### 1 Objectively measured physical activity among people with and

# without HIV in Uganda: associations with cardiovascular risk and coronary artery disease

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#### 25 ABSTRACT

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Background: Africa has a disproportionate burden of HIV-related cardiovascular
disease. We aimed to describe physical activity in people living with HIV (PLHIV) and
people without HIV (PWOH) in Uganda and characterize its relationship with the
presence of computed tomography angiography-detected (CCTA) coronary artery
disease (CAD).

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33 **Methods:** We performed a cross-sectional analysis of the Ugandan Study of HIV

- 34 Effects on the Myocardium and Atherosclerosis using Computed Tomography
- 35 (mUTIMA-CT) cohort. From 2017-2019, physical activity in PLHIV and PWOH was
- 36 assessed by accelerometry over seven days. Participants additionally underwent CCTA.
- 37 Univariable and multivariable modified Poisson regression was used to analyze the
- 38 relationship between physical activity and CAD presence.
- 39
- Results: 168 participants were analyzed. The median (IQR) age was 57 (53-58) years
  old and 64% were female. Males had more moderate-to-vigorous physical activity per
  week [68 minutes (12-144) vs 15 minutes (0-50), *P*<0.001] and less light physical</li>
  activity [788 minutes (497-1,202) vs [1,059 (730-1490), *P*=0.001] compared to females,
  but there was no difference by HIV status. After adjusting for age, which accounted for
  10% of the variation in steps taken, and sex, no significant associations were found
  between physical activity and coronary plaque.
- 47

48 Conclusion: Objectively measured physical activity was low compared to guideline 49 recommendations, with males being somewhat more active than females and without 50 significant differences by HIV status. Physical activity was not associated with the 51 presence of CAD independently of age and sex. 52

53 Keywords: HIV, cardiovascular disease, sedentary, accelerometry, correlation

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#### 59 CLINICAL PERSPECTIVE

#### 60 What is new?

- For the first time, we describe objective physical activity patterns in people living with HIV (PLHIV) and people without HIV (PWOH) in the Ugandan context.
   Overall, few people met guideline recommendations for physical activity. Males had more moderate-to-vigorous physical activity and were more likely to meet guideline recommendations compared to females, without significant difference by HIV status.
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In contrast, females had more light physical activity compared to males. Although light physical activity appeared to have a stronger inverse relationship with coronary artery disease (CAD) in PLHIV compared to PWOH in stratified models, the relationship was significantly confounded by age and sex.

#### 73 What are the clinical implications?

- Larger studies are needed to further investigate the relationship between
   physical activity and CAD in Africa—including any modifying influence of sex or
   HIV status. In the meantime, our study suggests there is significant room to
   enhance physical activity in Uganda.
- Age informs the relationship between physical activity and CAD, and our study suggests efforts to emphasize exercise as the population ages may play a role in reducing CAD burden.

#### 82 INTRODUCTION

- 83 Africa is disproportionately impacted by HIV and HIV-related cardiovascular disease
- 84 (CVD). Mirroring outcomes in higher-resourced countries, increased life-expectancy due
- to more widely available antiretroviral therapy (ART) has led to higher rates of age-
- 86 related comorbidities, such as CVD, non-Autoimmune Deficiency Syndrome (AIDS)
- 87 malignancies and liver disease<sup>1</sup>. Over the past two decades, the global burden of HIV-
- 88 associated CVD has tripled and accounts for 2.6 million disability-adjusted life-years per
- 89 year, with the highest impact in Africa and the Asia-Pacific areas<sup>2</sup>. Key risk factors for
- 90 CVD in people living with HIV (PLHIV) include hypertension<sup>3</sup>, diabetes mellitus<sup>4</sup>,
- 91 dyslipidemia<sup>5,6</sup>, obesity<sup>3</sup>, inflammation<sup>6</sup>, low nadir CD4+ count, and smoking<sup>3</sup>.
- 92
- 93 Physical activity is a key preventive factor for CVD. Physical activity and exercise
- 94 training interventions improve cardiovascular health, decrease CVD risk, and mitigate
- 95 morbidity and mortality in those with CVD<sup>6</sup>. For instance, eight weeks of moderate
- 96 intensity exercise resulted in improved aerobic fitness, reduced blood pressure and
- 97 increased CD4 cells for PLHIV in Nigeria<sup>7</sup>. Despite the proven benefits, the majority of
- 98 PLHIV in Africa do not seem to engage in regular physical activity<sup>8</sup>. However, most prior
- 99 research has relied on self-reported measures of physical activity, which has been
- 100 shown to overestimate physical activity compared to gold-standard objective measures
- 101 of physical activity, such as accelerometry<sup>9</sup>.
- 102
- 103 Atherosclerotic cardiovascular disease (ASCVD) risk can be assessed using risk
- 104 prediction scores or objective measures of subclinical disease; however, risk prediction
- 105 scores may not strongly correlate with subclinical disease in Africa. For example,
- 106 research conducted in Uganda and Botswana demonstrated only modest correlations
- 107 between pre-clinical atherosclerosis measures and the pooled cohort equation's ASCVD
- 108 risk score<sup>3</sup>. More research is needed to address non-traditional risk factors unique to
- 109 this region, including infectious and environmental factors such as latent tuberculosis
- and air pollution<sup>3</sup>. In the meantime, enhancing physical activity and fitness is a low-cost
- 111 approach to ASCVD risk reduction in Africa.
- 112
- 113 Our study was designed to compare objective measures of physical activity among
- 114 PLHIV and a similar population of people without HIV (PWOH), which has not
- 115 previously been described in Uganda. Secondly, we aimed to evaluate the relationship
- 116 between physical activity metrics and ASCVD risk, coronary artery disease (CAD)
- 117 presence by coronary computed tomography angiography (CCTA), and severity of CAD
- 118 by coronary CTA. Lastly, we sought to assess whether HIV status and/or sex modify the
- 119 relationship between physical activity and CAD.
- 120

