmHg, SBP >160 mmHg) and hsCRP or hscTnI. Models were constructed on complete cases with no imputation. All analysis was carried out in R (Version 4.1.2).

Ethics statement

Patients were enrolled only after providing written informed consent prior to participation. After receiving site approval from the Coptic Hope Center for Infectious Diseases in Nairobi, we obtained ethics approval for data analysis from The Aga Khan University Hospital, Nairobi Research Ethics Committee (approval letter reference: 2018/REC-84). The research was carried out in accordance with the Helsinki Declaration's principles.

Patient and public involvement

No patient involved

Results

Two hundred patients (median age 46 years [IQR 38 to 53 years], 61% females) were recruited in this cross-sectional study consisting (*Figure S1*). Prevalence of smoking was 2.5% across the cohort and higher in males compared to females. Hypertension was the most common cardiovascular risk factor at 30% with rates higher in males (33%) compared to females (28%). Self-reported dyslipidemia was low at 0.5% but much higher when classified according to a total cholesterol concentration >6.1 mmol/L (19%). The prevalence of elevated LDL ≥ 4.2 mmol/L was 14%. Seventeen percent of the population had a systolic blood pressure ≥ 140 mmHg and 15% of the population had a diastolic blood pressure ≥ 90 mmHg. Obesity rates were high with 29% considered obese and 36% overweight. Obesity rates were higher in women at 34% compared to males (22%). Past history of malaria and tuberculosis remained high at 32% and 18% respectively. Over 90% of participants were receiving antiretroviral therapy and median duration of diagnosis to study recruitment was 12 years (*Table 1 and Table 2*). Given differences in the population served at Aga Khan University and Coptic hospitals, we observed important differences in baseline characteristics. Patient treated at Coptic hospital has lower income levels and higher rates of elevated blood pressure (*Table S1*).

Stored serum was available to measure hscTnI concentrations in 169 of the 200 participants. Despite using a hscTnI assay, the majority had concentrations below the limit of quantification at <2.5 ng/L ($n=109/169$, 65%). Fifty-nine patients ($n = 59/169$, 35%) had concentration levels above the limit of quantification but below the 99th centile upper reference limit. Serum hsCRP was measured in 198 of the 200 participants. The median hsCRP was 2 mg/L (IQR 0.8 to 4.2 mg/L). Levels were numerically higher in women compared to men (2.2 mg/L versus 1.5 mg/L). High-sensitivity CRP categorised 75 (38%) patients as having a high level (> 3 mg/L).

with 65 (33%) and 58 (29.3) at intermediate (1-3 mg/L) and low (<1 mg/L) levels. Levels of hscTnI and hsCRP did not differ when stratified by site (*Table S2*).

Table 1: Baseline demographics and clinical characteristics¹

Characteristics	All patients (n=200)	Sex		<i>p</i> -value ²
		Females (n= 121)	Males (n = 79)	
Age, median (Q1, Q3), years	45.5 (37.7, 52.6)	44.2 (37.3, 50.5)	47.3 (38.0, 53.1)	0.206
Years of education, median (Q1, Q3)	14.0 (12.0, 16.0)	14.0 (12.0, 16.0)	15.0 (12.0, 16.5)	0.174
Highest level of education attained				
Primary/none/don't know, %	30/200 (15.0)	18/121 (14.9)	12/79 (15.2)	0.825
Secondary, %	45/200 (22.5)	29/121 (24.0)	16/79 (20.3)	
Higher Education/University, %	125/200 (62.5)	74/121 (61.2)	51/79 (64.6)	
Marital status				
Married (monogamous/polygamous) , %	128/200 (64.0)	64/121 (52.9)	64/79 (81.0)	<0.001
Single	26/200 (13.0)	23/121 (19.0)	3/79 (3.8)	
Separated/widowed/divorced/refused/ cohabiting/others, %	46/200 (23.0)	34/121 (28.1)	12/79 (15.2)	
Employment status				
Salaried Job or self-employed, %	180/200 (90.0)	105/121 (86.8)	75/79 (94.9)	0.148
Unemployed/housewife/retiree, %	13/200 (6.5)	11/121 (9.1)	2/79 (2.5)	
Casual labourer, %	7/200 (3.5)	5/121 (4.1)	2/79 (2.5)	
Household income per month				
< 15,001 KES ³ , %	34/198 (17.2)	26/119 (21.8)	8/79 (10.1)	0.051
> 15,001 KES, %	164/198 (82.8)	93/119 (78.2)	71/79 (89.9)	
Cardiovascular risk factors				
Smoking				
Current smoker, %	5/200 (2.5)	2/121 (1.7)	3/79 (3.8)	<0.001
Ex-smoker, %	44/200 (22.0)	11/121 (9.1)	33/79 (41.8)	
Never smoker, %	151/200 (75.5)	108/121 (89.3)	43/79 (54.4)	
Diabetes, %	7/200 (3.5)	4/121 (3.3)	3/79 (3.8)	0.661
Self-reported hypertension ⁴ , %	44/200 (22.0)	30/121 (24.8)	14/79 (17.7)	0.315
Cumulative hypertension ⁵ , %	60/200 (30.0)	34/121 (28.1)	26/79 (32.9)	0.570
Self-reported dyslipidemia, %	1/197 (0.5)	1/119 (0.8)	0/78 (0.0)	0.153
Chronic kidney disease, %	2/200 (1.0)	1/121 (0.8)	1/79 (1.3)	0.863
HIV				
Time since (months) HIV ⁶ infection, Median (Q1, Q3)	143.0 (59.0, 191.0)	144.0 (62.0, 191.0)	131.0 (56.5, 191.0)	0.574

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the variable.

² *p*-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon test for continuous variables, two-sided; bold *p*-values indicate statistical significance (*p*<0.05).

³ KES, Kenya shillings currency code

⁴ Self-reported physician-diagnosed hypertension.

⁵ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

⁶ HIV, human immunodeficiency virus,

Characteristics	All patients (n=200)	Sex		<i>p</i> -value ²
		Females (n= 121)	Males (n = 79)	
Currently on ART ⁷ , %	195/200 (97.5)	119/121 (98.3)	76/79 (96.2)	0.385
Past medical history				
Malaria, %	21/200 (10.5)	10/121 (8.3)	11/79 (13.9)	0.298
Tuberculosis, %	12/200 (6.0)	7/121 (5.8)	5/79 (6.3)	1.000
Clinical characteristics				
Body mass index, BMI (Kg/m ²), median (Q1, Q3)	26.8 (23.4, 30.8)	27.9 (23.8, 32.3)	26.0 (23.2, 29.6)	0.010
<i>BMI <25</i> , %	71/200 (35.5)	37/121 (30.6)	34/79 (43.0)	0.100
<i>BMI 25 to 29</i> , %	71/200 (35.5)	43/121 (35.5)	41/79 (33.9)	
<i>BMI >30</i> , %	58/200 (29.0)	41/121 (33.9)	17/79 (21.5)	
Systolic blood pressure (mmHg), Median (Q1, Q3), n = 200	120.0 (110.0, 133.0)	120.0 (110.0, 130.0)	122.0 (111.5, 133.0)	0.272
<i>SBP < 130 mmHg</i> , %	136/200 (68.0)	86/121 (71.1)	50/79 (63.3)	0.173
<i>SBP 130 -139 mmHg</i> , %	30/200 (15.0)	19/121 (15.7)	11/79 (13.9)	
<i>SBP 140-159 mmHg</i> , %	19/200 (9.5)	7/121 (5.8)	12/79 (15.2)	
<i>SBP >160 mmHg</i> , %	15/200 (7.5)	9/121 (7.4)	6/79 (7.6)	
Diastolic blood pressure (mmHg), Median (Q1, Q3), n = 200	78.0 (71.0, 85.0)	77.0 (71.0, 84.0)	80.0 (72.0, 85.0)	0.301
<i>DBP < 85 mmHg</i> , %	149/200 (74.5)	92/121 (76.0)	57/79 (72.2)	0.417
<i>DBP 85 – 89 mmHg</i> , %	22/200 (11.0)	10/121 (8.3)	12/79 (15.2)	
<i>DBP 90 – 99</i> , %	17/200 (8.5)	12/121 (9.9)	5/79 (6.3)	
<i>DBP > 100</i> , %	12/200 (6.0)	7/121 (5.8)	5/79 (6.3)	
Heart rate (bpm) median (Q1, Q3)	78.0 (74.0, 82.0)	76.5 (74.8, 84.2)	78.0 (72.0, 81.0)	0.474
Current cardiovascular medications				
RAAS modulators, %	16/200 (8.0)	11/121 (9.1)	5/79 (6.3)	0.662
Calcium channel blockers, %	8/200 (4.0)	5/121 (4.1)	3/79 (3.8)	1.000
Beta-blockers, %	8/200 (4.0)	5/121 (4.1)	3/79 (3.8)	1.000
Diuretics, %	10/200 (5.0)	8/121 (6.6)	2/79 (2.5)	0.321
Statins, %	2/200 (1.0)	1/121 (0.8)	1/79 (1.3)	1.000

⁷ ART, antiretroviral therapy.

