BACKGROUND
Increased urinary albumin excretion reflects general vascular damage and predicts adverse cardiovascular and renal outcomes. Albuminuria can be determined from easily collected spot urine samples, especially in low-resource settings. However, no prognostic evidence exists for Africans.

METHODS
We followed clinical outcomes in 1,061 randomly selected non diabetic, human immunodeficiency virus (HIV)–negative Africans (mean age: 51.5 years; 62.0% women). Baseline urinary albumin-to-creatinine ratio was assessed from spot urine samples.

RESULTS
Over a median follow-up of 4.52 years, 132 deaths occurred, of which 47 were cardiovascular related. The urinary albumin-to-creatinine ratio averaged 6.1 μg/mg (5th to 95th percentile interval: 1.2–70.0). In multivariable-adjusted analyses, urinary albumin excretion predicted all-cause mortality (hazard ratio (HR), 1.26; 95% confidence interval (CI), 1.07–1.48; P = 0.006), and a tendency existed for cardiovascular mortality (HR, 1.26; 95% CI, 0.97–1.63; P = 0.087), which seemed to be driven by fatal stroke (HR, 1.72; 95% CI, 1.17–2.54; P = 0.006) rather than cardiovascular mortality (HR, 1.24; 95% CI, 0.41–1.07; P = 0.094). The predictive value remained in 528 hypertensives for both all-cause (HR, 1.38; 95% CI, 1.13–1.69; P = 0.001) and cardiovascular (HR, 1.45; 95% CI, 1.07–1.96; P = 0.017) mortality, again driven by stroke. Our findings also remained significant after we excluded participants with macroalbuminuria, those on antihypertensive treatment, as well as participants who died within 1 year after enrollment.

CONCLUSION
In nondiabetic HIV-negative Africans, albuminuria predicts all-cause and stroke mortality.

Keywords: urinary albumin excretion; spot urine sampling; mortality; Africans.

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Urinary albumin excretion is an accepted marker of general endothelial dysfunction \(^1\)–\(^5\) and relates adversely to measures of vascular structure and function. \(^6\), \(^7\) It is a risk factor or risk indicator for cardiovascular events in patients with diabetes \(^8\) and hypertension, \(^9\) in nondiabetic and normotensive individuals, \(^7\) as well as in the general population. \(^9\) Urinary albumin excretion determined from easily collected spot urine samples is comparable to 24-hour samples, \(^9\) is inexpensive, has prognostic value, \(^10\) and, today, is recommended as a diagnostic tool for albuminuria. \(^11\)

An urgent need exists, particularly in sub-Saharan Africa, for easily measurable, low-cost screening tools in order to identify people at high risk for adverse health outcomes. Apart from infectious diseases, death from cardiovascular disease is reaching alarming levels. \(^12\) Some suggest that South Africa and the rest of sub-Saharan Africa are facing epidemics of hypertension, \(^13\) vascular disease, \(^14\) and related morbidity and mortality, especially from congestive heart failure, \(^15\) renal failure, \(^16\) and stroke. \(^17\) This contributes to the low life expectancy among South Africans of 52.6 years (2011), which is comparable to that in other African countries. \(^18\)

In light of the available evidence, urinary albumin excretion in Africans seems to be a prime candidate for use by clinicians as a way to achieve early risk stratification and initiate appropriate intervention strategies. Although albuminuria has been shown to associate with ambulatory blood pressure, arterial stiffness, and left ventricular hypertrophy in cross-sectional studies from African countries, \(^19\), \(^20\) to our knowledge, the predictive value of albumin excretion for mortality from any type of urine collection is unknown in Africans. We therefore investigated its prognostic significance using morning spot urine samples from 1,061 randomly selected Africans as part of the international Prospective Urban and Rural Epidemiology (PURE) study.

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METHODS

Study population

The Ethics Committee of the North-West University, Potchefstroom; South Africa, approved this substudy as part of the PURE study. The PURE study tracks changes in lifestyle, cardiovascular disease risk factors, and chronic diseases in people from urban and rural areas of developing countries. At baseline (2005), the South African leg included 2,010 randomly selected black South Africans, hereafter referred to as Africans (1,004 urban and 1,006 rural) from the North West Province. The rural communities had to be far away from cities and still be under tribal law with as little urban influence as possible, while the urban communities had to reflect true urbanization. A household census of number of people, their ages, and their health profiles was done on 6,000 randomly selected households, from which the 2,010 participants aged >35 years were selected. If a person declined participation or was not at home, the next house was selected.