# 121 METHODS

# 122 Participant Selection

- 123 The <u>Ugandan sTudy of HIV effects on the Myocardium and A</u>therosclerosis using
- 124 **C**omputed **T**omography (mUTIMA-CT), conducted in Kampala, Uganda, is an ongoing
- 125 prospective cohort investigation examining the impact of HIV on the myocardium and
- 126 atherosclerosis. In this phase of the study, PLHIV were age- (within 3 years) and sex-
- 127 matched in a 1:1 ratio with PWOH controls. PLHIV were recruited from the Joint Clinical

128 Research Centre (JCRC) in Lubowa, Uganda, which is near Kampala. PWOH were

- recruited from community or hospital-based internal medicine clinics in Kampala. To be
- eligible for inclusion, PLHIV must have been on ART for more than six months without
- any changes in regimen within 12 weeks prior to enrollment. All participants, regardless
- 132 of HIV status, were  $\geq$  45 years old and had at least one cardiovascular disease (CVD)
- risk factor, such as hypertension, low high-density lipoprotein cholesterol, diabetes
- mellitus, smoking, or a family history of early CAD. Exclusion criteria were a history of
   known CVD, peripheral artery disease, ischemic stroke, uncontrolled chronic
- 136 inflammatory conditions, pregnancy, use of chemotherapy or immunomodulating
- 137 agents, or an estimated glomerular filtration rate (eGFR) less than 30 ml/minute.
- 138
- The original cohort comprised of 100 PLHIV and 100 PWOH enrolled from April 2015 to
- 140 May 2017. Previous publications have detailed the findings and methods of the baseline
- 141 examination of the original cohort<sup>10–13</sup>. Follow-up examinations were conducted from
- 142 2017 to 2019, with total cohort size of 200 participants maintained by replacing those
- 143 lost to follow-up with age- and sex-matched individuals. This follow-up consisted of 2
- 144 study visits separated by 7 days, during which physical activity metrics were collected
- 145 via accelerometry. This current study is a cross-sectional analysis of those data among
- participants with accelerometry data duration of at least 10 hours per day on at least 4
- 147 days<sup>14,15</sup>, which is described as valid wear time.
- 148

The study protocol was approved by the University Hospitals Cleveland Medical Center
 Institutional Review Board, the JCRC Research Ethics Committee, and the Uganda
 National Council for Science and Technology, with all participants providing written

- 152 informed consent prior to any study procedures.
- 153

# 154 Physical Activity

155 Self-reported measures of physical activity were assessed using the International 156 Physical Activity Questionnaire – Short Form (IPAQ-SF). This was developed as a tool for international monitoring of physical activity and sedentary time<sup>16</sup>. The IPAQ-SF 157 contains a series of 7 questions, requiring participant recall of light, moderate, and 158 159 vigorous physical activity time, as well as sedentary time over the preceding 7 days. The 160 amount of light, moderate, and vigorous physical activity per day was multiplied by the 161 number of days performing those activities to get the amount of activity per week. The 162 amount of time spent sitting per day was multiplied by 7 to obtain the amount of

- 163 sedentary time per week.
- 164

165 Objective measures of physical activity were assessed by accelerometry. Participants

- 166 were instructed to wear an Actigraph®wGT3X+-BT monitor (Actigraph, LLC, Pensacola,
- 167 FL) for 7 days on their non-dominant hip. Physical activity metrics of interest were steps
- 168 per day, light physical activity time per week, moderate-to-vigorous physical activity time 169 per week, and sedentary time per week. The number of steps per day was derived by
- 170 dividing the number of total steps recorded by the number of valid wear days. Other
- 171 physical activity metrics were derived by dividing the amount of activity time by the
- 172 number of valid days and multiplying by 7. Data was sampled at 30 Hz, using 60-
- 173 second epochs and the normal filter. Bouted physical activity was used to measure

- physical activity accumulation over 10 minutes or more. Different intensities of physical 174
- activity were defined by adult cut-points for tri-axial accelerometers<sup>17</sup>. In this validation, 175
- 176 moderate-to-vigorous activity was defined as achieving at least 3 metabolic equivalents
- 177 and was predicted by achieving at least 2,960 triaxial counts per minute. Valid wear time
- 178 was determined by data recorded for at least 10 hours per day for at least 4 days.
- 179 Accelerometry data was analyzed using Actilife software.
- 180

#### 181 Atherosclerotic Cardiovascular Disease Risk

- 182 10-year ASCVD risk was quantified using the pooled-cohort equation<sup>18</sup>. The following 183 variables were utilized: age, sex, and smoking status were obtained by self-report; 184 diabetes was defined as a chart confirmed diagnosis or on medication for diabetes;
- 185 hypertension treatment was defined as receiving medication to lower blood pressure.
- 186 Systolic and diastolic blood pressure were obtained at the initial visit by trained study
- 187 staff. Total cholesterol, high density lipoprotein, and calculated low-density lipoprotein
- 188 concentrations were measured by the JCRC clinical lab from fasting blood drawn at the
- 189 initial visit. Notably, we chose to use the "other race" term, since the African American
- 190 term has not been validated in the East African population. Further, the nature of
- 191 atherosclerotic cardiovascular disease risk may be different in the East African
- 192 population compared to the population from which the pooled-cohort equation was
- derived<sup>10</sup>. Elevated ASCVD risk was defined as 10-year ASCVD risk ≥5%, which is the 193
- 194 threshold to consider use of statin therapy to reduce ASCVD risk<sup>18</sup>.
- 195

