


# BMJ Open Hypertension incidence among middle-aged and older adults: findings from a 5-year prospective study in rural South Africa, 2010–2015

Brian Houle <sup>1,2</sup> Thomas A Gaziano,<sup>3,4</sup> Nicole Angotti,<sup>2,5</sup> Sanyu A Mojola,<sup>2,6</sup> Chodziwadziwa W Kabudula,<sup>2</sup> Stephen M Tollman,<sup>2,7,8</sup> F Xavier Gómez-Olivé<sup>2,7,9</sup>

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For numbered affiliations see end of article.

## Correspondence to

Dr Brian Houle;  
[brian.houle@anu.edu.au](mailto:brian.houle@anu.edu.au)

## ABSTRACT

**Objectives** There is a scarcity of 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 years 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 non-response 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 aged 40 years 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 who became hypertensive were more likely to be older, have a high waist circumference (incidence rate ratio (IRR): 1.557, 95% CI: 1.074 to 2.259) and be employed (IRR: 1.579, 95% CI: 1.071 to 2.329) at baseline. Being HIV positive and not on antiretroviral therapy at baseline was associated with lower risk of incident hypertension.

**Conclusions** Over a 5-year period, 29% of respondents developed hypertension. Given the high burden of hypertension in South Africa, continued longitudinal follow-up is needed to understand the complex interplay of non-communicable and infectious diseases and their underlying and modifiable risk factors to inform public health prevention strategies and programmes.

## INTRODUCTION

Hypertension is one of the most important non-communicable disease (NCD) risk factors and the largest contributor to the global burden of disease, with high blood pressure (BP) accounting for 7% of global disability-adjusted life years.<sup>1</sup> The burden of hypertension is greatest in low/

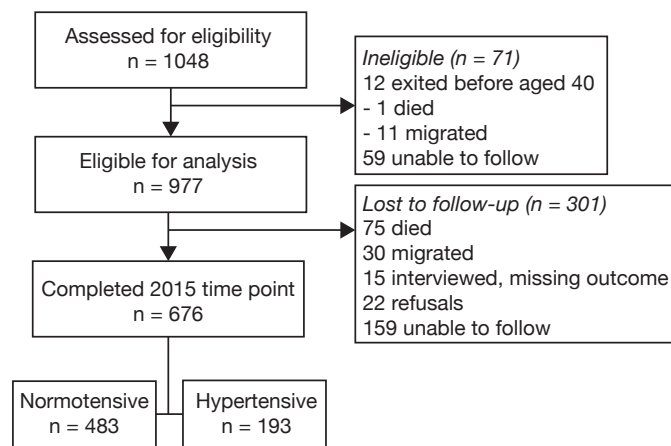
## Strengths and limitations of this study

- We provide longitudinal evidence on hypertension incidence from a population-based cohort in rural South Africa including both HIV-positive and HIV-negative individuals.
- Associations between HIV status and incident hypertension may be sensitive to survivorship bias if those who died due to HIV/AIDS over the 5-year period were also more likely to develop hypertension.
- A longer period of follow-up is needed to assess the effects of HIV and antiretroviral therapy on hypertension and related cardiometabolic conditions.

middle-income countries (LMICs),<sup>2</sup> and has increased rapidly in sub-Saharan Africa.<sup>3–7</sup> A study of people aged 50 years and over from six countries found markedly high prevalence in South Africa (77.9%).<sup>8</sup>

Rapid demographic and epidemiological changes in LMICs, such as population ageing, 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 population with hypertension in South Africa is expected to grow by 105% by 2050.<sup>9</sup> 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 individuals with hypertension being on treatment.<sup>10–12</sup> In South Africa, an estimated 38%–64% of hypertensives were aware of their status and 7.8%–22.8% effectively controlled.<sup>8 13</sup>

Longitudinal data from sub-Saharan Africa are needed to examine changes in population-specific hypertension risk factors over time,<sup>14</sup> particularly given differences in sociocultural environments and related health factors (eg, diet, concurrent infectious diseases), and