All participants gave informed consent and could withdraw at any stage. The protocol complied with the 1975 Declaration of Helsinki (as revised in 1983) for investigation of human participants.

Of the 2,010 participants, we excluded 949 because they were human immunodeficiency virus (HIV) infected at baseline (n = 322), had missing information (n = 190), were lost to follow-up (n = 377), or had a fasting blood glucose level ≥7 mmol/l (n = 60). Thus, the number of participants statistically analyzed totaled 1,061.

Measurements at baseline

At baseline, participants arrived at the research locality of the rural and urban areas at 8:00 a.m. after a 10–15 minute drive (provided by the research team) from their communities. We introduced the participants to the research setup and explained the procedures before they gave informed consent. If irregularities were identified, referrals to the local clinic or hospital, if necessary, as well as feedback on general health were given to all participants. Trained fieldworkers completed the demographic and lifestyle questionnaires in the participants’ home languages. Lifestyle data included self-reported height, body weight, and alcohol use as well as medical history.

Anthropometrists measured body height to the nearest 1.0 cm with a stadiometer (SECA, Hamburg, Germany). For body weight measurement, participants wore light indoor clothing and no shoes, and weight was measured on portable electronic scales (A&D Company, Tokyo, Japan). Body mass index was weight, in kilograms, divided by the square of height, in meters. Physical activity was assessed using the Baecke physical activity questionnaire, which is usable for various socioeconomic classes in the general population.

We measured systolic and diastolic blood pressure (OMRON HEM-757; Omron Healthcare, Kyoto, Japan) on the right arm after a 10-minute rest in duplicate with a 5-minute rest between measurements. Appropriate-sized cuffs were used for obese subjects. Hypertension was a blood pressure equal to or exceeding 140 mm Hg systolic or 90 mm Hg diastolic, or the use of antihypertensive medication.

Registered nurses obtained fasting venous blood samples from the antebrachial vein using a sterile winged infusion set and syringes. Serum was prepared according to appropriate methods and stored at –80 °C in the laboratory. In rural areas, serum were stored at –18 °C and transported within 5 days to the laboratory facility for storage at –80 °C until analysis.

Serum total cholesterol, glucose, gamma glutamyltransferase, and creatinine were analyzed using the sequential multiple analyzer computer (Konelab 20i auto-analyzer; Thermo Fisher Scientific Oy, Vantaa, Finland). We calculated the estimated creatinine clearance using the Cockcroft–Gault formula.

Albumin and creatinine in urine were determined using the measurement of immunoturbidimetric assay (Cobas Integra 400 plus; Roche, Basel, Switzerland). The urinary albumin-to-creatinine ratio measured in spot urine samples is highly correlated with 24-hour urine albumin excretion. Normo-, micro-, and macroalbuminuria were defined as albumin-to-creatinine ratios of <30 μg/mg, 30–<300 μg/mg, and ≥300 μg/mg, respectively. All biochemical measurements were performed by an independent laboratory, blinded to the subjects’ cardiovascular profiles.

Assessment of outcome

To retain subjects and ascertain the vital status of all participants, three monthly follow-up visits to the participants’ homes were performed by fieldworkers under supervision of the senior researcher. The cause of death was obtained from family death certificates and verbal autopsy and coded by a physician according to the International Classification of Diseases codes for the immediate and underlying causes. All persons involved in these assessments were unaware of the participants’ albuminuria status.

Cardiovascular mortality included all fatal cardiac and stroke events and death noted as “due to hypertension.” Cardiovascular-related illnesses that caused death included heart failure, myocardial infarction, congestive heart failure, or any other cardiac-related reason. Death due to stroke included any stroke or cerebral vascular incident.

Statistical analysis

For database management and statistical analysis, we used SAS software, version 9.3 (SAS Institute Inc., Cary, NC). We compared means and proportions by the standard normal z test and the χ2 statistic, respectively, and survival curves by Kaplan-Meier survival function estimates and the log-rank test. Statistical significance was set at a level of 0.05 on two-sided tests.