#### 196 **Coronary Artery Disease**

- 197 At visit 2, all participants underwent coronary computed tomography angiography
- 198 (CCTA) on a 128-slice Siemens Somatom scanner at Nsambya St. Francis Hospital in
- 199 Kampala. Participants were ineligible to have intravenous contrast for CCTA if their
- 200 estimated GFR was not greater than 60 mL/min/1.73m<sup>2</sup>. Data acquisition was
- 201 additionally limited for some participants by other technical reasons (e.g., inability to
- 202 adequately lower the heart rate with betablockers) (Figure 1). The acquisition and image
- 203 analysis protocols were developed in alignment with the Society of Cardiovascular Computed Tomography Guidelines<sup>19</sup>. Participants were given 100 mg of oral metoprolol 204
- 205 two hours prior to the scan. They were additionally given another 50 mg dose 30
- 206 minutes prior to the scan if the heart rate was elevated above 60 beats per minute.
- 207
- The CT scans were first read by a local radiologist for clinically significant findings and 208
- 209 were subsequently read offline in batch by a single expert reader (MSB) for research.
- 210 Scans that were of poor technical quality were excluded from analysis. Segment
- 211 involvement score (SIS) was defined as the total number of disease segments.
- 212 Segment severity score (SSS) was calculated using a luminal obstruction weight for that
- 213 segment (x1 if <25% obstruction, x2 if 25-50%, x3 if 50-70%, x4 if 70-99% and x5 if 214 totally occluded), giving a
- 215
- maximum possible SSS of 90 for an 18-segment model. The presence of CAD was
- 216 defined as SIS>0 and more severe CAD was defined as an SSS greater than the
- 217 median among those with CAD.
- 218
- 219 **Statistical Analysis**

220 Demographic and clinical characteristics were described by frequency (percent) for 221 categorical variables and median (interquartile range) for continuous variables, stratified 222 by HIV status and sex. Physical activity measures were described in a similar manner. 223 Spearman's correlation coefficient was used to evaluate the relationship between selfreported and gold-standard objective measures of physical activity. Bland-Altman plots 224 225 were used to assess the degree of agreement between the two measures of physical 226 activity. The objective measures were subtracted from the self-reported measures to 227 obtain measurement differences and the limits of agreement were defined as the mean 228 difference ± 1.96 times the standard deviation of the differences. Spearman's correlation 229 was additionally used to assess the relationship between age and objective measures 230 of physical activity. Additionally, the Wilcoxon rank-sum test was used to compare 231 physical activity metrics in their continuous version across binary subgroups of HIV 232 status and sex. Chi-square tests were used to compare the proportion of those 233 achieving at least 150 minutes of moderate-to-vigorous exercise per week and those 234 achieving at least ten thousand steps per day by HIV status and sex.

235

236 Unadjusted and adjusted Poisson regression models with robust standard errors were 237 used to estimate prevalence ratios to analyze the relationship between binary measures 238 of physical activity, by median cut points, with elevated ASCVD risk, presence of CAD 239 among those with available CTA data, and presence of more severe CAD among those 240 with CAD. Binary measures of physical activity were used to meet the linearity 241 assumption of log transformation of the outcomes of interest with their physical activity 242 predictors. Median cut points were used to allow for sufficient sample size on both sides 243 of the selected cut points. Covariates – age and sex – were chosen a priori to build the 244 adjustment models. HIV status and sex interaction terms, along with likelihood ratio

- tests, were used individually to assess for effect modification in the relationship between
- binary objective physical activity metrics and the presence of CAD. A schematic of the
- 247 data analysis approach may be found in Supplementary Figure 1.
- 248

R version 4.3.1 was used for analysis: *P*<0.05 was considered statistically significant.

250 251 **RESULTS** 

## 252 Study cohort

The cohort began with 200 participants (Figure 1). The overall cohort for this analysis included 168 participants with valid accelerometry wear time, 48% of whom were PLHIV. 139 participants among those with valid accelerometry wear time had coronary angiography available for analysis (46% PLHIV). The most common reasons for missing coronary angiography were tachycardia and low eGFR.

258

# 259 Baseline characteristics of study participants

260 The median (IQR) age of the overall cohort was 57 (53, 62) years old and 64% were

261 female (Table 1). The median age was similar across HIV status and sex. 84% of PLHIV

had viral load suppression, and males were more likely to have HIV viral load

suppression than females (94% vs 77%). Overall, smoking rates were low (2.4%) and

264 no females reported smoking. The median systolic blood pressure was higher in males

265 than in females [155 mmHg (139-171) vs 146 (131-162)]. Males had higher ASCVD 10-

266 year risk than females [13% (8-24) vs 6% (3-10)]. Males had lower body mass index
267 than females [25 (23-28) vs 31 (27-34)].

268

# 269 Relationship between self-reported and objective measures of physical activity

270 There was no statistically significant correlation between self-reported measures of

- 271 physical activity and objective gold-standard measures of physical activity ( $\rho$ =0.06,
- 272 P=0.529 for sedentary time; p=-0.04, P=0.703 for light activity time; p=-0.16, P=0.172
- for moderate-to-vigorous activity time; Supplementary Figure 2). Additionally,
- 274 participants overestimated their moderate-to-vigorous activity and underestimated their
- light activity; and these errors in estimation were enhanced as self-reported or
- objectively measured physical activity increased. Objective measures of physical activity
- were used for the remainder of the analysis.
- 278

