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Hypertension incidence among middle-aged and older adults: Findings from a 5-year prospective study in rural South Africa, 2010-2015

Brian Houle,^{1,2,3} Thomas Gaziano,^{4,5} Nicole Angotti,^{2,3,6} Sanyu A Mojola,⁷ Chodziwadziwa W Kabudula,^{2,8} Stephen M Tollman,^{2,8,9} F Xavier Gómez-Olivé^{2,8,10}

1 School of Demography, The Australian National University, Canberra, ACT, Australia

2 MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

3 Institute of Behavioral Science, University of Colorado Boulder, Boulder, Colorado, USA

4 Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA, USA

5 Harvard Medical School, Harvard University, Boston, MA, USA

6 Department of Sociology and Center on Health, Risk and Society, American University, Washington, DC, USA

7 Department of Sociology and Woodrow Wilson School of Public and International Affairs, and Office of Population Research, Princeton University, Princeton, NJ, USA

8 INDEPTH Network, Accra, Ghana

9 Centre for Global Health Research, Umeå University, Umeå, Sweden

10 Harvard Center for Population and Development Studies, Harvard University, Cambridge, MA, USA

Correspondence to: Brian Houle; brian.houle@anu.edu.au

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ABSTRACT

Objectives: There have been urgent calls for longitudinal cohort studies in sub-Saharan Africa to understand the epidemiology of cardiovascular disease as a basis for intervention. We estimated incident hypertension and associated sociodemographic, health and behavioural risk factors in a population aged 40 and older over a 5-year period.

Design: We assessed the association between incident hypertension and sociodemographic, health and behavioural factors using Poisson regression. We adjusted for nonresponse in 2015 using inverse probability sampling weights from a logistic regression including sex and age at baseline.

Setting: Rural South Africa.

Participants: We used a population-based cohort of normotensive adults in 2010 who were ages 40 and older at retest in 2015.

Results: Of 676 individuals completing baseline and 5-year follow-up, there were 193 incident cases of hypertension. The overall hypertension incidence rate was 8.374/100 person-years. In multivariable analyses, those that became hypertensive were more likely to have a high waist circumference (incidence rate ratio (IRR): 1.557 95% CI: 1.074-2.259) and be employed (IRR: 1.579 95% CI 1.071-2.329) at baseline. Being HIV-positive (regardless of antiretroviral therapy status) at baseline was inversely associated with incident hypertension.

Conclusions: Over a 5-year period, 29% of respondents developed hypertension. As the burden of hypertension continues to increase in sub-Saharan Africa, this study provides evidence of modifiable risk factors in a poor, rural South African setting to inform public health prevention strategies and programs. Continued longitudinal follow-up is needed to understand the complex interplay of noncommunicable and infectious diseases and their underlying and modifiable risk factors.

Keywords: Hypertension; incidence; South Africa; rural population; cohort

Strengths and limitations of this study

- In response to the urgent call for longitudinal sub-Saharan African studies, we provide longitudinal evidence on hypertension incidence from a population-based cohort in rural South Africa.
- Our results that being HIV-positive was inversely related to increased BP may be sensitive to survivorship bias if those who died due to HIV/AIDS over the five-year period were also more likely to develop hypertension.
- A longer period of follow-up is needed to assess the effects of HIV and ART on hypertension and related cardiometabolic conditions.

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INTRODUCTION

Hypertension is one of the most important noncommunicable disease (NCD) risk factors and the largest contributor to the global burden of disease, with high blood pressure accounting for 7% of global disability-adjusted life years.¹ The burden of hypertension is greatest in low and middle-income countries (LMIC),² and has increased rapidly in sub-Saharan Africa.^{3–7} A study of people aged 50 years and over from six countries found markedly high prevalence in South Africa (77.9%).⁸

Rapid demographic and epidemiological changes in LMICs, such as population aging, are expected to dramatically increase hypertension prevalence. Results from a modelling study found that without any changes in the age-specific prevalence of hypertension, the hypertensive population in South Africa is expected to grow by 105% by 2050.⁹ These dramatic changes on the epidemiology of hypertension are further complicated by a lack of awareness by those with a hypertensive condition, with serious consequences of a low proportion of hypertensive individuals being on treatment.^{10–12} In South Africa, an estimated 38–64% of hypertensives were aware of their status and 7.8–22.8% effectively controlled.^{8 13}