Table 2: Biochemistry and haematology¹

Characteristics	All patients (n=200)	Sex		p-value ²
		Females (n=121)	Males (n=79)	
Creatinine, median (Q1, Q3), n=197	85.0 (73.0, 101.0)	77.5 (69.0, 89.3)	99.0 (89.0, 113.0)	<0.001
Urea, median (Q1, Q3), n=196	3.7 (3.1, 4.6)	3.6 (3.0, 4.3)	3.8 (3.2, 5.0)	0.013
Hemoglobin, mean (SD) , n=98* ³	14.01 (2.06)	12.90 (1.77)	15.31 (1.55)	<0.001
Glucose, median (Q1, Q3), n=197	4.8 (4.4, 5.3)	4.8 (4.3, 5.3)	4.9 (4.5, 5.3)	0.169
HbA1c, median (Q1, Q3), n=98*	5.6 (5.4, 5.9)	5.6 (5.4, 5.8)	5.8 (5.4, 6.1)	0.013
HbA1c <5.7, %	50/98 (51.0)	34/53 (64.2)	16/45 (35.6)	0.004
HbA1c 5.7 – 6.4, %	45/98 (45.9)	19/53 (35.8)	26/45 (57.8)	
HbA1c >= 6.5, %	3/98 (3.1)	0/53 (0.0)	3/45 (6.7)	
Lipid profiles				
Total cholesterol, median (Q1, Q3), n=196	4.6 (3.9, 5.1)	4.7 (3.9, 5.2)	4.5 (3.9, 5.1)	0.706
TC < 4.7, %	107/196 (54.6)	59/118 (50.0)	48/78 (61.5)	0.393
TC 4.8 – 5.1, %	22/196 (11.2)	15/118 (12.7)	7/78 (9.0)	
TC 5.2 – 6.1, %	30/196 (15.3)	21/118 (17.8)	9/78 (11.5)	
TC >= 6.2, %	37/196 (18.9)	23/118 (19.5)	14/78 (17.9)	
LDL, median (Q1, Q3), n=196	3.0 (2.3, 3.6)	3.0 (2.4, 3.7)	3.0 (2.3, 3.5)	0.747
LDL < 2.6	75/196 (38.3)	46/118 (39.0)	29/78 (37.2)	0.619
LDL 2.6 – 3.3	53/196 (27.0)	30/118 (25.4)	23/78 (29.5)	
LDL 3.4 – 4.1	41/196 (20.9)	23/118 (19.5)	18/78 (23.1)	
LDL >= 4.2	27/196 (13.8)	19/118 (16.1)	8/78 (10.3)	
HDL, median (Q1, Q3), n=196	1.2 (1.0, 1.5)	1.2 (1.1, 1.5)	1.1 (1.0, 1.3)	0.001
Trigylcerides, median (Q1, Q3), n=196	1.4 (0.9, 2.0)	1.2 (0.9, 1.7)	1.7 (1.0, 2.7)	0.0005
Trig < 1.7	123/196 (62.8)	86/118 (72.9)	37/78 (47.4)	<0.0001
Trig 1.7 – 2.2	32/196 (16.3)	19/118 (16.1)	13/78 (16.7)	
Trig >2.3	41/196 (20.9)	13/118 (11.0)	28/78 (35.9)	
Cardiac and inflammatory biomarkers				
High sensitivity troponin I, median (Q1, Q3), n=169	2.5 (2.5, 3.0)	2.5 (2.5, 2.5)	2.7 (2.5, 3.8)	<0.0001
hscTnI < 2.5 ng/L, %	109/169 (64.5)	78/103 (75.7)	31/66 (47.0)	<0.001
hscTnI 2.5 – 45 ng/L	59/169 (34.9)	24/103 (23.3)	35/66 (53.0)	
hscTnI >= 45 ng/L	1/169 (0.6)	1/103 (1.0)	0/66 (0.0)	

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the laboratory marker.
² p-value from Chi-square test or Fisher’s exact test for categorical variables and unpaired two-sample Wilcoxon test or Student’s t-test for continuous variables, two-sided; bold p-values indicate statistical significance (p<0.05).
³ * Hemoglobin and hemoglobin A1c (HbA1c) summaries are from Aga Khan University Hospital only.

Characteristics	All patients (n=200)	Sex		<i>p</i> -value ²
		Females (n=121)	Males (n=79)	
High-sensitivity CRP, median (Q1, Q3), n=198	2.0 (0.8, 4.2)	2.2 (0.9, 4.5)	1.5 (0.8, 3.8)	0.144
hsCRP < 1mg/L	58/198 (29.3)	31/120 (25.8)	27/78 (34.6)	0.300
hsCRP 1 - 3 mg/L	65/198 (32.8)	39/120 (32.5)	26/78 (33.3)	
hsCRP >3 mg/L	75/198 (37.9)	50/120 (41.7)	25/78 (32.1)	

Using the sex stratified Framingham laboratory-based risk score with lipids, the majority of the HIV population was classified at low risk (83%) with 12% at intermediate risk and 5% at high risk. Although sample sizes remained limited when stratified by sex and risk category, the prevalence of hypertension remained higher in women compared to men (*Table 3*) and as expected higher in the intermediate and high-risk groups across the population (*Table S3*).

Association between hscTnI and hsCRP and traditional cardiovascular risk factors were also evaluated (*Table 4*). The findings from cumulative logit models showed that older patients were more likely to have higher hscTnI levels (adjusted odds ratio (aOR) per year: 1.05, 95% confidence interval (CI): 1.01–1.09, $p < 0.011$). Female patients, compared to male patients, were identified as having lower hscTnI levels. Systolic blood pressures (SBP) of 140–159 mmHg and SBP >160 mmHg were associated with higher hscTnI concentrations (aOR 2.96 (95% CI: 1.09–7.90, $p = 0.030$) and 4.68 (95% CI: 1.55–14.1, $p = 0.006$, respectively) compared to those with SBP <130 mmHg. Our study did not find any strong associations between hsCRP and traditional cardiovascular risk factors including age, hypertension, diabetes and smoking. We also did not find any association between SBP levels and hsCRP. Levels of hsCRP were higher for HIV-patients with higher hscTnI levels. Study site - as a surrogate for socioeconomic status – was not associated with hscTnI or hsCRP.