# 279 Objective physical activity outcomes of study participants

- The median (IQR) accelerometry valid wear days for the total cohort was 6 (6-7) days 280 281 during the 7 days in which objective measures of physical activity were collected. The 282 median step counts per day was higher for males than for females [6,534 steps (5,073-9,178) vs 5,382 steps (3,808-7,316), P= 0.005], and males were more likely to achieve 283 284 at least 10,000 steps per day than females (16% vs 5%, P=0.023). Males had more 285 moderate-to-vigorous physical activity per week [68 minutes (12-144) vs 15 minutes (0-286 50), P<0.001] than females and a greater proportion of men achieved at least 150 287 minutes of moderate-to-vigorous physical activity per week than females (21% vs 5%. 288 P=0.002). Males had less light physical activity per week [788 minutes (497-1,202) vs 289 [1,059 (730-1490), P=0.001] than females. There was no significant difference in 290 objective physical activity outcomes when comparing PLHIV and POWH.
- 291

There was a statistically significant positive correlation between age and sedentary time (Spearman's correlation coefficient,  $\rho$ =0.22, P=0.004) and a statistically significant negative correlation between age and moderate-to-vigorous physical activity ( $\rho$ =-0.25, P=0.001), and steps per day ( $\rho$ =-0.31, P<0.001) (Supplementary Figure 3). The negative correlation between age and light physical activity was not statistically significant ( $\rho$ =-0.12, P=0.113).

298

# Association of objective physical activity outcomes and atherosclerotic cardiovascular disease risk and coronary artery disease

301 Prior to adjusting for age and sex, participants who achieved at least 15.7 hours of light physical activity per week (the median in the total cohort) had non-statistically significant 302 303 19% lower prevalence of elevated ASCVD risk compared to those who had less than 304 15.7 hours of light physical activity per week (unadjusted prevalence ratio (PR) 0.807, 95% CI 0.649-1.002, P=0.053). This association was weakened after adjustment for age 305 306 and sex. Prior to adjustment, there was a general non-statistically significant association 307 of decreased risk of elevated ASCVD risk with more physical activity and increased risk 308 of elevated ASCVD risk with more sedentary time for the overall cohort.

309

310 For the total cohort, no statistically significant association was found between physical

311 activity metrics and presence of CCTA-detected CAD prior to and after adjustment. Prior

- to adjustment, there was a general non-statistically significant trend of lower risk of CTA-
- detected CAD with more physical activity and greater risk of CAD with greater sedentary
- time for the overall cohort.
- 315
- After stratifying by HIV status and prior to adjustment, there was a trend of lower risk of
- 317 CT-detected CAD in PLHIV with more light physical activity compared to PWOH
- 318 [unadjusted PR 0.259, 95% CI 0.057-1.188, P=0.082 vs unadjusted PR 1.461, 95% CI
   319 0.675-3.160, P=0.336] with a statistically significant interaction P-value of 0.025. After
- 320 adjustment, the interaction was no longer statistically significant.
- 321
- 322 Similarly, there was no significant interaction of sex on the relationship between physical 323 activity metrics and the presence of CTA-detected CAD prior to and after adjustment.
- 324
- Prior to and after adjustment, there was a general non-statistically significant trend of lower risk of more severe CTA-detected CAD with more physical activity and higher risk
- 327 of more severe CTA-detected CAD with more sedentary time.
- 327 of more severe CTA-detected CAD with more sedentary time328

# 329 DISCUSSION

- 330 Self-reported measures of physical activity, such as IPAQ-SF have been described as a
- cost-effective method to assess physical activity<sup>20</sup>. In this study, we collected and
- 332 compared self-reported and objective measures of physical activity by way of the IPAQ-
- 333 SF and accelerometry, respectively. We demonstrated self-reported moderate-to-
- 334 vigorous activity was overestimated while self-reported light activity was
- 335 underestimated, and we did not find a statistically significant correlation between self-
- reported and objective physical activity metrics. These results were consistent with other investigations applying to validate IBAO  $SE^9$  and highlights the potential rate of chiesting
- investigations seeking to validate IPAQ-SF<sup>9</sup>, and highlights the potential role of objective
   measurement instruments in physical activity studies.
- 339
- This is the first study to describe objective measures of physical activity among PLHIV and PWOH living in Uganda. While we did not find a significant difference in physical activity patterns between well-matched PLHIV and PWOH, we found significant differences between males and females. On average, males had 21% more steps per day and spent almost five times as much time engaging in moderate-to-vigorous physical activity. On the other hand, females spent 34% more time in light physical
- activity. These results are generally in line with traditional gender roles among males
  and females observed in Uganda<sup>13</sup>. Importantly, objectively measured physical activity
  was low in this population in urban Uganda, as only 11% of participants overall achieved
- moderate-to-vigorous physical activity time of at least 150 minutes, with just 5% of females achieving this target. Several studies have demonstrated the all-cause and cardiovascular mortality benefit from achieving this level of physical activity<sup>21–23</sup>, and this target has been recommended by several international cardiovascular organizations for the mitigation of ASCVD<sup>24–27</sup>.
- 353 354

A large volume of population-level evidence supports the reduction in ASCVD events with increased physical activity<sup>28,21–23</sup>, and this benefit may be mediated by an inverse relationship between physical activity and sub-clinical cardiovascular disease<sup>29</sup>. Despite 358 this, we did not find a significant association between the varied levels of physical activity and inactivity with elevated ASCVD risk after adjusting for age and sex. Similarly, 359 360 we did not find a significant association between physical activity metrics with presence 361 of CTA-detected CAD or severity of CAD with multivariable analyses. However, our 362 univariable analyses demonstrate an overall non-statistically significant trend of lower 363 risk of elevated ASCVD risk, CTA-detected CAD, and CAD severity with higher levels of 364 physical activity metrics for the overall cohort, with an opposite relationship with 365 increased sedentary time. This trend was maintained in the multivariable analysis for 366 CAD severity. Additionally, we demonstrated that increased light physical activity had a 367 non-statistically significant association with lower prevalence of elevated ASCVD risk, 368 with a 19% prevalence reduction for the total cohort. We also demonstrated a significant 369 moderating effect of HIV, such that the inverse relationship between light physical 370 activity and CAD was stronger among PLHIV compared to PWOH. While larger studies 371 are needed to further characterize this finding, it does suggest that even light levels of physical activity may help reduce the burden of HIV-related cardiovascular disease. 372 373