Longitudinal data from sub-Saharan Africa are needed to examine changes on population-specific hypertension risk factors over time,¹⁴ particularly given differences in socio-cultural environments and related health factors (e.g., diet, concurrent infectious diseases), and differentials in rural versus urban risk factor level.¹⁵ This is particularly important as increased availability of antiretroviral therapy (ART) has reduced HIV/AIDS mortality^{16 17} and the subsequent aging of people living with HIV.¹⁸ The aging population will be at higher risk of developing hypertension, and the effect of HIV and ART may also increase the incidence of hypertension.^{19–22} In South Africa, an emerging dual burden of disease, along

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with urban-rural differences due to the legacy of the apartheid era also highlight the importance of understanding location-specific hypertension risk factors over time.²³ However, there is currently a limited number of longitudinal studies examining risk factors for incident hypertension in the region.²⁴⁻²⁷

We use a population-based cohort of adults in rural South Africa who were normotensive in 2010-11 and were 40 years or older in 2014-15 to estimate hypertension incidence and identify sociodemographic, health and behavioural risk factors over a five-year period.

METHODS

We use data from two survey studies conducted in 2010-11 and 2014-2015 in the Agincourt Health and socio-Demographic Surveillance System (HDSS) study area in rural northeast South Africa.²⁸ Since 1992, the Medical Research Council (MRC)/Wits Rural Public Health and Health Transitions Unit has been conducting an annual census update of the population living in the study site, including information on vital events (births, deaths, migrations) and household and individual socio-demographic information. In 2010-11, the baseline study (Ha Nakekela) included a sex-age stratified random sample of 7,662 men and women aged 15 and older who were permanent residents from the 2009 HDSS census.²⁹ A follow-up study from November 2014 to November 2015 (The Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI)) included a random sample of 6,281 men and women aged 40 years and older who were permanent residents from the 2013 HDSS census,³⁰ including those in the baseline study who fulfilled the inclusion criteria. Both studies included information on sociodemographic factors and self-reported health and conditions, anthropometric and blood pressure measurements, and point of care blood tests for glucose and lipids, and dried blood spots (DBS) for HIV status.

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Outcome measure

Blood pressure (BP) and hypertension. BP was measured three times using a Boso BP instrument in 2010 and an Omron M6W automated cuff in 2015. Validation studies of similar blood pressure monitoring devices indicate that they can provide accurate measurements.^{31–33} We used the average of the second and third measurements consistent with national surveillance guidance.³⁴ Hypertension was defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or if the respondent self-reported taking hypertensive medication.

2010 risk factors

Anthropometry and high waist circumference. Height, weight, and waist circumference were measured using a flexible stadiometer (Seca). High waist circumference was defined as >102 cm for men and >88 cm for women. Obesity was classified as a body mass index (BMI; kg/m^2) ≥ 30 .

Random blood glucose and diabetes. Point of care instruments were used to measure glucose (Caresens POP blood glucose meter). Diabetes was defined as a random blood glucose level of ≥ 11.1 mmol/L or if the respondent self-reported medication use for diabetes.

High triglycerides. A Cardiocheck instrument was used to measure lipid levels. High triglycerides was defined as ≥ 1.7 mmol/l.³⁵

HIV status. HIV DBS were tested using screening assay Vironostika Uniform 11 (Biomerieux, France); with positive results retested using the SD Bioline HIV ELISA test

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(SD; Standard Diagnostics Inc., Korea). If the two tests were inconsistent, we conducted a third assay (Elecys, Roche, USA) that determined the final result.

Socio-demographics and behaviours. Respondents were asked about smoking and alcohol history, physical activity, and if they were using ART. Information on years of completed education, employment (currently working for pay), union (informal or formal) and socioeconomic status (based on tertiles of an asset index³⁶) were extracted from the most recent surveillance census.

Cause of death: For those who died between the baseline and follow-up study and for whom a death was identified from census updates, a verbal autopsy (VA) was conducted using a standardized VA instrument. For each identified death, a specially trained team conducted a VA interview with the closest living care taker to record signs and symptoms experienced before the death. We categorized cause of death using InterVA-4³⁷ – assigning a single cause for the largest likelihood for each death.