We analyzed the prognostic significance of urinary albumin excretion using both categorical and continuous analyses. In categorical analysis, we determined the incidence rates by tertiles of the urinary albumin-to-creatinine ratio distribution, while standardizing rates for gender and age. For the continuous analysis, we used Cox proportional hazard regression to calculate standardized relative hazard ratios, while allowing for covariables and confounders. Covariables were identified by using Cox regression
models with a stepwise procedure, with \( P \) values for variables to enter and to stay in the model set at 0.05. Covariates included in the model were age, gender, urban/rural locality, systolic blood pressure, body mass index, total cholesterol, estimated creatinine clearance, fasting glucose, gamma-glutamyltransferase, physical activity, tobacco use, and antihypertensive medication. Of these variables, gender, urban/rural locality, systolic blood pressure, estimated creatinine clearance, fasting glucose, tobacco use, and antihypertensive medication did not enter any of the models. We checked the proportional hazards assumption by the Kolmogorov-type supremum test, as implemented in the PROC PHREG procedure of the SAS package. We tested heterogeneity in the hazard ratios across subgroups by introducing the appropriate interaction term in the Cox model.

**RESULTS**

**Baseline characteristics**

Baseline characteristics of the participants are presented in Table 1. In the entire study population, the urinary albumin-to-creatinine ratio averaged 6.1 (5th to 95th percentile interval, 1.2–70.0) μg/mg. Per definition, there were 954 (89.9%), 97 (9.2%), and 10 (0.9%) participants with normoalbuminuria (4.5; 1.1–21.0 μg/mg), microalbuminuria (67.9; 31.7–215.7 μg/mg), and macroalbuminuria (82.3; 30.9–245.5 μg/mg), respectively. Of these normo-, micro-, and macroalbuminuric participants, 105 (11.0%), 24 (24.7%), and 3 (30.0%) died, respectively. Urinary albumin excretion did not differ between men and women (5.6 (1.1–64.4) vs. 6.4 (1.1–71.6) μg/mg, \( P = 0.14 \)).

**Incidence of mortality**

In the entire study population, median follow-up was 4.52 years (5th to 95th percentile interval, 2.58–4.60 years). During 4,825 person-years of follow-up, 132 participants died (27.4 per 1,000 person-years), which included 47 (35.6%) cardiovascular and 54 (40.9%) noncardiovascular deaths and 31 (23.5%) deaths from unknown causes. Forty-seven cardiovascular deaths occurred (9.7 per 1,000 person-years), comprising 18 (38.3%) fatal strokes, 19 (40.4%)

### Table 1. Baseline characteristics of 1,061 participants by tertiles of urinary albumin excretion

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total group</th>
<th>Category of albumin-to-creatinine ratio</th>
<th>( P ) trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limits (μg/mg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3.2</td>
<td>3.2 to 8.3</td>
<td>&gt;8.3</td>
<td></td>
</tr>
<tr>
<td>Means (5th, 95th)</td>
<td>6.1 (1.2–70.0)</td>
<td>1.8 (0.9–3.0)</td>
<td>5.0 (3.3–7.7)</td>
</tr>
<tr>
<td><strong>Number of subjects (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All participants in category</td>
<td>1,061</td>
<td>353</td>
<td>354</td>
</tr>
<tr>
<td>Women</td>
<td>658 (62.0)</td>
<td>206 (58.4)</td>
<td>231 (65.3)</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>528 (49.8)</td>
<td>147 (41.6)</td>
<td>161 (45.5)</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td>122 (11.5)</td>
<td>29 (8.2)</td>
<td>43 (12.1)</td>
</tr>
<tr>
<td>Smoker</td>
<td>556 (52.4)</td>
<td>176 (49.9)</td>
<td>187 (52.8)</td>
</tr>
<tr>
<td>Drink alcohol</td>
<td>413 (38.9)</td>
<td>127 (36.5)</td>
<td>125 (35.3)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>132 (12.4)</td>
<td>39 (11.0)</td>
<td>35 (9.9)</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>47 (4.4)</td>
<td>11 (3.1)</td>
<td>13 (3.7)</td>
</tr>
<tr>
<td><strong>Mean (standard deviation) of characteristic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>51.5 (10.2)</td>
<td>50.5 (10.6)</td>
<td>51.7 (9.5)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.7 (7.1)</td>
<td>25.0 (6.9)</td>
<td>25.9 (6.9)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>135 (25)</td>
<td>130 (21)</td>
<td>133 (24)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>88 (14)</td>
<td>85 (13)</td>
<td>87 (14)</td>
</tr>
<tr>
<td>Heart rate (beats per minute)</td>
<td>73 (16)</td>
<td>70 (14)</td>
<td>74 (16)</td>
</tr>
<tr>
<td>Serum total cholesterol (mg/dl)</td>
<td>197 (51)</td>
<td>192 (52)</td>
<td>199 (51)</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>85.9 (13.7)</td>
<td>85.8 (14.1)</td>
<td>85.8 (13.2)</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.91 (0.51–4.26)</td>
<td>0.91 (0.53–4.25)</td>
<td>0.93 (0.52–4.27)</td>
</tr>
<tr>
<td>Estimated creatinine clearance (ml/min)</td>
<td>0.99 (0.48)</td>
<td>1.02 (0.45)</td>
<td>0.97 (0.48)</td>
</tr>
<tr>
<td>Gamma glutamyltransferase (UI)</td>
<td>57.4 (19.8–379.7)</td>
<td>50.2 (18.9–296.4)</td>
<td>55.8 (20.0–425.6)</td>
</tr>
<tr>
<td><strong>Median (interquartile range)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity (Kcal/day)</td>
<td>2.84 (1.98–3.77)</td>
<td>2.92 (1.96–3.85)</td>
<td>2.81 (2.01–3.70)</td>
</tr>
</tbody>
</table>