- We further assessed the correlation of age with physical activity metrics. We found that age was positively correlated with sedentary time. We demonstrated that age was
- 376 negatively correlated with moderate-to-vigorous physical activity time and steps per day
- and explained as much as 10% of the variation in steps per day. We further
- demonstrated a trend of negative correlation between age and light physical activity
  time. These correlations help inform the relationship between physical activity metrics
  and ASCVD risk, CAD, and presence of more severe CAD within the Ugandan context.
  Given the trends of physical activity benefits seen in this study, it may indicate a role for
  encouraging lifelong exercise, especially as one ages. This further attracts attention to
  the potential need to promote physical activity in Africa, especially as it continues to
  industrialize.
- 384 385

# 386 Strengths and Limitations

This work contains several important strengths including the use of gold-standard objective measures of physical activity and atherosclerotic CAD. We have shown that self-reported physical activity is not a good measure of objectively measured physical activity, arguing for the use of objective measures whenever feasible. Our prior research has also shown that ASCVD risk scores do not correlate well with objectively measured subclinical atherosclerosis in Uganda, and thus risk scores should not be used as a surrogate marker of subclinical ASCVD<sup>10</sup>.

394

395 However, our study also has limitations. First, it is possible that our sample size was 396 not sufficient to detect significant associations between physical activity metrics and the 397 outcomes described. Secondly, this was a cross-sectional analysis where measures of 398 physical activity were assessed for a short period of 7 days. Although wearing the 399 physical activity monitor during 7 days with a minimum of 4 days of valid data is recommended<sup>30</sup>, this did not capture the majority of lifetime physical activity habits that 400 401 would inform the relationship with ASCVD risk, CAD, and severity of CAD. Thirdly, it is 402 possible some participants may have altered their physical activity habits with the 403 awareness of monitoring. Additionally, as this was an observational study, the

- 404 univariable trends and associations seen cannot be construed as causal. Lastly, this
- was a single-center study based near the commercial capital of Uganda and the resultsmight not be generalizable to those living in more rural areas.
- 407

### 408 CONCLUSION

- 409 In this unique study from Africa, objectively measured physical activity was low in Urban
- 410 Uganda compared to guideline recommendations, with males being somewhat more
- 411 active than females and without significant differences by HIV status. Physical activity
- 412 was not statistically significantly associated with the presence of CAD independently of
- 413 age and sex. However, these hypothesis generating findings require further research
- 414 with larger studies.
- 415

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- 419

#### 420 **DISCLOSURES**

421 The authors have no relevant conflicts of interest.

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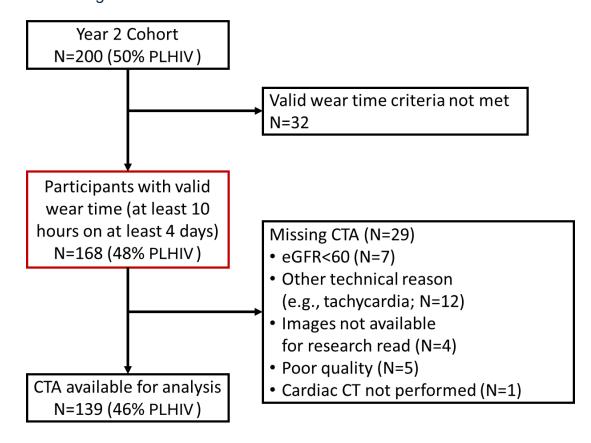
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- 539 Figure 1. Derivation of the study population from the mUTIMA-CT cohort. Definitions:
- 540 PLHIV, people living with HIV; CTA, computed tomography angiography; eGFR, 541 estimated glomerular filtration rate.



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	HIV (+) Male	HIV (+) Female	HIV (-) Male	HIV (-) Female
	N = 32	N = 48	N = 29	N = 59
Age in years, median (IQR)	55.00 (51.50,	56.50 (53.00,	60.00 (51.00,	58.00 (55.00,
	62.25)	62.00)	62.00)	63.50)
Diabetes, (%)	9 (28.1)	14 (29.2)	17 (58.6)	22 (37.3)
Hypertension, (%)	26 (81.2)	43 (89.6)	23 (79.3)	56 (94.9)
Smoking status, (%)				
Smoke every day	1 (3.1)	0 (0.0)	1 (3.4)	0 (0.0)
Smoke, not every day	2 (6.2)	0 (0.0)	0 (0.0)	0 (0.0)
No smoking	29 (90.6)	48 (100.0)	28 (96.6)	59 (100.0)
Alcohol use frequency, (%)				
Never	20 (62.5)	41 (89.1)	17 (60.7)	44 (78.6)
Monthly or less	9 (28.1)	3 (6.5)	3 (10.7)	8 (14.3)
2-4 times per month	0 (0.0)	1 (2.2)	5 (17.9)	2 (3.6)
2-3 times per week	2 (6.2)	0 (0.0)	3 (10.7)	0 (0.0)
4 or more times per week	1 (3.1)	1 (2.2)	0 (0.0)	2 (3.6)
Alcohol drinks per use, (%)			, , ,	(
1 or 2	8 (66.7)	4 (66.7)	5 (45.5)	11 (84.6)
3 or 4	4 (33.3)	1 (16.7)	5 (45.5)	2 (15.4)
5 or 6	0 (0.0)	1 (16.7)	1 (9.1)	0 (0.0)
Systolic blood pressure, median (IQR)	153 (142, 171)	146 (128, 161)	155 (132, 171)	144 (132, 163)
ASCVD 10-year risk score, median (IQR)	11 (7, 21)	5 (3, 8)	17 (11, 24.83)	6 (3, 12)
Total cholesterol, median (IQR)	201 (1651, 235)	214(182, 242)	194 (167, 218)	195 (180, 233)
Body mass index, median (IQR)	24 (22, 27)	28 (25, 33)	28 (24, 31)	33 (30, 34)
Waist hip ratio, median (IQR)	0.93 (0.91, 0.98)	0.88 (0.83, 0.92)	0.94 (0.88, 0.97)	0.86 (0.81, 0.91
Years with HIV, median (IQR)	14.02 (12.26, 15.92)	13.97 (11.97, 4.54)	-	-
Years with ART, median (IQR)	12.74 (10.73,	4.54) 12.41 (9.80,		