Analysis

We calculated hypertension incidence for those aged 40 years and older at the time of the second survey over five years overall, and by sex, age, and other socio-demographic factors. We calculated age-adjusted incidence using the Agincourt 2009 census population. We used Poisson regression to examine the association of hypertension status with socio-demographic, health and behavioural factors from the baseline study. To adjust for nonresponse in the follow-up study, we developed inverse probability sampling weights (IPSW) based on a logistic regression including sex and age at August 2010. We multiplied the IPSW for nonresponse by the inverse probability weights from the 2010 sample selection to derive our

final weights for analysis. For our fully adjusted multivariable models, we fit separate models with and without HIV/ART status given a reduced sample of 2010 respondents with measured HIV status (particularly for the eligible sample estimates, see next paragraph).

We used two approaches to estimating exposure time for our incidence estimates. For the first approach, we included only those individuals who participated in both surveys. For incident cases, we defined exposure time as the midpoint between the dates of the first and second survey assessments. For the second approach, we included all eligible individuals from the first survey who were able to be tracked from census data. For those who out-migrated or died before the start of the second study, we allowed them to contribute exposure time between their blood pressure measurement in the first study and time at death or out-migration. For those who were not found or refused to participate in the second survey, we allowed exposure time between the first study's measurement and the start of the second study. As the second approach includes additional exposure time but no new incident cases, it provides a lower bound for our estimate of hypertension incidence. Individuals who aged to 40 during the follow-up time only contributed to exposure when they had reached 40 years or older. We used Stata 15 for all statistical analyses.³⁸

We also tested the sensitivity of our results. We tested models using either BMI or waist-to-hip ratio instead of waist circumference. We also tested a model of hypertension based on only BP thresholds to assess if there were differences in the associations between predictors and incident BP only. Finally, we tested a competing-risk model for those eligible individuals who either died, migrated, or completed the follow-up study to test for bias in our risk factor associations. We modelled incident hypertension as the main event and death due to any cause as a competing event (censoring those who out-migrated) using the Fine-Grey model.³⁹

Patient and public involvement

Neither study participants nor public were involved in study design or conduct of the study.

The HDSS Learning, Information dissemination and Networking with Community (LINC) office manages community liaison with the HDSS study communities and their leaders.

Annual feedback of findings from the HDSS and projects are provided to open village meetings with participation commonly from local service providers.

RESULTS

Figure 1 shows the participant flowchart. A total of 977 individuals were eligible for analysis from the first study and 676 (69%) also completed the second study. Table 1 presents sample characteristics from the baseline study comparing those who completed the second study and those who did not. Women, those with a high waist circumference, those in older ages and in a union with lower completed education were more likely to participate in the second study.

There were 193 incident cases of hypertension since baseline. The overall hypertension incidence rate was 8.374 per 100 person-years for those completing both studies (men 9.097; women 8.159; Table 2). The overall age adjusted hypertension incidence rate for those completing both studies was 8.372 per 100 person-years (men 8.955; women 8.50). Rates were lower when including the full eligible sample (Online supplemental table 1). By age, men in their 40s and 50s had higher incidence compared to same aged women, while women showed higher rates than men from ages 60-plus (Figure 2).

Table 2 shows incident rates and ratios for those completing both studies by baseline socio-demographic, health, and behavioural factors. Older age individuals were associated with

higher incident hypertension risk compared to those ages 40-49. Those with high waist circumference and elevated triglycerides had a higher risk of incident hypertension. Respondents engaging in high physical activity levels had a lower risk of incident hypertension compared to those with low physical activity levels. Those HIV-positive and not on ART at baseline had a 55% lower risk of developing hypertension over the 5 years of follow-up, while those on ART also had lower hypertensive risk than those HIV-negative at baseline. Results for the full eligible sample are presented in online supplemental table 1.