Table 3: Cardiovascular risk factors, markers of myocardial injury and inflammation by cardiovascular risk category¹

Variable	Framingham risk score classification (FRS lipid) ²			p-value for trend ³	
	Low	Intermediate	High	Increasing	Two-sided
Males					
All (%)	58 (73.4)	14 (17.7)	7 (8.9)		
Smoking				–	0.503
Current smoker, %	3/58 (5.2)	0/14 (0.0)	0/7 (0.0)		
Ex-smoker, %	22/58 (37.9)	6/14 (42.9)	5/7 (71.4)		
Never smoker, %	33/58 (56.9)	8/14 (57.1)	2/7 (28.6)		
Diabetes, %	3/58 (5.2)	0/14 (0.0)	0/7 (0.0)	0.163	0.326
Hypertension ⁴ , %	12/58 (20.7)	6/14 (42.9)	7/7 (100.0)	<0.001	<0.001
Hyperlipidemia, %	0/58 (0.0)	0/13 (0.0)	0/7 (0.0)	–	–
Lipid profiles					
Total cholesterol, median (Q1, Q3)	4.3 (3.8, 4.9)	4.5 (4.3, 5.4)	6.2 (5.0, 6.8)	0.005	0.007
TC < 4.7, %	39/57 (68.4)	8/14 (57.1)	1/7 (14.3)	–	<0.001
TC 4.8 – 5.1, %	7/57 (12.3)	0/14 (0.0)	0/7 (0.0)		
TC 5.2 – 6.1, %	5/57 (8.8)	4/14 (28.6)	0/7 (0.0)		
TC ≥ 6.2, %	6/57 (10.5)	2/14 (14.3)	6/7 (85.7)		
LDL, median (Q1, Q3)	3.0 (2.3, 3.4)	3.2 (2.3, 3.5)	3.9 (3.5, 5.2)	0.016	0.039
Cardiac and inflammatory biomarkers					
High sensitivity troponin I, median (Q1, Q3)	2.5 (2.5, 3.4)	3.4 (2.8, 5.2)	4.1 (2.9, 7.1)	0.013	0.020
hscTnI < 2.5 ng/L, %	26/48 (54.2)	3/11 (27.3)	2/7 (28.6)	–	0.083
hscTnI 2.5 – 45 ng/L	22/48 (45.8)	8/11 (72.7)	5/7 (71.4)		
hscTnI ≥ 45 ng/L	0/48 (0.0)	0/11 (0.0)	0/7 (0.0)		
High-sensitivity CRP, median (Q1, Q3)	1.5 (0.8, 4.0)	2.3 (0.8, 3.1)	1.0 (0.7, 3.6)	0.523	0.95
hsCRP < 1mg/L	19/57 (33.3)	5/14 (35.7)	3/7 (42.9)	–	0.782

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the cardiovascular risk factor/marker.

² Risk categories classified as low (<10%), intermediate (10-19%) and high (≥ 20%)

³ p-values for trend were calculated Jonckheere-Terpstra for continuous variables and Cochran-Armitage, or Cochran-Mantel-Haenszel tests, appropriate, for categorical variables.

⁴ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

Variable	Framingham risk score classification (FRS lipid) ²			p-value for trend ³	
	Low	Intermediate	High	Increasing	Two-sided
hsCRP 1 - 3 mg/L	20/57 (35.1)	414 (28.6)	2/7 (28.6)	0.702	0.610
hsCRP >3 mg/L	18/57 (31.6)	514 (35.7)	2/7 (28.6)		
Creatinine, median (Q1, Q3)	100.0 (89.5, 113.2)	98.5 (94.8, 115.0)	91.0 (79.0, 104.5)		
Females					
All (%)	108 (89.3)	9 (7.4)	4 (3.3)		
Smoking					
Current smoker, %	2/108 (1.9)	0/9 (0.0)	0/4 (0.0)	–	0.241
Ex-smoker, %	11/108 (10.2)	0/9 (0.0)	0/4 (0.0)		
Never smoker, %	95/108 (88.0)	9/9 (100.0)	4/4 (100.0)		
Diabetes, %	0/108 (0.0)	2/9 (22.2)	2/4 (50.0)	1.000	<0.0001
Hypertension ⁵ , %	24/108 (22.2)	7/9 (77.8)	3/4 (75.0)	<0.0001	<0.001
Hyperlipidemia, %	0/106 (0.0)	1/9 (11.1)	0/4 (0.0)	0.976	0.048
Lipid profiles					
Total cholesterol, median (Q1, Q3)	4.6 (3.8, 5.1)	5.4 (4.9, 6.1)	4.4 (4.3, 4.7)	0.07	0.031
TC < 4.7, %	54/105 (51.4)	2/9 (22.2)	3/4 (75.0)	–	0.883
TC 4.8 – 5.1, %	13/105 (12.4)	2/9 (22.2)	0/4 (0.0)		
TC 5.2 – 6.1, %	18/105 (17.1)	2/9 (22.2)	1/4 (25.0)		
TC ≥ 6.2, %	20/105 (19.0)	3/9 (33.3)	0/4 (0.0)		
LDL, median (Q1, Q3)	2.9 (2.4, 3.5)	4.0 (3.3, 4.2)	2.9 (2.6, 3.2)	0.042	0.082
Cardiac and inflammatory biomarkers					
High sensitivity troponin I, median (Q1, Q3)	2.5 (2.5, 2.5)	2.8 (2.5, 4.1)	2.7 (2.6, 5.2)	0.003	0.006
hscTnI < 2.5 ng/L, %	74/92 (80.4)	3/7 (42.9)	1/4 (25.0)	–	0.003
hscTnI 2.5 – 45 ng/L	17/92 (18.5)	4/7 (57.1)	3/4 (75.0)		
hscTnI ≥ 45 ng/L	1/92 (1.1)	0/7 (0.0)	0/4 (0.0)		
High-sensitivity CRP, median (Q1, Q3)	2.0 (0.9, 4.3)	6.9 (2.2, 10.3)	2.6 (2.5, 4.4)	0.012	0.022
hsCRP < 1mg/L	30/107 (28.0)	1/9 (11.1)	0/4 (0.0)	–	0.128
hsCRP 1 - 3 mg/L	34 (31.8)	2/9 (22.2)	3/4 (75.0)		
hsCRP >3 mg/L	43 (40.2)	6/9 (66.7)	1/4 (25.0)		
Creatinine, median (Q1, Q3)	76.0 (69.0, 85.5)	88.0 (75.0, 94.0)	91.0 (84.2, 99.5)	0.047	0.047

⁵ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

Table 4: Relationship between baseline markers of myocardial injury and inflammation and traditional cardiovascular risk factors, displayed as multivariable-adjusted odds ratios¹⁶ for hscTnI and multivariable-adjusted mean differences¹⁷ for hsCRP

	High-sensitivity troponin I			High-sensitivity C-Reactive Protein		
Risk factor	Model I AOR ¹⁸ (95% CI) ¹⁹	Model II AOR (95% CI)	Model III AOR (95% CI)	Model I Adjusted Coef. ²⁰ (95% CI)	Model II Adjusted Coef. (95% CI)	Model III Adjusted Coef. (95% CI)
Age (years)	1.05 (1.02 to 1.09, p= 0.004)	1.05 (1.01 to 1.09, p= 0.021)	1.04 (1.00 to 1.08, p= 0.032)	0.004 (-0.12 to 0.12, p=0.952)	0.01 (-0.11 to 0.14, p=0.860)	0.02 (-0.13 to 0.17, p=0.775)
Sex						
Male	Reference	Reference	Reference	Reference	Reference	Reference
Female	0.32 (0.14 to 0.70, p= 0.004)	0.39 (0.16 to 0.93, p= 0.035)	0.38 (0.17 to 0.84, p= 0.018)	1.66 (-0.85 to 4.18, p=0.194)	1.49 (-1.28 to 4.25, p=0.290)	0.04 (-3.39 to 3.47, p=0.980)
Study Site ²¹						
AKUNH	Reference	Reference	Reference	Reference	Reference	Reference
Coptic	1.08 (0.54 to 2.16, p=0.832)	0.97 (0.48 to 1.99, p=0.941)	0.91 (0.44 to 1.90, p=0.805)	0.78 (-1.70 to 3.27, p=0.536)	0.91 (-1.63 to 3.45, p=0.481)	0.87 (-2.02 to 3.76, p=0.553)
Hypertension	–	2.76 (1.36 to 5.63, p= 0.005)	–	–	1.23 (-3.91 to 6.45, p=0.366)	–
Diabetes	–	0.53 (0.06 to 3.37, p=0.513)	–	–	1.41 (-6.24 to 9.06, p=0.903)	–
Smoking						
Never smoker	Reference	Reference	–	–	Reference	–

¹⁶ Cumulative Logit Model with high-sensitivity Troponin-I response as myocardial injury marker. Bold *p*-values indicate statistical significance (*p*<0.05). Model I adjusts for age, sex, creatinine and study site; Model II as for Model I plus history of hypertension, diabetes and smoking status; Model III as for Model I plus systolic blood pressure and hsCRP levels

¹⁷ Linear Regression with high-sensitivity C-Reactive Protein (hsCRP) response as inflammation marker. Bold *p*-values indicate statistical significance (*p*<0.05). Model I adjusts for age, sex and creatinine; Model II as for Model I plus history of hypertension, diabetes and smoking status; Model III as for Model I plus systolic blood pressure and hsCRP levels

¹⁸ AOR, adjusted odds ratio.