**Figure 1** Participant flow chart.

differentials in rural versus urban risk factor levels.<sup>15</sup> This is particularly important as wide-scale availability of antiretroviral therapy (ART) has reduced HIV/AIDS-related mortality<sup>16 17</sup> thereby increasing the population of those ageing with HIV.<sup>18</sup> The ageing population will be at higher risk of developing hypertension, and the effect of HIV and ART may also increase the incidence of hypertension.<sup>19–22</sup> In South Africa, an emerging dual burden of disease, along 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.<sup>23</sup> However, there are currently a limited number of longitudinal studies examining risk factors for incident hypertension in the region, with most of these restricted to HIV-positive individuals only.<sup>24–27</sup>

## METHODS

We use a population-based cohort of adults in rural South Africa who were normotensive in 2010–2011 and were 40 years or older in 2014–2015 to estimate hypertension incidence and identify sociodemographic, health and behavioural risk factors over a 5-year period.

We use data from two survey studies conducted in 2010–2011 and 2014–2015 in the Agincourt Health and socio-Demographic Surveillance System (HDSS) study area in rural northeast South Africa.<sup>28</sup> The area is a low rainfall setting with limited subsistence farming. Since 1992, the Medical Research Council/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 sociodemographic information. In 2010–2011, the baseline study (Ha Nakekela) included a sex/age-stratified random sample of 7662 men and women aged 15 years and older who were permanent residents from the 2009 HDSS census.<sup>29</sup> 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) included a random sample of 6281 men and women aged 40 years and older who were permanent

residents from the 2013 HDSS census,<sup>30</sup> 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 BP measurements, and point-of-care blood tests for glucose and lipids, and dried blood spots (DBS) for HIV status.

## Outcome measure

### BP and hypertension

BP was measured three times using a Boso BP instrument 2 min apart in 2010 and an Omron M6W automated cuff 2 min apart in 2015. Validation studies of similar BP monitoring devices indicate that they can provide accurate measurements.<sup>31–33</sup> Consistent with national surveillance guidance, we used the average of the second and third measurements.<sup>34</sup> Hypertension was defined as a systolic BP  $\geq 140$  mm Hg or diastolic BP  $\geq 90$  mm Hg or if the respondent self-reported taking antihypertensive 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.<sup>35</sup> Obesity was classified as a body mass index (BMI;  $\text{kg}/\text{m}^2$ )  $\geq 30$ .<sup>35</sup>

### Random blood glucose and diabetes

Point-of-care instruments were used to measure glucose (Caresens POP blood glucose metre). Diabetes was defined as a random blood glucose level of  $\geq 11.1$  mmol/L or if the respondent self-reported medication use for diabetes.<sup>36</sup>

### High triglycerides

A Cardiocheck instrument was used to measure lipid levels. High triglycerides were defined as  $\geq 1.7$  mmol/L.<sup>37</sup>

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

### Sociodemographics and behaviours

Respondents were asked about smoking (never, prior, current) and alcohol history (not in past 30 days, less than weekly, weekly), physical activity (using the International Physical Activity Questionnaire) 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 index<sup>38</sup>) was extracted from the most recent surveillance census.