Table 3 shows the multivariable-adjusted results from the full Poisson regression excluding HIV status for those completing both studies (see online supplemental table 2 for the full eligible sample results). Older ages, being employed (IRR: 1.579 95% CI: 1.071-2.329), and having a high waist circumference (IRR: 1.557 95% CI: 1.074-2.259) were associated with higher risk of incident hypertension in 2015. Those engaging in high levels of physical activity had an approximately 43% lower risk of incident hypertension, although the 95% CI overlapped with the null value of 1 (95% CI: 0.319-1.018)

Table 4 shows the same multivariable-adjusted Poisson model as Table 3 including HIV status, with similar results to those risk factors from the model without HIV status. The results for high waist circumference were in the same direction but the 95% CI overlapped with the null value of 1, likely due to the reduced sample size. Those who were HIV-positive and not on ART had an approximately 52% lower risk of incident hypertension compared to those HIV-negative at baseline (95% CI 0.301-0.778), while those HIV-positive and on ART showed similar associations to those not on ART.

Results of the sensitivity analyses of alternate anthropometry measures showed similar associations for BMI as for waist circumference (online supplemental table 3). There were not enough cases of high waist-to-hip ratio to include in the models. A model examining an outcome based only on BP thresholds also showed similar associations to the original models (online supplemental table 4). For the competing risk model, high rates of missingness on HIV/ART status precluded including that indicator. Results omitting HIV/ART status at baseline are presented in online supplemental table 5, showing similar results to the full eligible sample (online supplemental table 2). Cause of death information according to broad cause groups is presented in online supplemental table 6.

DISCUSSION

In 1998, South Africa had approximately 6.3 million adults with hypertension.⁴⁰ Now it is estimated to be close to 12 million, nearly doubling despite population growth of about 34% over the same time period, with prevalence increasing from 24% to over 40% in some populations.⁴¹ Based on our finding of 8.37 per 100 person-years, roughly 1.4 million adults over the age of 40 will develop hypertension over the next five years. Given an increase of nearly 50% in the risk of ischemic heart disease and stroke death for each 10 mmHg increase,⁴² the results suggest a significant increase in the number of people required for additional treatment and premature mortality if not adequately controlled.

We found that 29% of older adults in our study developed hypertension over a five-year period. Our results were similar to another study from South Africa following individuals ages 30-plus who started with optimal blood pressure over five years (2005-2010). They found a relatively similar incidence of 24%²⁷ given the slightly younger age range.

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We showed that men have higher hypertension incidence rates in mid-life, while women had higher rates in older ages. This is likely due at least in part to the smaller sample size of men in our study. A potentially similar pattern was shown in a study in South Africa (2004-2016) of patients initiating ART at 10 public sector clinics (9 urban, 1 rural) and including a wider age range (ages 18-50-plus).²⁴ They found that men had higher hypertension incidence rates at ages 18-39, while women had higher rates at ages 40-49 and 50-plus. Our finding may also be due in part to greater employment for middle-aged men⁴³ and higher survival^{17 44} or obesity^{45 46} among older women.

In multivariable-adjusted models, we found that being employed and having a high waist circumference at baseline were risk factors for incident hypertension. In another study in South Africa, they also found that high waist circumference was a key risk factor, along with alcohol intake.²⁷ While we showed no association with alcohol use, our sample also had low self-reported use of alcohol, with 80% reporting not drinking in the past month, which may be due in part to response bias.⁴⁷ Given the limited employment opportunities in our setting,²⁸ a higher risk of hypertension amongst employed individuals may represent those more likely to be exposed to workplace-related stress and other behavioural factors such as diet^{48 49} that may differ from those not employed.

We found that being HIV-positive at baseline was associated with a lower risk of incident hypertension. This also aligns with an earlier study in South Africa that showed that being HIV-positive was inversely related to increased BP.²⁷ However, our results may be sensitive to survivorship bias if those who died due to HIV/AIDS over the five-year period were also more likely to develop hypertension. Of the 71 individuals for which mortality information is available, about 28% died due to HIV/AIDS or TB. If a substantial portion of those

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contexts. We include a wide range of potential risk factors based on existing studies. Other factors, however, such as migration history, would be important to consider given the high levels of circular labour migration in this setting and potential links of rural to urban migration to increased blood pressure.^{52–55} Further, food insecurity is highly prevalent in this setting⁵⁶ and may lead to differential hypertension risk due to dietary differences. Given the high level of missingness on HIV/ART status amongst the eligible population who did not complete the follow-up study, we were unable to assess the effect of HIV/ART in a competing risk framework. Our measure of ART status is also based on self-report and may be subject to response bias, as well as factors related to HIV awareness such as engagement with health services.⁵⁷