	14.71)	14.00)		
HIV viral load suppressed, (%)	30 (93.8)	37 (77.1)	-	-
Viral load if not suppressed, %				
21-500	1 (3.1)	9 (18.8)	-	-
501-1,000	0 (0.0)	0 (0.0)	-	-
>1,000	1 (3.1)	2 (4.2)	-	-

Definitions: IQR, interquartile range; ART, antiretroviral therapy; ASCVD, atherosclerotic cardiovascular disease risk.

Table 2. Objectively measured physical activ	vity stratified by (a) HIV statu	s and (b) sex	
(a). Stratified by HIV status			
	PLHIV, n=80	PWOH, n=88	P-value
Valid wear days, median (IQR)	6.00 (6.00, 7.00)	6.00 (5.75, 7.00)	0.993
Total step counts per day, median (IQR)	5859.05 (4308.05, 7735.14)	5814.08 (4027.48, 7556.35)	0.574
Light activity time per week in minutes, median (IQR)	949.08 (666.87, 1369.08)	934.00 (649.03, 1342.00)	0.881
Moderate-to-vigorous activity time per week in minutes, median (IQR)	18.38 (0.00, 95.88)	35.50 (0.00, 74.31)	0.889
Sedentary time per week in minutes, median (IQR)	1234.50 (951.56, 1806.58)	1,301.00 (883.31, 1959.13)	0.906
Achieved 150 minutes moderate-to-vigorous activity or more per week, (%)	11 (13.8)	7 (8.0)	0.335
Achieved 10 thousand steps or more per day, %)	9 (11.2)	6 (6.8)	0.462
(b). Stratified by sex			
	Male, n=61	Female, n=107	P-value
Valid wear days, median (IQR)	6.00 (6.00, 7.00)	6.00 (6.00, 7.00)	0.757
Total step counts per day, median (IQR)	6534.00 (5073.00, 9177.50)	5382.33 (3807.58, 7316.42)	0.005
Light activity time per week in minutes, median (IQR)	788.00 (497.00, 1201.67)	1059.00 (730.40, 1490.42)	0.001
Moderate-to-vigorous activity time per week in minutes, median (IQR)	68.00 (11.67, 143.50)	15.17 (0.00, 49.50)	<0.001
Sedentary time per week in minutes, median (IQR)	1320.67 (1079.17, 1850.33)	1203.00 (873.25, 1916.83)	0.303
Achieved 150 minutes moderate-to-vigorous activity or more per week, (%)	13 (21.3)	5 (4.7)	0.002
Achieved 10 thousand steps or more per day, %)	10 (16.4)	5 (4.7)	0.023

Definitions: IQR, interquartile range; PLHIV, people living with HIV; PWOH, people without HIV

Table 3. Unadjusted and adjusted associations of objective physical activity metrics with ASCVD 10-year risk ≥ 5%, n=168

	Unadjusted		Adjusted	
	PR (95% CI)	P-value	PR	P-value
Total step counts per day $\geq$ 5.9 thousand	0.954 (0.770- 1.181)	0.663	1.042 (0.850- 1.277)	0.694
Light activity time per week ≥ 15.7 hours	0.807 (0.649- 1.002)	0.053	0.991 <sup>´</sup> (0.821- 1.195)	0.922
Moderate-to-vigorous activity time per week $\geq 0.4$ hours	0.909 (0.734- 1.126)	0.383	0.934 (0.770- 1.134)	0.491
Sedentary time per week ≥ 21 hours	1.049 (.847-1.299)	0.663	0.864 (0.714- 1.045)	0.131

Definitions: ASCVD, atherosclerotic cardiovascular disease risk; PR, prevalence ratio; CI, confidence interval. Adjusted for age and sex.

Table 4. Unadjusted and adjusted associations of objective physical activity metrics with presence of CTAdetected CAD for (a) the overall cohort with available CTA, stratified by HIV status [(b) and (c)] and by sex [(d) and (e)]