**Table 1** Sample characteristics at baseline (2010), by study participation in 2015 for eligible individuals (n=977)

	Lost to follow-up (n=301)		Completed 2015 (n=676)		P value	Total (n=977)	
	n	%	n	%		n	%
<b>Gender</b>							
Male	140	46.5	239	35.4	0.001	379	38.8
Female	161	53.5	437	64.6		598	61.2
<b>Age groups</b>							
35–44	130	43.2	227	33.6	0.003	357	36.5
45–54	71	23.6	180	26.6		251	25.7
55–64	34	11.3	126	18.6		160	16.4
65–74	29	9.6	81	12.0		110	11.3
75+	37	12.3	62	9.2		99	10.1
<b>Education</b>							
None	40	34.2	277	41.0	0.018	317	40.0
Less than secondary	54	46.2	327	48.4		381	48.0
Secondary or more	23	19.7	72	10.7		95	12.0
<b>Union status</b>							
Not in union	166	55.1	302	44.7	0.002	468	47.9
Formal/informal union	135	44.9	374	55.3		509	52.1
<b>SES*</b>							
Low	130	43.2	253	37.7	0.258	383	39.4
Middle	86	28.6	216	32.2		302	31.1
High	85	28.2	202	30.1		287	29.5
<b>Employment status</b>							
Not employed	80	68.4	498	74.1	0.196	578	73.3
Employed	37	31.6	174	25.9		211	26.7
<b>Smoking history</b>							
Never	236	78.4	548	81.1	0.206	784	80.2
Prior	18	6.0	49	7.2		67	6.9
Current	47	15.6	79	11.7		126	12.9
<b>Alcohol use</b>							
Not in past 30 days	235	78.1	544	80.5	0.686	779	79.7
Less than weekly	24	8.0	47	7.0		71	7.3
Weekly	42	14.0	85	12.6		127	13.0
<b>Physical activity†</b>							
Low	27	9.4	40	6.0	0.128	67	7.0
Moderate	80	27.9	209	31.3		289	30.3
High	180	62.7	419	62.7		599	62.7
<b>High waist circumference‡</b>							
No	205	72.7	430	65.8	0.04	635	67.9
Yes	77	27.3	223	34.2		300	32.1
<b>Diabetes§</b>							
No	293	98.0	655	97.2	0.46	948	97.4
Yes	6	2.0	19	2.8		25	2.6
<b>High triglycerides¶</b>							
No	213	72.7	479	73.5	0.805	692	73.2

Continued

**Table 1** Continued

	Lost to follow-up (n=301)		Completed 2015 (n=676)		P value	Total (n=977)	
	n	%	n	%		n	%
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.

\*Based on a household asset index score.

†Based on the International Physical Activity Questionnaire.

‡Greater than 102 cm for men and 88 cm for women.

§Blood glucose greater than or equal to 11.1.

¶Greater than or equal to 1.7 mmol/L.

ART, antiretroviral therapy; SES, socioeconomic status.

### 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 standardised VA instrument. For each identified death, a specially trained team conducted a VA interview with the closest living caretaker to record signs and symptoms experienced before the death. We categorised cause of death using InterVA-4<sup>39</sup>—assigning a single cause for the largest likelihood for each death.

### Analysis

We calculated hypertension incidence (over 5 years) for those aged 40 years and older at the time of the second survey overall, and by sex, age, and other sociodemographic factors. We calculated age-adjusted incidence using the Agincourt 2009 census population. We used Poisson regression with robust SEs to examine the association of hypertension status with sociodemographic, health and behavioural risk factors from the baseline study. To adjust for non-response in the follow-up study, we developed inverse probability sampling weights (IPSW) based on a logistic regression including sex and age in August 2010. We multiplied the IPSW for non-response 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 below).

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 BP 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

**Table 2** Hypertension incidence rates (IRs) and incidence rate ratios (IRRs) per 100 person-years (PYRS) over 5 years of follow-up (2010–2015), by sociodemographic, health and behavioural factors among those completing both time points