Over a period of five years, 29% of individuals developed hypertension in a population-based cohort of individuals ages 40 and older given an incidence rate of 8.374 per 100 person-years. Abdominal obesity was one of the most consistent risk factors. Being employed was also a predictor of incident hypertension. As South Africa continues to undergo a complex health and epidemiological transition, continued longitudinal follow-up is needed to understand the complex interplay of noncommunicable and infectious diseases, along with their underlying and modifiable risk factors. In response to the urgent call for longitudinal sub-Saharan African studies, an increasing evidence base can help inform and target public health strategies to reduce preventable morbidity and mortality.

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Contributions: BH wrote the first draft and designed and completed the statistical analyses. FXG, BH, TG and SMT conceptualized the work. FXG, NA, CWK, and SMT designed and implemented the baseline study. TG, FXG, CWK, and SMT designed and implemented the follow-up study. TG, NA, SAM, CWK, SMT, and FXG revised the manuscript for important intellectual content and contributed to interpretation of the data. All authors read and approved the final manuscript.

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Competing interests: None declared.

Ethics approval: Ethical clearance for both surveys and the HDSS were obtained from the University of the Witwatersrand Human Research Ethics Committee (Medical) [M10458 and M141159] and the Mpumalanga Provincial Research and Ethics Committee. The baseline study also received ethical approval from the Institutional Review Board of the University of Colorado – Boulder [11-0549] and the follow-up study from the Harvard TH Chan School of Public Health, Office of Human Research Administration [C13-1608-02]. Written consent to participate was obtained for all participants in the baseline study. Each respondent in the follow-up study also provided written, informed consent (or by a proxy, when needed).

Data sharing: The datasets generated and/or analysed for the follow-up study are available at the Harvard Center for Population and Development Studies (HCPDS) program website: www.haalsi.org. The data supporting the findings of this study are available from the corresponding author on reasonable request.

FIGURE CAPTIONS

Figure 1. Participant flowchart.

Figure 2. Proportion of participants with incident hypertension, by age and gender, 2015.

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Moderate	80	(27.9)	209	(31.3)	289	(30.3)
High	180	(62.7)	419	(62.7)	599	(62.7)
High waist circumference ^c						
No	205	(72.7)	430	(65.8)	0.04	635 (67.9)
Yes	77	(27.3)	223	(34.2)	300	(32.1)
Diabetes ^d						
No	293	(98.0)	655	(97.2)	0.46	948 (97.4)
Yes	6	(2.0)	19	(2.8)	25	(2.6)
High triglycerides ^e						
No	213	(72.7)	479	(73.5)	0.805	692 (73.2)
Yes	80	(27.3)	173	(26.5)	253	(26.8)

HIV/ART is not included given missing values (n=297) for the vast majority of those lost to follow-up.

^a Based on a household asset index score.

^b Based on the International Physical Activity Questionnaire (IPAQ).

^c Greater than 102cm for men and 88cm for women.

^d Blood glucose greater than or equal to 11.1.

^e Greater than or equal to 1.7 mmol/l.

High waist circumference ^c	0.57	0.319	1.018	0.057
No	1			
Yes	1.557	1.074	2.259	0.02
Diabetes ^d				
No	1			
Yes	0.932	0.399	2.178	0.87
High triglycerides ^e				
No	1			
Yes	1.297	0.932	1.805	0.123

^a Based on a household asset index score.

^b Based on the International Physical Activity Questionnaire (IPAQ).

^c Greater than 102cm for men and 88cm for women.

^d Blood glucose greater than or equal to 11.1.

^e Greater than or equal to 1.7 mmol/l.

High waist circumference ^c	0.56	0.309	1.015	0.056
No	1			
Yes	1.448	0.975	2.149	0.066
Diabetes ^d				
No	1			
Yes	0.907	0.392	2.102	0.82
High triglycerides ^e				
No	1			
Yes	1.34	0.956	1.877	0.089
HIV and ART status				
Negative	1			
Positive, not on ART	0.484	0.301	0.778	0.003
Positive, on ART	0.462	0.197	1.082	0.075

^a Based on a household asset index score.