Values are number of subjects (%), arithmetic mean ± standard deviation, or geometric mean (5th to 95th percentile interval). \( P \) denotes the significance of the linear trend across categories of albumin-to-creatinine ratio. Significance of the difference with the adjacent lower tertile: * \( P \leq 0.05 \).
cardiac deaths, and 10 (21.3%) deaths noted as “due to hypertension.”

**Risk prediction by urinary albumin excretion**

The sex- and age-standardized rates for all-cause ($P < 0.0001$) and cardiovascular ($P = 0.013$) mortality increased across tertiles of urinary albumin-to-creatinine ratio (Table 2). In analyses of Kaplan-Meier estimates, the log-rank test was significant for all-cause mortality (Figure 1A; $P = 0.020$) and borderline significant for cardiovascular mortality (Figure 1B; $P = 0.075$) across tertiles of urinary albumin-to-creatinine ratio. The urinary albumin-to-creatinine ratio fulfilled the proportional hazard assumption for all-cause mortality ($P = 0.69$), cardiovascular mortality ($P = 0.63$), stroke ($P = 0.92$), and cardiac ($P = 0.92$) mortality. Also, there were no interactions between gender, hypertensive status, and urban or rural locality with all-cause, cardiovascular, stroke, or cardiac mortality (all $P > 0.05$). The multivariable-adjusted standardized hazard ratios for mortality in relation to urinary albumin-to-creatinine ratio are presented in Figure 2. In the total group, urinary albumin excretion predicted all-cause mortality (hazard ratio (HR), 1.26; 95% confidence interval (CI), 1.07–1.48; $P = 0.006$), but a borderline significant association existed with cardiovascular mortality (HR, 1.26; 95% CI, 0.97–1.63; $P = 0.075$).

**Table 2.** All-cause and cardiovascular event rates by tertiles of urinary albumin excretion in 1,061 participants

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Category of albumin-to-creatinine ratio</th>
<th>$P$ trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limits (μg/mg)</td>
<td>&lt;3.1</td>
<td>3.2 to 8.3</td>
</tr>
<tr>
<td>Means (5th, 95th)</td>
<td>1.8 (0.9, 3.0)</td>
<td>5.0 (3.3, 7.7)</td>
</tr>
<tr>
<td><strong>All-cause mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>38</td>
<td>35</td>
</tr>
<tr>
<td>Event rate per thousand person-years of follow-up (SE)</td>
<td>24.9 (3.9)</td>
<td>24.7 (4.1)</td>
</tr>
<tr>
<td><strong>Cardiovascular mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Event rate per thousand person-years of follow-up (SE)</td>
<td>7.3 (2.2)</td>
<td>8.7 (2.5)</td>
</tr>
</tbody>
</table>

Incidence rates were standardized for sex and age by the direct method. The number of endpoints contributing to the rates is presented. $P$ denotes significance for trend. Abbreviation: SE, standard error.

**Figure 1.** Kaplan-Meier survival function estimates for all-cause (A) and cardiovascular mortality (B) by tertiles of urinary albumin-to-creatinine ratio. $P$ values refer to the significance of the log-rank test across three tertiles.
Our results after excluding participants who died within 1 year after enrollment (all-cause mortality: HR, 1.27; 95% CI, 1.07–1.51; P = 0.007; stroke mortality: HR, 1.73; 95% CI, 1.13–2.65; P = 0.012).