## (a) Participants with available CTA, n=139

Line Pro-	4 - 1				
PR (95% CI)	<i>P</i> -value	PR	<i>P</i> -value	$P_i$	
0.904 (0.467-	0.765	1.699 (0.854-	0.131	-	
1.752)		3.381)			
0.878 (0.453-	0.701	1.459 (0.691-	0.322	-	
1.702)		3.079)			
0.678 (0.347-	0.256	0.957 (0.534-	0.883	-	
1.326)		1.717)			
1.240 (0.638-	0.526	0.715 (0.364-	0.331	-	
2.409)		1.406)			
PLWHIV,	n=64	PWOH, r	<b>1=75</b>		
PR (95% CI)	<i>P</i> -value	PR (95% CI)	<i>P</i> -value	$P_i$	
0.778 (0.213-	0.704	1.027 (0.485-	0.945	0.162	
2.839)		2.176)			
0.259 (0.057-	0.082	1.461 (0.657-	0.336	0.025	
1.188)		3.160)			
0.939 (0.257-	0.925	0.583 (0.270-	0.171	0.137	
3.434)		1.261)			
2.012 (0.525-	0.308	0.974 (0.460-	0.945	0.121	
7.713)		2.063)			
PLWHIV,	n=64	<b>PWOH</b> , n=75			
PR (95% CI)	P-value	PR (95% CI)	P-value	$P_i$	
1.151 (0.296-	0.840	2.332 (1.031-	0.042	0.332	
		5.277)			
0.300 (0.068-	0.112	2.436 (1.019-	0.045	0.192	
	PR (95% CI) 0.904 (0.467- 1.752) 0.878 (0.453- 1.702) 0.678 (0.347- 1.326) 1.240 (0.638- 2.409) PLWHIV, PR (95% CI) 0.778 (0.213- 2.839) 0.259 (0.057- 1.188) 0.939 (0.257- 3.434) 2.012 (0.525- 7.713) PLWHIV, PR (95% CI) 1.151 (0.296- 4.472)	0.904 (0.467-       0.765         1.752)       0.878 (0.453-       0.701         0.878 (0.453-       0.701         1.702)       0.678 (0.347-       0.256         1.326)       1.240 (0.638-       0.526         2.409)	PR (95% Cl) <i>P</i> -value         PR           0.904 (0.467-         0.765         1.699 (0.854-           1.752)         3.381)           0.878 (0.453-         0.701         1.459 (0.691-           1.702)         3.079)           0.678 (0.347-         0.256         0.957 (0.534-           1.326)         1.717)           1.240 (0.638-         0.526         0.715 (0.364-           2.409)         1.406)           PLWHIV, n=64         PWOH, n           PR (95% Cl) <i>P</i> -value         PR (95% Cl)           0.778 (0.213-         0.704         1.027 (0.485-           2.839)         2.176)         2.176)           0.259 (0.057-         0.082         1.461 (0.657-           1.188)         3.160)         0.939 (0.257-           0.925         0.583 (0.270-         3.434)           2.012 (0.525-         0.308         0.974 (0.460-           7.713)         2.063)         PWOH, n           PR (95% Cl) <i>P</i> -value         PR (95% Cl)           1.151 (0.296-         0.840         2.332 (1.031-           4.472)         5.277)         5.277)	PR (95% Cl)         P-value         PR         P-value           0.904 (0.467-         0.765         1.699 (0.854-         0.131           1.752)         3.381)         0.0378         0.453-         0.701         1.459 (0.691-         0.322           1.702)         3.079)         0.678 (0.347-         0.256         0.957 (0.534-         0.883           1.326)         1.717)         1.240 (0.638-         0.526         0.715 (0.364-         0.331           2.409)         1.406)         PWOH, n=75           PR (95% Cl)         P-value         PR (95% Cl)         P-value           0.778 (0.213-         0.704         1.027 (0.485-         0.945           2.839)         2.176)         0.259 (0.057-         0.082         1.461 (0.657-         0.336           0.939 (0.257-         0.925         0.583 (0.270-         0.171         3.434)         1.261)           2.012 (0.525-         0.308         0.974 (0.460-         0.945         7.713)         2.063)           PLWHIV, n=64         PWOH, n=75           PR (95% Cl)         P-value         P.value         1.151 (0.296-         0.840         2.332 (1.031-         0.042           1.151 (0.296-         0.840         2.332 (1.031-	

Moderate-to-vigorous activity time per week ≥ 0.4 hours	1.110 (0.324- 3.802)	0.868	1.130 (0.572- 2.232)	0.726	0.440
Sedentary time per week $\geq$ 21 hours	1.229 (0.290- 5.203)	0.780	0.545 (0.249- 1.193)	0.129	0.421

# (d) Stratification by sex status, unadjusted

	Male, n=51		Female,	Female, n=88	
	PR (95% CI)	<i>P</i> -value	PR (95% CI)	<i>P</i> -value	$P_i$
Total step counts per day $\geq$ 5.9 thousand	1.129 (0.379- 3.366)	0.828	0.767 (0.321- 1.831)	0.550	0.843
Light activity time per week $\geq$ 15.7 hours	0.886 (0.297- 2.641)	0.828	0.900 <sup>°</sup> (0.379- 2.137)	0.810	0.977
Moderate-to-vigorous activity time per week $\geq$ 0.4 hours	0.800 <sup>°</sup> (0.273- 2.348)	0.685	0.548 <sup>´</sup> (0.211- 1.424)	0.217	0.769
Sedentary time per week ≥ 21 hours	1.556 (0.519- 4.666)	0.431	1.067 <sup>°</sup> (0.454- 2.508)	0.882	0.866

### (e) Stratification by sex status, adjusted

	Male, n=51		Female, i		
	PR (95% CI)	<i>P</i> -value	PR (95% CI)	<i>P</i> -value	$P_i$
Total step counts per day $\geq$ 5.9 thousand	2.217 (0.861- 5.710)	0.099	1.455 (0.566- 3.740)	0.437	0.567
Light activity time per week ≥ 15.7 hours	1.535 (0.401- 5.884)	0.532	1.400 (0.588- 3.336)	0.448	0.805
Moderate-to-vigorous activity time per week ≥ 0.4 hours	1.462 (0.608- 3.515)	0.396	0.704 (0.304- 1.629)	0.412	0.349
Sedentary time per week ≥ 21 hours	0.830 (0.258- 2.676)	0.755	0.675 (0.297- 1.534)	0.348	0.958