^b Based on the International Physical Activity Questionnaire (IPAQ).

^c Greater than 102cm for men and 88cm for women.

^d Blood glucose greater than or equal to 11.1.

^e Greater than or equal to 1.7 mmol/l.

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Supplementary Materials

Online Supplemental Tables 1-6

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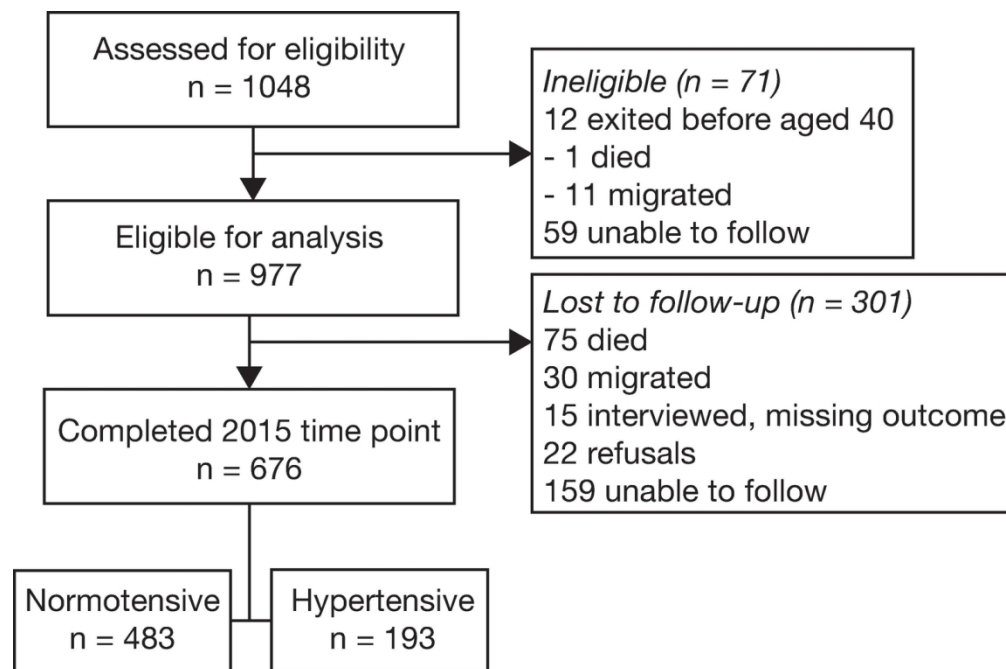


Figure 1

134x89mm (300 x 300 DPI)