¹⁹ CI, confidence interval

²⁰ Coef., coefficient as multivariable mean difference.

²¹ AKUHN, Aga Khan University Hospital, Nairobi; Coptic, Coptic Hope Center for Infectious Diseases.

	High-sensitivity troponin I			High-sensitivity C-Reactive Protein		
Risk factor	Model I AOR ¹⁸ (95% CI) ¹⁹	Model II AOR (95% CI)	Model III AOR (95% CI)	Model I Adjusted Coef. ²⁰ (95% CI)	Model II Adjusted Coef. (95% CI)	Model III Adjusted Coef. (95% CI)
Former smoker	–	1.19 (0.51 to 2.70, p=0.685)	–	–	0.45 (-3.61 to 4.52, p=0.781)	–
Current smoker	–	1.36 (0.15 to 9.11, p=0.762)	–	–	0.22 (-7.47 to 7.92, p=0.954)	–
Systolic Blood Pressure						
SBP < 130 mmHg	Reference	–	Reference	–	–	Reference
SBP 130 - 139 mmHg	–	–	2.29 (0.87 to 5.87, p=0.087)	–	–	-2.40 (-6.37 to 1.58, p=0.235)
SBP 140- 159 mmHg	–	–	3.08 (1.13 to 8.34, p=0.026)	–	–	-3.47 (-8.13 to 1.19, p=0.143)
SBP > 160 mmHg	–	–	5.40 (1.75 to 16.6, p=0.003)	–	–	-2.09 (-7.45 to 3.26, p=0.441)
High-sensitivity CRP mg/L	–	–	1.05 (1.01 to 1.10, p=0.014)	–	–	–
High-sensitivity troponin-I						
< 2.50 ng/L	Reference	Reference	Reference	Reference	Reference	Reference
2.50–3.02 ng/L	–	–	–	–	–	4.42 (0.78 to 8.07, p=0.018)
3.02–7.12 ng/L	–	–	–	–	–	1.20 (-2.43 to 4.84, p=0.514)
≥ 7.12 ng/L	–	–	–	–	–	0.57 (-3.23 to 4.38, p=0.766)
Creatinine mg/L	1.00 (0.98 to 1.03, p= 0.671)	1.01 (0.99–1.03, p=0.399)	1.01 (0.99 to 1.04, p=0.177)	-0.01 (-0.05 to 0.02, p=0.568)	0.01 (-0.04 to 0.03, p=0.644)	-0.11 (-0.20 to -0.03, p=0.010)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Discussion

In this small, descriptive, cross-sectional study across two sites in urban Kenya, we evaluated the prevalence of traditional cardiovascular risk factors. We also explored how biochemical markers of inflammation and myocardial injury are associated with traditional cardiovascular risk factors in PLHIV. We make a number of observations. First, in a relatively young population with HIV, some traditional cardiovascular risk factors were common. Smoking and diabetes rates, however, were low. Second, using traditional risk estimation systems, the majority of the young HIV population were categorized as low-risk for future cardiovascular events. Third, across the majority of patients, hsTnI values were below the limit of detection. Fourth, in exploratory analysis we found no associations between hsCRP levels and traditional cardiovascular risk factors but did observe a positive association between hscTnI levels and increasing age and higher systolic blood pressure.

Some traditional cardiovascular risk factors were common in the HIV population studied. Hypertension was self-reported in 1 in 5 individuals and higher, at 1 in 3, when classified by office systolic blood pressure measurement and/or use of anti-hypertensives. Self-reported dyslipidemia was low at 1 in 20 but much higher when based on total cholesterol concentration >6.1 mmol/L (19%). This discordance likely reflects individuals being unaware of their cholesterol status. Smoking and diabetes rates, however, remained relatively low in contrast to PLHIV in high income countries.²² Our prevalence rates of traditional cardiovascular risk factors are in agreement with other studies from the sub-Saharan African region²³⁻²⁵ and discordant to those evaluating PLHIV in high-income settings.^{22 26} Whilst North American / European studies contribute to most of the evidence evaluating cardiovascular disease in HIV,

the region only hosts 6% of the global HIV population compared to 75% for sub-Saharan Africa.^{27 28} PLHIV in sub-Saharan Africa and North America / Europe are different by virtue of the factors associated with HIV acquisition. HIV remains firmly established in the general population in SSA but overwhelmingly affects men who have sex with men and intravenous drug users in North America / Europe.²⁹ These differences probably account for regional discordance in the association between HIV status and prevalence of cardiovascular risk factors that has been observed in the published literature. Positive associations in North America / Europe either become null or even reverse in sub-Saharan Africa.^{22-26 30-33}

Using the sex stratified Framingham laboratory-based risk score, the overwhelming majority of the HIV population was classified at low risk (83%) with 12% at intermediate risk and 5% at high risk. Similar risk categorizations were obtained when using the Framingham non-laboratory-based risk scores. All established cardiovascular risk estimation systems – predominantly developed in high-income countries and not accounting for HIV status are highly influenced by age. As such, our findings likely reflect the younger age distribution in our study.^{12 34} Whether this estimation of low-risk, using generalized risk scores developed predominantly in high-income countries, reflects the observed cardiovascular risk of HIV individuals in sub-Saharan Africa remains uncertain.

Previous studies have shown how biochemical markers, such as hsCRP and hscTnI, may hold promise in improving cardiac risk estimation systems.³⁵ Our study showed that the majority of individuals had undetectable levels of hscTnI with only 1 in 3 patients demonstrating levels above the limit of detection. Previous studies in high-income settings have shown that during acute HIV infection, troponin levels are higher but drop 3-fold once viremic control is achieved.³⁶ A large proportion of our patients were established on antiretroviral therapy and

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

with the duration of diagnosis to study recruitment being nearly 12 years. Two studies showed contrasting results when evaluating the association between troponin levels and presence of coronary plaques, with results primarily applicable to men with HIV in non-endemic regions.³⁷
³⁸ Levels of hsCRP, suggestive of underlying inflammation, were high in this study with women having higher concentrations. Whether higher baseline hsCRP levels relate to increased risk of cardiovascular events in HIV, however, remains uncertain with contrasting data in the published literature.^{39,40} Higher levels of hsCRP in people with HIV is biologically plausible and supported by previous studies^{28 41}, but may not just be reflective of vascular disease.⁴² As such the specificity of hsCRP for cardiovascular disease in PLHIV may be low.

Our study showed, hscTnI levels were higher in males, associated with increasing age, measured systolic blood pressure, and reported history of hypertension. This is similar to what has been observed in the general population.^{43 44} However, surprisingly, in our study, much of the population had troponin concentrations below the limit of quantification despite using a high-sensitivity assay likely reflective of a younger population. Unlike in the general population⁴⁵, We did not show any robust association between hsCRP and traditional cardiovascular risk factors. This may reflect the younger age of our population with previous studies showing higher hsCRP values in the elderly.⁴⁶

This is one of the few studies that has quantified the prevalence of cardiovascular risk factors and explored their association with biochemical markers of inflammation and myocardial injury in HIV populations from two distinct centres in urban Kenya. However, several limitations should be considered. First, our study was cross-sectional and we were unable to evaluate the associations between novel biochemical markers and future cardiovascular events. Second, HIV populations in our study were recruited across two centres in Nairobi,

representing a predominantly urban population. Whether our findings are generalisable to rural populations remains uncertain. Third, given resource limitations, we did not study age- and sex-matched non-HIV populations and were limited to a finite choice of biochemical biomarkers. As such our study is unable to comment on associations between a wider range of biochemical markers and cardiovascular risk factors in the general population and how these may differ to those infected with HIV. For the same reason we were also unable to measure metric if infection control (viral load and CD4 count) at the time of recruitment. Fourth, some of the risk factors such as diabetes status depended on self-reporting – as such, the absence of associations may reflect exposure misclassification. Lastly, we cannot exclude the possibility that associations between biomarkers and outcomes may in part be due to residual confounding or unmeasured confounders.