Value	Events	PYRS	IR	95% CI		IRR	95% CI		P value
				Lower	Upper		Lower	Upper	
Overall	193	2311	8.374	7.242	9.721				
Gender									
Male	74	815	9.097	7.266	11.496	1			
Female	119	1496	8.159	6.832	9.804	0.897	0.67	1.2	0.463
Age groups									
40–49	56	975	5.04	3.837	6.73	1			
50–59	47	556	8.897	6.667	12.077	1.765	1.177	2.647	0.006
60–69	42	399	11.104	8.282	15.14	2.203	1.464	3.315	<0.001
70–79	28	239	11.875	8.285	17.436	2.356	1.486	3.735	<0.001
80+	20	141	16.197	10.647	25.379	3.213	1.931	5.348	<0.001
Education									
None	85	986	9.256	7.491	11.536	1			
Less than secondary	92	1090	8.21	6.645	10.229	0.887	0.655	1.202	0.439
Secondary or more	16	235	5.318	3.112	9.652	0.575	0.319	1.034	0.065
Union status									
Not in union	91	1034	8.613	6.983	10.709	1			
Formal/informal union	102	1277	8.165	6.685	10.051	0.948	0.706	1.273	0.722
SES*									
Low	68	867	8.064	6.328	10.397	1			
Middle	64	736	8.715	6.798	11.305	1.081	0.759	1.539	0.667
High	60	689	8.389	6.449	11.056	1.04	0.723	1.497	0.831
Employment status									
Not employed	144	1701	8.336	7.048	9.911	1			
Employed	48	595	8.511	6.375	11.557	1.021	0.726	1.435	0.905
Smoking history									
Never	163	1861	8.644	7.392	10.155	1			
Prior	11	171	6.356	3.501	12.447	0.735	0.391	1.381	0.339
Current	19	279	6.715	4.293	10.956	0.777	0.478	1.262	0.308
Alcohol use									
Not in past 30 days	153	1852	8.416	7.167	9.931	1			
Less than weekly	10	167	5.459	2.879	11.284	0.649	0.331	1.272	0.208
Weekly	30	292	9.789	6.708	14.649	1.163	0.766	1.765	0.478
Physical activity†									
Low	20	122	15.468	9.85	24.91	1			
Moderate	71	687	10.641	8.402	13.61	0.688	0.412	1.149	0.153
High	100	1471	6.98	5.718	8.59	0.451	0.275	0.742	0.002
High waist circumference‡									
No	104	1512	6.519	5.326	8.046	1			
Yes	78	735	10.571	8.483	13.283	1.621	1.197	2.196	0.002
Diabetes§									
No	186	2240	8.298	7.156	9.662	1			
Yes	6	64	10.06	4.451	26.006	1.212	0.529	2.778	0.649
High triglycerides¶									
No	122	1660	7.262	6.049	8.775	1			
Yes	59	575	10.59	8.177	13.88	1.458	1.057	2.012	0.022

Continued

Table 2 Continued

Value	Events	PYRS	IRR	95% CI		IRR	95% CI		P value
				Lower	Upper		Lower	Upper	
HIV and ART status									
Negative	155	1514	10.452	8.909	12.318	1			
Positive, not on ART	25	486	4.749	3.15	7.439	0.454	0.289	0.713	0.001
Positive, on ART	6	178	3.553	1.52	10.122	0.34	0.142	0.811	0.015

\*Based on a household asset index score.

†Based on the International Physical Activity Questionnaire.

‡Greater than 102 cm for men and 88 cm for women.

§Blood glucose greater than or equal to 11.1.

¶Greater than or equal to 1.7 mmol/L.

ART, antiretroviral therapy; SES, socioeconomic status.

additional exposure time but no new incident cases, it provides a lower bound for our estimate of hypertension incidence. Individuals who aged to 40 years during the follow-up time only contributed to exposure when they had reached 40 years or older. We used Stata V.15 for all statistical analyses.<sup>40</sup>

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.<sup>41</sup>

### Patient and public involvement

Neither study participants nor the public were involved in study design or conduct of the study. The HDSS Learning, Information dissemination and Networking with Community office manages community liaison activities with the HDSS study communities and their leaders. Annual feedback of findings from the HDSS census and research projects conducted in the site are provided through open village meetings, with frequent participation from local service providers.

### RESULTS

Figure 1 shows the participant flow chart. 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 (95% CI: 7.242 to 9.721) for those completing both studies (men 9.097 (95% CI: 7.266 to 11.496); women 8.159 (95% CI: 6.832 to 9.804); 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). Men in their 40s and 50s had higher incidence compared with same-aged women; from ages 60+ years, women showed higher rates than men (figure 2).