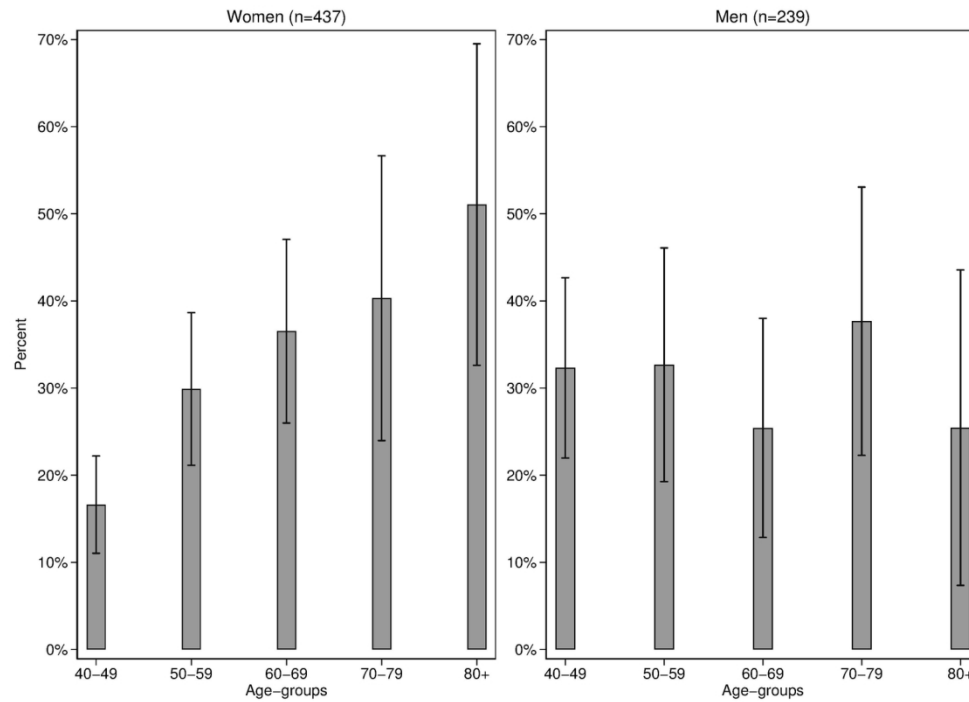


Figure 2

139x101mm (300 x 300 DPI)

Weekly	30	414	5.546	3.691	8.558	1.227	0.784	1.92	0.372
Physical activity ^b									
Low	20	199	6.424	3.801	11.185	1			
Moderate	71	913	6.323	4.899	8.246	0.984	0.548	1.769	0.958
High	100	2017	3.798	3.073	4.733	0.591	0.335	1.043	0.07
High waist circumference ^c									
No	104	2106	3.629	2.936	4.523	1			
Yes	78	974	5.796	4.544	7.455	1.597	1.151	2.215	0.005
Diabetes ^d									
No	186	3095	4.513	3.851	5.311	1			
Yes	6	81	6.868	2.92	18.668	1.522	0.64	3.621	0.342
High triglycerides ^e									
No	122	2269	4.084	3.367	4.989	1			
Yes	59	817	5.344	4.014	7.203	1.309	0.922	1.857	0.132
HIV and ART status									
Negative	155	1522	10.254	8.726	12.104	1			
Positive, not on ART	25	490	4.615	3.054	7.246	0.45	0.286	0.708	0.001
Positive, on ART	6	178	3.553	1.52	10.122	0.346	0.145	0.827	0.017

^a Based on a household asset index score.
^b Based on the International Physical Activity Questionnaire (IPAQ).
^c Greater than 102cm for men and 88cm for women.
^d Blood glucose greater than or equal to 11.1.
^e Greater than or equal to 1.7 mmol/l.

High waist circumference ^c	0.639	0.342	1.195	0.161
No	1			
Yes	1.564	1.047	2.335	0.029
Diabetes ^d				
No	1			
Yes	1.047	0.438	2.506	0.917
High triglycerides ^e				
No	1			
Yes	1.126	0.776	1.633	0.532

^a Based on a household asset index score.
^b Based on the International Physical Activity Questionnaire (IPAQ).
^c Greater than 102cm for men and 88cm for women.
^d Blood glucose greater than or equal to 11.1.
^e Greater than or equal to 1.7 mmol/l.

Low	1				
Moderate	0.721	0.419	1.242	0.239	
High	0.506	0.289	0.886	0.017	
Obesity ^c					
No	1				
Yes	1.902	1.315	2.751	0.001	
Diabetes ^d					
No	1				
Yes	0.916	0.371	2.263	0.849	
High triglycerides ^e					
No	1				
Yes	1.346	0.965	1.876	0.08	
HIV and ART status					
Negative	1				
Positive, not on ART	0.504	0.315	0.809	0.004	
Positive, on ART	0.507	0.221	1.165	0.11	

^a Based on a household asset index score.

^b Based on the International Physical Activity Questionnaire (IPAQ).

^c Greater than or equal to 30 BMI.

^d Blood glucose greater than or equal to 11.1.

^e Greater than or equal to 1.7 mmol/l.

High waist circumference ^c	0.669	0.33	1.355	0.264
No	1			
Yes	1.361	0.882	2.102	0.164
Diabetes ^d				
No	1			
Yes	0.341	0.05	2.309	0.27
High triglycerides ^e				
No	1			
Yes	1.19	0.792	1.789	0.402
HIV and ART status				
Negative	1			
Positive, not on ART	0.28	0.151	0.518	<0.001
Positive, on ART	0.313	0.108	0.908	0.033

^a Based on a household asset index score.
^b Based on the International Physical Activity Questionnaire (IPAQ).
^c Greater than 102cm for men and 88cm for women.
^d Blood glucose greater than or equal to 11.1.
^e Greater than or equal to 1.7 mmol/l.