Conclusions

In conclusion, we show that whilst some traditional cardiovascular risk factor prevalences remain high in HIV populations in sub-Saharan Africa, important ones such as smoking are low. This is in contrast to HIV populations in non-endemic regions²². The majority of PLHIV - using traditional risk estimation systems - have a low estimated CVD risk likely reflecting a younger aged population predominantly consisting of women. Whilst hscTnI values were associated with increasing age and higher blood pressure, no associations between hsCRP levels and traditional cardiovascular risk factors were observed.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Contributors: ASVS and MC conceived and designed the study. HA recruited the patients. ASVS and HA wrote the first draft of the manuscript. IA, HA and JS analysed the data. ASVS, JM, IA, KL, SA, PP, JS, MA, SE and MC made critical revisions on the paper.

Competing interests: ASVS’s institution has received speaker fees from Abbott Diagnostics. The authors declare no other conflicts of interest.

Funding: Supported by the Global Challenges Research Fund UKRI and the British Heart Foundation Intermediate Clinical Research Fellowship

Data availability statement: Data will be available on request to the corresponding author (anoop.shah@lshtm.ac.uk)

Ethical approval: Ethical approval was obtained from the Aga Khan University Nairobi Research Ethics committee (2018/REC-84). Written informed consent was obtained from all subjects participating in the study.

References

1. Global AIDS Update 2016: Joint United Nations Programme on HIV/AIDS. Available at: <https://www.unaids.org/en/resources/documents/2016/Global-AIDS-update-2016#:~:text=The%20world%20has%20committed%20to,8%20to%2010%20June%202016.>
2. Mensah GA, Roth GA, Sampson UK, et al. Mortality from cardiovascular diseases in sub-Saharan Africa, 1990-2013: a systematic analysis of data from the Global Burden of Disease Study 2013. *Cardiovasc J Afr* 2015;26(2 Suppl 1):S6-10. doi: 10.5830/CVJA-2015-036
3. Murray CJ, Ortblad KF, Guinovart C, et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014;384(9947):1005-70. doi: 10.1016/S0140-6736(14)60844-8
4. Palella FJ, Jr., Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* 1998;338(13):853-60. doi: 10.1056/NEJM199803263381301
5. Neuhaus J, Angus B, Kowalska JD, et al. Risk of all-cause mortality associated with nonfatal AIDS and serious non-AIDS events among adults infected with HIV. *Aids* 2010;24(5):697-706. doi: 10.1097/QAD.0b013e3283365356
6. Mocroft A, Reiss P, Gasiowski J, et al. Serious fatal and nonfatal non-AIDS-defining illnesses in Europe. *Journal of acquired immune deficiency syndromes* 2010;55(2):262-70. doi: 10.1097/QAI.0b013e3281e9be6b [published Online First: 2010/08/12]
7. Antiretroviral Therapy Cohort C. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2010;50(10):1387-96. doi: 10.1086/652283
8. Shah ASV, Stelzle D, Lee KK, et al. Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV. *Circulation* 2018;138(11):1100-12. doi: 10.1161/circulationaha.117.033369 [published Online First: 2018/07/04]
9. Rao SG, Galaviz KI, Gay HC, et al. Factors Associated With Excess Myocardial Infarction Risk in HIV-Infected Adults: A Systematic Review and Meta-analysis. *Journal of acquired immune deficiency syndromes* 2019;81(2):224-30. doi: 10.1097/QAI.0000000000001996 [published Online First: 2019/03/14]
10. Gaziano TA, Abrahams-Gessel S, Gomez-Olive FX, et al. Cardiometabolic risk in a population of older adults with multiple co-morbidities in rural south africa: the HAALSI (Health and Aging in Africa: longitudinal studies of INDEPTH communities) study. *BMC Public Health* 2017;17(1):206. doi: 10.1186/s12889-017-4117-y [published Online First: 2017/02/19]
11. Gaziano TA, Bitton A, Anand S, et al. Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr Probl Cardiol* 2010;35(2):72-115. doi: 10.1016/j.cpcardiol.2009.10.002
12. So-Armah K, Benjamin LA, Bloomfield GS, et al. HIV and cardiovascular disease. *Lancet HIV* 2020;7(4):e279-e93. doi: 10.1016/S2352-3018(20)30036-9 [published Online First: 2020/04/04]
13. Chung MH, Drake AL, Richardson BA, et al. Impact of prior HAART use on clinical outcomes in a large Kenyan HIV treatment program. *Curr HIV Res* 2009;7(4):441-6. doi: 10.2174/157016209788680552 [published Online First: 2009/07/16]

14. Performance Evaluation of the Atellica High-Sensitivity Troponin I Assay: Siemens Healthcare Diagnostics Inc. 2020 [Available from: <https://www.siemens-healthineers.com/en-uk/laboratory-diagnostics/assays-by-diseases-conditions/cardiac-assays/cardiac-troponin-assays> accessed 19th March 2021].

15. Healthineers S. High Sensitivity C-Reactive Protein (hsCRP) Assay [Available from: <https://www.siemens-healthineers.com/en-uk/cardiac/cardiac-assays/high-sensitivity-c-reactive-protein> accessed 19th March 2021].

16. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):e13-e115. doi: 10.1161/HYP.0000000000000065 [published Online First: 2017/11/15]

17. Roth GA, Fihn SD, Mokdad AH, et al. High total serum cholesterol, medication coverage and therapeutic control: an analysis of national health examination survey data from eight countries. *Bull World Health Organ* 2011;89(2):92-101. doi: 10.2471/BLT.10.079947 [published Online First: 2011/02/25]

18. Kramer CK, Araneta MR, Barrett-Connor E. A1C and diabetes diagnosis: The Rancho Bernardo Study. *Diabetes Care* 2010;33(1):101-3. doi: 10.2337/dc09-1366 [published Online First: 2009/10/20]

19. Zacho J, Tybjaerg-Hansen A, Jensen JS, et al. Genetically elevated C-reactive protein and ischemic vascular disease. *N Engl J Med* 2008;359(18):1897-908. doi: 10.1056/NEJMoa0707402 [published Online First: 2008/10/31]

20. Shah AS, Newby DE, Mills NL. High sensitivity cardiac troponin in patients with chest pain. *Bmj* 2013;347:f4222. doi: 10.1136/bmj.f4222 [published Online First: 2013/07/24]

21. Liu Q, Shepherd BE, Li C, et al. Modeling continuous response variables using ordinal regression. *Statistics in medicine* 2017;36(27):4316-35. doi: 10.1002/sim.7433 [published Online First: 2017/09/06]

22. Johnston PI, Wright SW, Orr M, et al. Worldwide relative smoking prevalence among people living with and without HIV. *Aids* 2021;35(6):957-70. doi: 10.1097/QAD.0000000000002815 [published Online First: 2021/01/21]

23. Clark SJ, Gomez-Olive FX, Houle B, et al. Cardiometabolic disease risk and HIV status in rural South Africa: establishing a baseline. *BMC Public Health* 2015;15:135. doi: 10.1186/s12889-015-1467-1 [published Online First: 2015/04/18]

24. Mugisha JO, Schatz EJ, Randell M, et al. Chronic disease, risk factors and disability in adults aged 50 and above living with and without HIV: findings from the Wellbeing of Older People Study in Uganda. *Glob Health Action* 2016;9:31098. doi: 10.3402/gha.v9.31098 [published Online First: 2016/05/27]