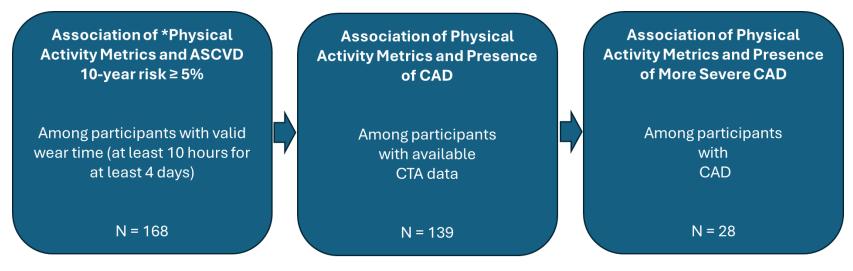
Definitions: CAD, coronary artery disease; PR, prevalence ratio; CI, confidence interval; P<sub>i</sub>, P-value for interaction. Adjusted for age and sex.

Table 5. Unadjusted and adjusted associations of objective physical activity metrics with more severe CTAdetected CAD, n=28

	Unadjusted		Adjusted	
	PR (95% CI)	P-value	PR	P-value
Total step counts per day $\geq$ 5.9 thousand	0.429 (0.138- 1.329)	0.142	0.480 (0.128- 1.797)	0.276
Light activity time per week $\geq$ 15.7 hours	0.429 (0.138- 1.329)	0.142	0.464 (0.138- 1.559)	0.214
Moderate-to-vigorous activity time per week $\geq 0.4$ hours	0.571 <sup>°</sup> (0.185- 1.763)	0.330	0.624 (0.199- 1.955)	0.418
Sedentary time per week ≥ 21 hours	2.022 (0.653- 6.262)	0.222	1.676 (0.464- 6.051)	0.430

Definitions: CAD, coronary artery disease; PR, prevalence ratio; CI, confidence interval. Adjusted for age and sex.

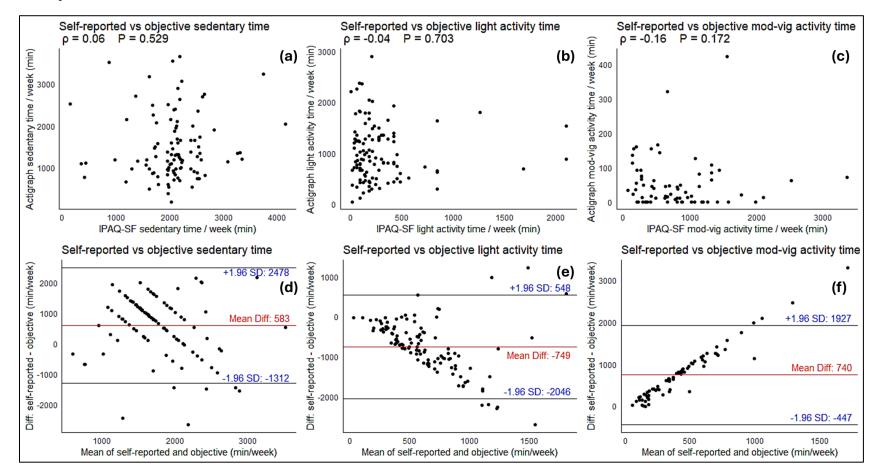
Supplementary Figure 1. Depicts flow of data analysis among study participants. Objective physical activity metrics were used for analysis. Definitions: ASCVD, atherosclerotic cardiovascular disease risk; CAD, coronary artery disease.



\*Binary cut point for physical activity metrics = median values of individual metrics among those with valid wear time

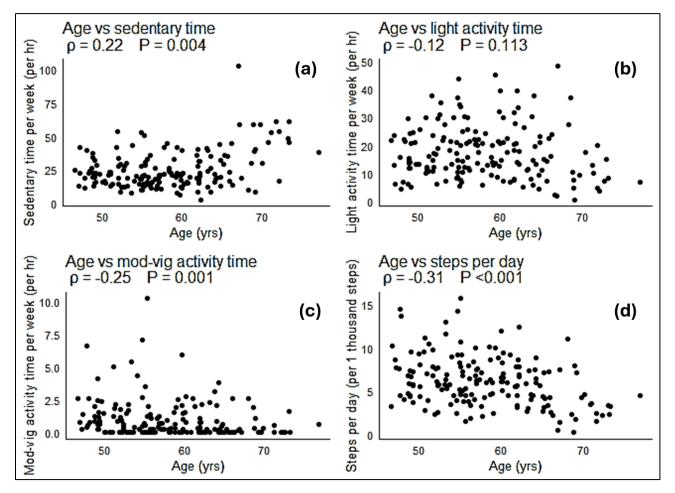
- Steps per day 5,900 steps
- Light physical activity per week 15.7 hours
- Moderate-to-vigorous activity per week 0.4 hours
- Sedentary time per week 21.0 hours

Supplementary Figure 2. Relationship between self-reported and objective measures of physical activity. (a), (b), and (c) demonstrate scatter plots and Spearman's correlation for self-reported vs objectively measured sedentary, light activity, and moderate-to-vigorous activity time, respectively. (d), (e), and (f) demonstrate Bland-Altman plots discerning the degree of agreement between self-reported vs objectively measured sedentary, light activity, and moderate-to-vigorous activity time.



Definitions:  $\rho$  = rho = Spearman's coefficient; Diff, difference; SD, standard deviation

Supplementary Figure 3. Correlation of age with objective measures of (a) sedentary time, (b) light activity time, (c) moderate-to-vigorous activity time, and (d) steps per day.



Definitions:  $\rho$  = rho = Spearman's coefficient