Table 2 shows incidence rates and ratios (unadjusted) for those completing both studies by baseline sociodemographic, health and behavioural risk factors. Older individuals had higher incident hypertension risk compared with those aged 40–49 years. 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 with those with low physical activity levels. Compared with those HIV negative at baseline, those HIV positive and not on ART had a 55% lower risk of developing hypertension over the 5 years of follow-up, while those on ART also had lower hypertensive risk.

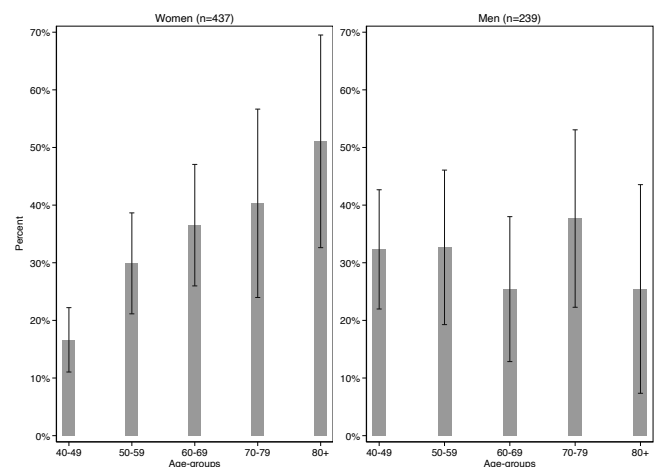


Figure 2 Proportion of participants with incident hypertension, by age and gender, 2015.

**Table 3** Multivariable Poisson regression of incident hypertension on sociodemographic, health and behavioural risk factors among those completing both time points (n=616)

	aIRR	95% CI		P value
		Lower	Upper	
<b>Gender</b>				
Male	1			
Female	0.818	0.512	1.305	0.399
<b>Age groups</b>				
40–49	1			
50–59	1.831	1.193	2.811	0.006
60–69	2.4	1.463	3.938	<0.001
70–79	2.607	1.451	4.684	<0.001
80+	2.561	1.196	5.488	<0.001
<b>Education</b>				
None	1			
Less than secondary	1.061	0.732	1.537	0.755
Secondary or more	0.741	0.372	1.478	0.395
<b>Union status</b>				
Not in union	1			
Formal/informal union	1.023	0.724	1.445	0.899
<b>SES*</b>				
Low	1			
Middle	1.068	0.715	1.593	0.749
High	0.915	0.59	1.42	0.693
<b>Employment status</b>				
Not employed	1			
Employed	1.579	1.071	2.329	0.021
<b>Smoking history</b>				
Never	1			
Prior	0.758	0.37	1.55	0.447
Current	0.709	0.373	1.349	0.295
<b>Alcohol use</b>				
Not in past 30 days	1			
Less than weekly	0.717	0.345	1.492	0.373
Weekly	1.07	0.652	1.755	0.789
<b>Physical activity†</b>				
Low	1			
Moderate	0.781	0.447	1.364	0.385
High	0.57	0.319	1.018	0.057
<b>High waist circumference‡</b>				
No	1			
Yes	1.557	1.074	2.259	0.02
<b>Diabetes§</b>				
No	1			
Yes	0.932	0.399	2.178	0.87

Continued

**Table 3** Continued

	aIRR	95% CI		P value
		Lower	Upper	
<b>High triglycerides¶</b>				
No	1			
Yes	1.297	0.932	1.805	0.123

\*Based on a household asset index score.

†Based on the International Physical Activity Questionnaire.

‡Greater than 102 cm for men and 88 cm for women.

§Blood glucose greater than or equal to 11.1.

¶Greater than or equal to 1.7 mmol/L.

aIRR, adjusted incidence rate ratio; SES, socioeconomic status.