25. Prioreschi A, Munthali RJ, Soepnel L, et al. Incidence and prevalence of type 2 diabetes mellitus with HIV infection in Africa: a systematic review and meta-analysis. *BMJ Open* 2017;7(3):e013953. doi: 10.1136/bmjopen-2016-013953 [published Online First: 2017/04/01]

26. Triant VA, Lee H, Hadigan C, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab* 2007;92(7):2506-12. doi: 10.1210/jc.2006-2190 [published Online First: 2007/04/26]

27. Lawal IO, Ankrah AO, Popoola GO, et al. Arterial inflammation in young patients with human immunodeficiency virus infection: A cross-sectional study using F-18 FDG

- PET/CT. *J Nucl Cardiol* 2019;26(4):1258-65. doi: 10.1007/s12350-018-1207-x [published Online First: 2018/02/09]
28. Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. *JAMA* 2012;308(4):379-86. doi: 10.1001/jama.2012.6698 [published Online First: 2012/07/24]
 29. UNAIDS Data 2020: UNAIDS. Available at: https://www.unaids.org/sites/default/files/media_asset/2020_aids-data-book_en.pdf
 30. Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. *Arch Intern Med* 2005;165(10):1179-84. doi: 10.1001/archinte.165.10.1179 [published Online First: 2005/05/25]
 31. van Zoest RA, Wit FW, Kooij KW, et al. Higher Prevalence of Hypertension in HIV-1-Infected Patients on Combination Antiretroviral Therapy Is Associated With Changes in Body Composition and Prior Stavudine Exposure. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2016;63(2):205-13. doi: 10.1093/cid/ciw285 [published Online First: 2016/05/05]
 32. Coetzee L, Bogler L, De Neve JW, et al. HIV, antiretroviral therapy and non-communicable diseases in sub-Saharan Africa: empirical evidence from 44 countries over the period 2000 to 2016. *J Int AIDS Soc* 2019;22(7):e25364. doi: 10.1002/jia2.25364 [published Online First: 2019/07/30]
 33. Davis K, Perez-Guzman P, Hoyer A, et al. Association between HIV infection and hypertension: a global systematic review and meta-analysis of cross-sectional studies. *BMC Med* 2021;19(1):105. doi: 10.1186/s12916-021-01978-7 [published Online First: 2021/05/14]
 34. Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk: a review for clinicians. *J Am Coll Cardiol* 2009;54(14):1209-27. doi: 10.1016/j.jacc.2009.07.020 [published Online First: 2009/09/26]
 35. Gilstrap LG, Wang TJ. Biomarkers and cardiovascular risk assessment for primary prevention: an update. *Clin Chem* 2012;58(1):72-82. doi: 10.1373/clinchem.2011.165712 [published Online First: 2011/11/30]
 36. Schuster C, Mayer FJ, Wohlfahrt C, et al. Acute HIV Infection Results in Subclinical Inflammatory Cardiomyopathy. *J Infect Dis* 2018;218(3):466-70. doi: 10.1093/infdis/jiy183 [published Online First: 2018/04/03]
 37. Rahman F, Zhang Z, Zhao D, et al. Association of High-Sensitivity Troponin with Cardiac CT Angiography Evidence of Myocardial and Coronary Disease in a Primary Prevention Cohort of Men: Results from MACS. *J Appl Lab Med* 2019;4(3):355-69. doi: 10.1373/jalm.2018.028860 [published Online First: 2019/10/30]
 38. Fitch KV, DeFilippi C, Christenson R, et al. Subclinical myocyte injury, fibrosis and strain in relationship to coronary plaque in asymptomatic HIV-infected individuals. *Aids* 2016;30(14):2205-14. doi: 10.1097/QAD.0000000000001186 [published Online First: 2016/06/18]
 39. De Luca A, de Gaetano Donati K, Colafigli M, et al. The association of high-sensitivity c-reactive protein and other biomarkers with cardiovascular disease in patients treated for HIV: a nested case-control study. *BMC Infect Dis* 2013;13:414. doi: 10.1186/1471-2334-13-414 [published Online First: 2013/09/06]
 40. Ford ES, Greenwald JH, Richterman AG, et al. Traditional risk factors and D-dimer predict incident cardiovascular disease events in chronic HIV infection. *Aids* 2010;24(10):1509-17. doi: 10.1097/QAD.0b013e32833ad914 [published Online First: 2010/05/28]

41. Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. *JAMA* 2012;308(4):379—86. doi: 10.1001/jama.2012.6698

42. Kulkarni M, Bowman E, Gabriel J, et al. Altered Monocyte and Endothelial Cell Adhesion Molecule Expression Is Linked to Vascular Inflammation in Human Immunodeficiency Virus Infection. *Open Forum Infect Dis* 2016;3(4):ofw224. doi: 10.1093/ofid/ofw224 [published Online First: 2016/10/15]

43. Willeit P, Welsh P, Evans JDW, et al. High-Sensitivity Cardiac Troponin Concentration and Risk of First-Ever Cardiovascular Outcomes in 154,052 Participants. *J Am Coll Cardiol* 2017;70(5):558—68. doi: 10.1016/j.jacc.2017.05.062

44. Blankenberg S, Salomaa V, Makarova N, et al. Troponin I and cardiovascular risk prediction in the general population: the BiomarCaRE consortium. *Eur Heart J* 2016;37(30):2428-37. doi: 10.1093/eurheartj/ehw172 [published Online First: 2016/05/14]

45. Saito M, Ishimitsu T, Minami J, et al. Relations of plasma high-sensitivity C-reactive protein to traditional cardiovascular risk factors. *Atherosclerosis* 2003;167(1):73-9. doi: 10.1016/s0021-9150(02)00380-5 [published Online First: 2003/03/06]

46. Puzianowska-Kuznicka M, Owczarz M, Wieczorowska-Tobis K, et al. Interleukin-6 and C-reactive protein, successful aging, and mortality: the PolSenior study. *Immun Ageing* 2016;13:21. doi: 10.1186/s12979-016-0076-x [published Online First: 2016/06/09]

SUPPLEMENT

Cardiovascular risk factors and markers of myocardial injury and inflammation in people living with HIV in Kenya

Hassan A Ahmed, MD¹; Mohammed Jeilan, MD¹; Isaiah G Akuku, MSc²; Kuan Ken Lee, MD³; Shirjel R Alam, MD⁴; Pablo Perel, MD⁴; Jasmit Shah, PhD¹; Mohammed K. Ali, MD;⁵ Sherry Eskander, MD;⁶ Michael H Chung, MD MPH^{5*} and Anoop S V Shah, MD^{4,7*}

*Contributed equally

¹ Department of Medicine, Aga Khan University

² Institute of Tropical and Infectious Diseases, University of Nairobi

³ BHF Centre for Cardiovascular Sciences, University of Edinburgh

⁴ Department of Non-communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

⁵ Emory University, Atlanta, Georgia, USA

⁶ Coptic Hospital, Nairobi, Kenya

⁷ Imperial College Hospital NHS Trust, London, UK

Correspondence and requests for reprints:

Dr Anoop Shah,
Room 249,
Department of Non-communicable Disease Epidemiology ,
London School of Hygiene and Tropical Medicine,
Keppel Street,
London,
UK
WC1E 7HT

Mobile: +(44) 7766 544 156

E-mail: Anoop.Shah@lshtm.ac.uk

Abstract: 299 (300)

Word count: 2,712

Table and Figures: 4

Figure S1: Study flow diagram

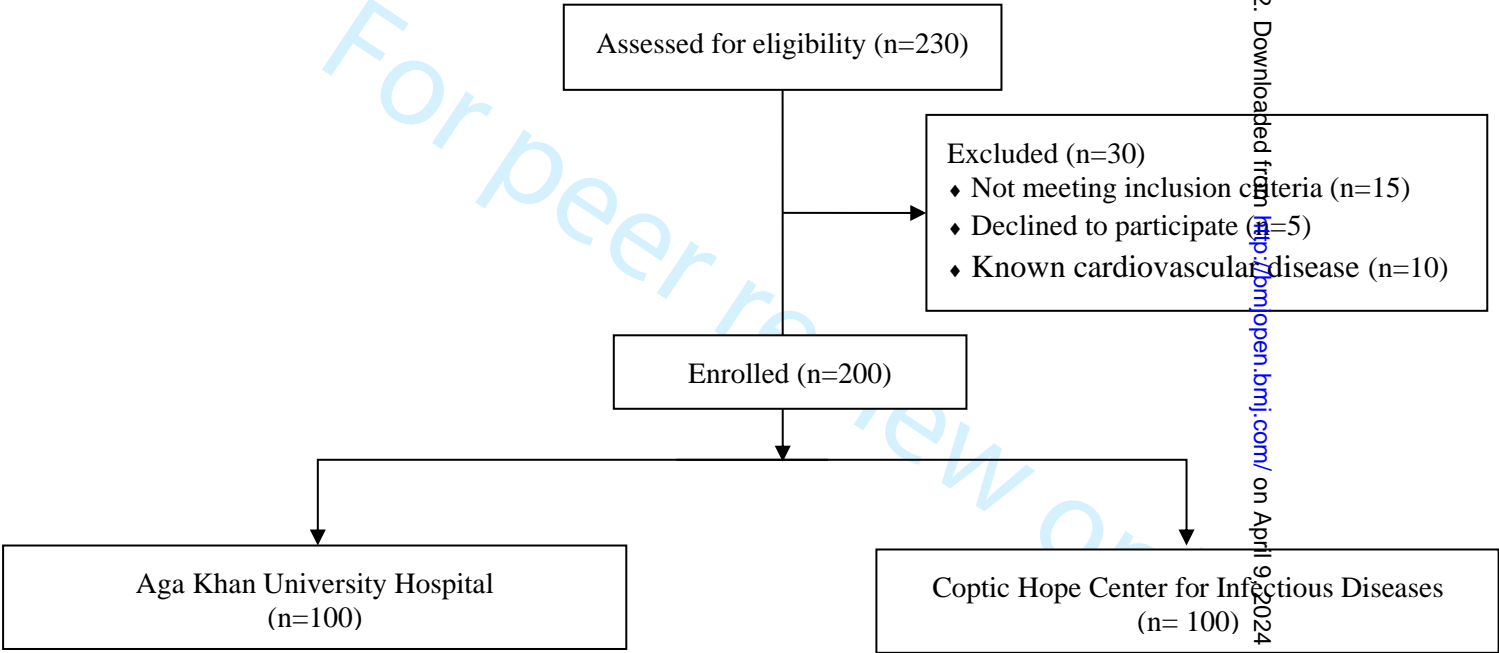


Table S1: Baseline demographics and clinical characteristics by clinical site¹

Characteristics	All patients (n=200)	Site		p-value ²
		Aga Khan University Hospital (n= 100)	Coptic Hope Center for Infectious Diseases (n = 100)	
Age, median (Q1, Q3), years	45.5 (37.7, 52.6)	41.9 (35.3, 49.4)	48.0 (40.5, 54.3)	<0.001
Gender				
Male, %	79/200 (39.5)	46/100 (46.0)	33/100 (33.0)	0.083
Female, %	121/200 (60.5)	54/100 (54.0)	67/100 (67.0)	
Years of education, median (Q1, Q3)	14.0 (12.0, 16.0)	16.0 (13.0, 16.0)	13.5 (10.8, 16.0)	<0.001
Highest level of education attained				
Primary/none/don't know, %	30/200 (15.0)	5/100 (5.0)	25/100 (25.0)	<0.001
Secondary, %	45/200 (22.5)	21/100 (21.0)	24/100 (24.0)	
Higher Education/University, %	125/200 (62.5)	74/100 (74.0)	51/100 (51.0)	
Marital status				
Married (monogamous/polygamous), %	128/200 (64.0)	70/100 (70.0)	58/100 (58.0)	0.119
Single	26/200 (13.0)	13/100 (13.0)	13/100 (13.0)	
Separated/widowed/divorced/refused/cohabiting/others, %	46/200 (23.0)	17/100 (17.0)	29/100 (29.0)	
Employment status				
Salaried Job or self-employed, %	180/200 (90.0)	91/100 (91.0)	89/100 (89.0)	0.117
Unemployed/housewife/retiree, %	13/200 (6.5)	8/100 (8.0)	5/100 (5.0)	
Casual labourer, %	7/200 (3.5)	1/100 (1.0)	6/100 (6.0)	
Household income per month				
< 15,001 KES ³ , %	34/198 (17.2)	6/100 (6.0)	28/98 (28.6)	<0.001
> 15,001 KES, %	164/198 (82.8)	94/100 (94.0)	70/98 (71.4)	
Cardiovascular risk factors				
Smoking				
Current smoker, %	5/200 (2.5)	3/100 (3.0)	2/100 (2.0)	1.000
Ex-smoker, %	44/200 (22.0)	22/100 (22.0)	22/100 (22.0)	
Never smoker, %	151/200 (75.5)	75/100 (75.0)	76/100 (76.0)	
Diabetes, %	7/200 (3.5)	5/100 (5.0)	2/100 (2.0)	0.444
Self-reported hypertension ⁴ , %	44/200 (22.0)	22/100 (22.0)	22/100 (22.0)	1.000
Cumulative hypertension ⁵ , %	60/200 (30.0)	25/100 (25.0)	35/100 (35.0)	0.165
Dyslipidemia, %	1/197 (0.5)	0/100 (0.0)	1/97 (1.0)	0.288
Chronic kidney disease, %	2/200 (1.0)	2/100 (2.0)	0/100 (0.0)	0.036
HIV				
Time since (months) HIV ⁶ infection, Median (Q1, Q3)	143.0 (59.0, 191.0)	106.0 (47.0, 191.0)	159.0 (95.0, 191.0)	0.037
Currently on ART ⁷ , %	195/200 (97.5)	95/100 (95.0)	100/100 (100.0)	0.059
Past medical history				
Malaria, %	21/200 (10.5)	0/100 (0.0)	21/100 (21.0)	<0.001
Tuberculosis, %	12/200 (6.0)	4/100 (4.0)	8/100 (8.0)	0.373
Clinical characteristics				

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the variable.

² p-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon test or Student's t-test for continuous variables, two-sided; bold p-values indicate statistical significance (p<0.05).

³ KES, Kenya shillings currency code

⁴ Self-reported physician-diagnosed hypertension.

⁵ Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

⁶ HIV, human immunodeficiency virus,

⁷ ART, antiretroviral therapy.