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 supplementary table 2 for the full eligible sample results). Older ages (eg, ages 60–69 years adjusted incidence rate ratio (aIRR): 2.4, 95% CI: 1.463 to 3.938), being employed (aIRR: 1.579, 95% CI: 1.071 to 2.329) and having a high waist circumference (aIRR: 1.557, 95% CI: 1.074 to 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 to 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. Those who were HIV positive and not on ART had an approximately 52% lower risk of incident hypertension compared with those HIV negative at baseline (95% CI 0.301 to 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 supplementary 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 missing data 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.

**Table 4** Multivariable Poisson regression of incident hypertension on sociodemographic, health and behavioural risk factors, and HIV and ART status among those completing both time points (n=581)

	aIRR	95% CI		P value
		Lower	Upper	
<b>Gender</b>				
Male	1			
Female	0.854	0.533	1.369	0.512
<b>Age groups</b>				
40–49	1			
50–59	1.846	1.183	2.879	0.007
60–69	2.128	1.281	3.535	0.004
70–79	2.339	1.256	4.356	0.007
80+	2.139	0.978	4.676	0.057
<b>Education</b>				
None	1			
Less than secondary	1.124	0.765	1.652	0.552
Secondary or more	0.754	0.368	1.542	0.439
<b>Union status</b>				
Not in union	1			
In union	0.939	0.662	1.332	0.724
<b>SES*</b>				
Low	1			
Middle	0.97	0.647	1.454	0.883
High	0.812	0.519	1.269	0.36
<b>Employment status</b>				
Not employed	1			
Employed	1.604	1.064	2.419	0.024
<b>Smoking history</b>				
Never	1			
Prior	0.727	0.34	1.554	0.411
Current	0.661	0.345	1.267	0.213
<b>Alcohol use</b>				
Not in past 30 days	1			
Less than weekly	0.751	0.358	1.574	0.448
Weekly	1.111	0.668	1.846	0.685
<b>Physical activity†</b>				
Low	1			
Moderate	0.77	0.434	1.365	0.371
High	0.56	0.309	1.015	0.056
<b>High waist circumference‡</b>				
No	1			
Yes	1.448	0.975	2.149	0.066
<b>Diabetes§</b>				
No	1			
Yes	0.907	0.392	2.102	0.82
<b>High triglycerides¶</b>				
No	1			
Yes	1.34	0.956	1.877	0.089
<b>HIV and ART status</b>				
Negative	1			

Continued

**Table 4** Continued

	aIRR	95% CI		P value
		Lower	Upper	
Positive, not on ART	0.484	0.301	0.778	0.003
Positive, on ART	0.462	0.197	1.082	0.075

\*Based on a household asset index score.

†Based on the International Physical Activity Questionnaire.

‡Greater than 102 cm for men and 88 cm for women.

§Blood glucose greater than or equal to 11.1.

¶Greater than or equal to 1.7 mmol/L.

aIRR, adjusted incidence rate ratio; ART, antiretroviral therapy; SES, socioeconomic status.

## DISCUSSION

In 1998, South Africa had approximately 6.3 million adults with hypertension.<sup>42</sup> 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.<sup>43</sup> Based on our finding of 8.37 per 100 person-years, we estimate that roughly 1.4 million adults over the age of 40 years will develop hypertension over the next 5 years. Given an increase of nearly 50% in the risk of ischaemic heart disease and stroke death for each 10 mm Hg increase,<sup>44</sup> the results suggest both a significant increase in the number of people in need of additional treatment and premature mortality if not adequately controlled.

We found that 29% of middle-aged and older adults in our study developed hypertension over a 5-year period. Our results were similar to another study from South Africa following individuals aged 30+ over 5 years (2005–2010) who started with optimal BP. They found a relatively similar incidence of 24%<sup>27</sup> given the slightly younger age range.

We showed that men have higher hypertension incidence rates in midlife, while women had higher rates at 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) which included a wider age range (ages 18–50+).<sup>24</sup> They found that men had higher hypertension incidence rates at ages 18–39 years, while women had higher rates at ages 40–49 and 50+ years. Our finding may also be due to greater employment for middle-aged men<sup>45</sup> and higher survival<sup>17 46</sup> or obesity<sup>47 48</sup> 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. Another study in South Africa also found that high waist circumference was a key risk factor, along with alcohol intake.<sup>27</sup> 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 to response bias.<sup>49</sup> Given the limited employment opportunities in our setting,<sup>28</sup> a higher risk of hypertension among employed individuals may represent those

more likely to be exposed to workplace-related stress and other behavioural factors such as diet<sup>50 51</sup> 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.<sup>27</sup> However, our results may be sensitive to survivorship bias if those who died due to HIV/AIDS over the 5-year period were also more likely to develop hypertension. Of the 71 individuals for whom mortality information is available, about 28% died due to HIV/AIDS or tuberculosis. If a substantial portion of those individuals developed hypertension, this may affect our estimates of the association between HIV/ART status and risk of incident hypertension. Further, as we lacked information on HIV/ART status for many individuals in the eligible sample who did not complete the follow-up study, this may affect our estimates if those individuals were more likely to be HIV positive.<sup>52</sup> A longer period of follow-up is needed to assess the effects of HIV and ART on hypertension and related cardiometabolic conditions. Longitudinal studies restricted to HIV-positive individuals have shown high hypertension incidence rates over relatively short periods of follow-up and similar risk factors to the HIV-negative population.<sup>25 26</sup>

Our longitudinal findings are particularly important given the complex health transition occurring in South Africa, with a concomitant burden of infections and NCDs.<sup>17 23 29 47</sup> A study from the same community as our study demonstrated a high and increasing burden of stroke morbidity and mortality.<sup>53</sup> While our findings are consistent with hypertension-related risk factors found in other regions, population-specific studies such as ours are important to contextualise the epidemiological findings from elsewhere and inform local prevention and treatment strategies.<sup>14</sup> They also provide an opportunity to understand the interaction between cardiometabolic and infectious diseases such as HIV. A longer period of follow-up, which will be possible as future waves of the study are completed, will permit a greater understanding of the interplay between hypertension, HIV, and treatment of both and related conditions.

We acknowledge our study limitations. While our study is one of the few population-based, longitudinal cohorts on hypertension incidence in Africa, the study comes from a defined region in rural northeast South Africa. Additional studies are needed in other settings, particularly given differences in exposures and differential risk factors in rural and urban 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 BP.<sup>54-57</sup> Other important factors to consider include nutritional factors such as consumption of fruits and vegetables and salt intake. Further, food insecurity is highly prevalent in this

setting<sup>58</sup> and may lead to differential hypertension risk due to dietary differences. Given the high level of missing data on HIV/ART status among 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.<sup>59</sup> Our self-reported measures may also be subject to social desirability and recall bias.

Over a period of 5 years, 29% of individuals developed hypertension in a population-based cohort of individuals aged 40 years 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 non-communicable and infectious diseases, along with their underlying and modifiable risk factors. In response to the call for longitudinal studies from sub-Saharan Africa on hypertension risk, this study contributes to the evidence base that can help inform and target public health strategies to reduce preventable morbidity and mortality.

#### Author affiliations

<sup>1</sup>School of Demography, The Australian National University, Canberra, Australian Capital Territory, Australia

<sup>2</sup>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

<sup>3</sup>Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA

<sup>4</sup>Harvard Medical School, Harvard University, Boston, Massachusetts, USA

<sup>5</sup>Department of Sociology, American University, Washington, District of Columbia, USA

<sup>6</sup>Department of Sociology, School of Public and International Affairs, and Office of Population Research, Princeton University, Princeton, New Jersey, USA

<sup>7</sup>INDEPTH Network, Accra, Ghana

<sup>8</sup>Centre for Global Health Research, Umea University, Umea, Sweden

<sup>9</sup>Center for Population and Development Studies, Harvard University, Cambridge, Massachusetts, USA

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#### ORCID iD

Brian Houle <http://orcid.org/0000-0003-2157-3118>

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