Table S2 Biochemistry and haematology by clinical site¹

Characteristics	All patients (n=200)	Site ²		p-value ³
		Aga Khan University Hospital (n=100)	Coptic Hope Center for Infectious Diseases (n=100)	
Creatinine, median (Q1, Q3), n=197	85.0 (73.0, 101.0)	89.0 (74.0, 106.0)	83.0 (71.8, 98.2)	0.102
Urea, median (Q1, Q3), n=196	3.7 (3.1, 4.6)	3.8 (3.1, 5.0)	3.5 (3.0, 4.2)	0.011
Hemoglobin, mean (SD), n=98*	—	14.01 (2.06)	—	—
Glucose, median (Q1, Q3), n=197	4.8 (4.4, 5.3)	5.2 (4.9, 5.6)	4.5 (4.1, 4.6)	<0.001
HbA1c, median (Q1, Q3), n=98*	5.6 (5.4, 5.9)	5.6 (5.4, 5.9)	—	—
HbA1c <5.7, %	—	50/98 (51.0)	—	—
HbA1c 5.7 – 6.4, %	—	45/98 (45.9)	—	
HbA1c >= 6.5, %	—	3/98 (3.1)	—	
Lipid profiles				
Total cholesterol, median (Q1, Q3), n=196	4.6 (3.9, 5.1)	4.6 (3.8, 5.3)	4.4 (4.0, 5.1)	0.665
TC < 4.7, %	107/196 (54.6)	52 (53.1)	55 (56.1)	0.955
TC 4.8 – 5.1, %	22/196 (11.2)	11 (11.2)	11 (11.2)	
TC 5.2 – 6.1, %	30/196 (15.3)	15 (15.3)	15 (15.3)	
TC >= 6.2, %	37/196 (18.9)	20 (20.4)	17 (17.3)	
LDL, median (Q1, Q3), n=196	3.0 (2.3, 3.6)	3.1 (2.3, 3.6)	3.0 (2.4, 3.5)	0.858
LDL < 2.6, %	75/196 (38.3)	36 (36.7)	39 (39.8)	0.978
LDL 2.6 – 3.3, %	53/196 (27.0)	27 (27.6)	26 (26.5)	
LDL 3.4 – 4.1, %	41/196 (20.9)	21 (21.4)	20 (20.4)	
LDL >= 4.2, %	27/196 (13.8)	14 (14.3)	13 (13.3)	
HDL, median (Q1, Q3), n=196	1.2 (1.0, 1.5)	1.2 (1.0, 1.4)	1.2 (1.0, 1.5)	0.457
Triglycerides, median (Q1, Q3), n=196	1.4 (0.9, 2.0)	1.5 (1.0, 2.2)	1.3 (0.9, 1.9)	0.196
Trig < 1.7, %	123/196 (62.8)	56 (57.1)	67 (68.4)	0.257
Trig 1.7 – 2.2, %	32/196 (16.3)	19 (19.4)	13 (13.3)	
Trig >2.3, %	41/196 (20.9)	23 (23.5)	18 (18.4)	
Cardiac and inflammatory biomarkers				
High sensitivity troponin I, median (Q1, Q3), n=169	2.5 (2.5, 3.0)	2.5 (2.5, 3.0)	2.5 (2.5, 3.2)	0.654
hscTnI < 2.5 ng/L, %	109/169 (64.5)	46 (66.7)	63 (63.0)	0.848
hscTnI 2.5 – 45 ng/L, %	59/169 (34.9)	23 (33.3)	36 (36.0)	
hscTnI >= 45 ng/L, %	1/169 (0.6)	0 (0.0)	1 (1.0)	
High-sensitivity CRP, median (Q1, Q3), n=198	2.0 (0.8, 4.2)	2.4 (1.1, 4.4)	1.6 (0.7, 4.2)	0.112
hsCRP < 1mg/L, %	58/198 (29.3)	23 (23.5)	35 (35.0)	0.197
hsCRP 1 - 3 mg/L, %	65/198 (32.8)	41 (41.8)	34 (34.0)	
hsCRP >3 mg/L, %	75/198 (37.9)	34 (34.7)	31 (31.0)	

¹ Number of patients may not sum to the corresponding column totals where there are missing data for the laboratory marker.

² *Data for Hemoglobin and hemoglobin A1c (HbA1c) was available for Aga Khan University Hospital only.

³ p-value from Chi-square test or Fisher's exact test for categorical variables and unpaired two-sample Wilcoxon test for continuous variables, two-sided; bold p-values indicate statistical significance ($p < 0.05$).

Table S3: Cardiovascular risk factors, markers of myocardial injury and inflammation by Framingham cardiovascular risk category

Variable	Framingham risk score classification (FRS lipid)			<i>p</i> -value for trend ¹
	Low	Intermediate	High	Two-sided
Overall				
All patients (%)	166 (83.0)	23 (11.5)	11 (5.5)	—
Male	58 (34.9)	14 (60.9)	7 (63.6)	0.006
Female	108 (65.1)	9 (39.1)	4 (36.4)	
Smoking				
Current smoker, %	5/166 (3.0%)	0/23 (0.0)	0/11 (0.0)	0.306
Ex-smoker, %	33/166 (19.9)	6/23 (26.1)	5/11 (45.5)	
Never smoker, %	128/166 (77.1)	17/23 (73.9)	6/11 (54.5)	
Diabetes, %	3/166 (1.8)	2/23 (8.7)	2/11 (18.2)	0.999
Hypertension ² , %	36/166 (21.7)	14/23 (60.9)	10/11 (90.9)	<0.001
Hyperlipidemia, %	0/164 (0.0)	1/22 (4.5)	0/11 (0.0)	0.145
Lipid profiles				
Total cholesterol, median (Q1, Q3)	4.5 (3.8, 5.0)	4.9 (4.3, 5.4)	5.1 (4.4, 6.4)	0.001
TC < 4.7, %	93/162 (57.4)	10/23 (43.5)	4/11 (36.4)	0.007
TC 4.8 – 5.1, %	20/162 (12.3)	2/23 (8.7)	0/11 (0.0)	
TC 5.2 – 6.1, %	23/162 (14.2)	6/23 (26.1)	1/11 (9.1)	
TC ≥ 6.2, %	26/162 (16.0)	5/23 (21.7)	6/23 (54.5)	
LDL, median (Q1, Q3)	3.0 (2.3, 3.5)	3.3 (2.4, 3.8)	3.6 (2.9, 4.5)	0.017
LDL < 2.6, %	65/162 (40.1)	8/23 (34.8)	2/11 (18.2)	0.016
LDL 2.6 – 3.3, %	47/162 (29.0)	4/23 (17.4)	2/11 (18.2)	
LDL 3.4 – 4.1, %	30/162 (18.5)	8/23 (34.8)	3/11 (27.3)	
LDL ≥ 4.2, %	12/162 (12.3)	3/23 (13.0)	4/11 (36.4)	
HDL, median (Q1, Q3)	1.2 (1.0, 1.5)	1.1 (0.9, 1.3)	1.0 (0.9, 1.2)	0.043
Triglycerides, median (Q1, Q3)	1.3 (0.9, 1.9)	1.9 (1.2, 3.1)	2.9 (1.8, 3.4)	<0.001
Trig < 1.7	110/162 (67.9)	11s/23 (47.8)	2/11 (18.2)	<0.001
Trig 1.7 – 2.2	26/162 (16.0)	3/23 (13.0)	3/11 (27.3)	
Trig >2.3	26/162 (16.0)	9/23 (39.1)	6/11 (54.5)	
Cardiac and inflammatory biomarkers				
High sensitivity troponin I, median (Q1, Q3)	2.5 (2.5, 2.7)	3.3 (2.5, 4.7)	3.3 (2.5, 7.1)	<0.001
hscTnI < 2.5 ng/L, %	100/140 (71.4)	6/18 (33.3)	3/11 (27.3)	<0.001
hscTnI 2.5 – 45 ng/L	39/140 (27.9)	12/18 (66.7)	8/11 (72.7)	
hscTnI ≥ 45 ng/L	1/140 (0.7)	0/18 (0.0)	0/11 (0.0)	
High-sensitivity CRP, median (Q1, Q3)	1.9 (0.8, 4.1)	2.9 (1.1, 5.3)	2.4 (0.9, 4.2)	0.283
hsCRP < 1mg/L	49/164 (29.9)	6/23 (26.1)	3/11 (27.3)	0.854
hsCRP 1 – 3 mg/L	54/164 (32.9)	6/23 (26.1)	5/11 (45.5)	
hsCRP >3 mg/L	61/164 (37.2)	11/23 (47.8)	3/11 (27.3)	
Creatinine, median (Q1, Q3)	83.0 (72.0, 100.5)	97.0 (87.0, 106.5)	91.0 (79.0, 104.5)	0.009

¹ *p*-values for trend were calculated using Jonckheere-Terpstra for continuous variables and Cochran-Armitage, or Cochran-Mantel-Haenszel tests, as appropriate, for categorical variables.

² Self-reported hypertension or measured systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or physician-prescribed blood pressure-lowering medications.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	Not provided as proof-of-concept study
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	6-7
		(c) Explain how missing data were addressed	7
		(d) If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	supplement

		(c) Consider use of a flow diagram	supplement
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
Outcome data	15*	Report numbers of outcome events or summary measures	Table 1 and 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 4
		(b) Report category boundaries when continuous variables were categorized	Tables 1 - 4
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplement
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.