**DISCUSSION**

We investigated the prognostic significance of urinary albumin excretion in a population sample of Africans without diabetes or HIV infection. The main finding was that albumin excretion from morning spot urine samples predicted all-cause and stroke mortality, but not cardiac mortality to a significant extent. In hypertensives, urinary albumin excretion also predicted cardiovascular mortality, but this seemed to be driven by the relationship with stroke mortality. These findings were, in addition to other covariates, independent of systolic blood pressure and renal function and remained robust after excluding participants with macroalbuminuria, those on antihypertensive treatment, as well as participants who died within 1 year after enrollment.

Evidence for urinary albumin excretion as a risk marker or indicator comes from various studies that included people with diabetes,\(^5\) diabetic nephropathy,\(^24\) and hypertension,\(^9\) as well as from the general population.\(^8,25\) Prognostic evidence also exists for low-grade albuminuria well below the level regarded as microalbuminuria.\(^26\) This is even seen in nondiabetic, normotensive individuals.\(^7\) Our study therefore adds to the available evidence from other population groups\(^7,10,27,28\) that, in Africans, inexpensive urinary albumin determinations from easily obtainable morning spot urine samples predict all-cause and stroke mortality.

In the present study, the relationship with all-cause mortality remained robust through group stratifications and sensitivity analyses, except in those with normoalbuminuria and normotension, which was also the case for all other outcome measures. Stroke, but not cardiac mortality, seemed to drive the relationship between urinary albumin excretion and cardiovascular mortality in the total group and the hypertensive subgroup. This is of interest, especially since the number of stroke events and the number of cardiac events were similar (P = 0.56). The relationship between cardiovascular mortality and urinary albumin excretion is complex. The most generally accepted explanation is that endothelial damage at the glomeruli, which results in albumin leakage, also reflects systemic endothelial damage\(^1,2\) and therefore the initial stage of thetherosclerosis/arteriosclerosis process. As the relationship between albuminuria and arterial stiffness is known in Africans\(^19\) and other populations,\(^3,29\) the mechanism linking albuminuria to heart failure seems more indirect through the known arterial stiffness—cardiac afterload—left ventricular hypertrophy pathway.\(^30\) On the other hand, more direct relationships exist between coronary artery disease,\(^31\) stroke,\(^32\) and albuminuria, as endothelial dysfunction can directly lead to an event. Indeed, human studies demonstrated a relationship between microalbuminuria and the presence and severity of coronary artery disease\(^33\) and that even low levels of albuminuria predict coronary events and death.\(^34\) Similarly, close relationships exist between microalbuminuria and cerebral small vessel disease, as determined by neuroimaging,\(^4,32\) and increased vascular risk, as shown in stroke survivors.\(^35\) Further evidence comes from prospective trials in diabetics.\(^36\)

**Sensitivity analyses**

Even though there was no interaction with hypertensive status, we repeated the analysis in hypertensive and normotensive participants. By doing so, the prognostic value of urinary albumin excretion seemed even more prominent in hypertensives, predicting all-cause mortality (HR, 1.38; 95% CI, 1.13–1.69; P = 0.001), cardiovascular mortality (HR, 1.45; 95% CI, 1.07–1.96; P = 0.017), stroke mortality (HR, 1.67; 95% CI, 1.10–2.53; P = 0.016) and, again, not cardiac mortality (HR, 0.72; 95% CI, 0.35–1.47; P = 0.37). No relationships existed in the normotensive group.

Systolic blood pressure, estimated creatinine clearance, gender, and urban/rural locality did not enter any of the Cox models. However, we repeated our analyses by forcing these potentially influencing variables into the models. However, we repeated our analyses by forcing these potentially influencing variables into the models. Variables that did not enter the models were gender, urban/rural locality, systolic blood pressure, estimated creatinine clearance, fasting glucose, tobacco use, and antihypertensive medication. Hazard ratios are given with 95% confidence intervals.

\(P = 0.087\). This relationship seemed to be driven by stroke mortality (HR, 1.72; 95% CI, 1.17–2.54; P = 0.006), and not cardiac mortality (HR, 0.67; 95% CI, 0.41–1.07; P = 0.094). We obtained similar results when 10 participants with macular diabetes were excluded. However, no relationship existed, with the exclusion of microalbuminuric participants (data not shown).

**Figure 2.** Adjusted standardized hazard ratios for endpoints in relation to the urinary albumin-to-creatinine ratio in the total group. The Cox models included age, body mass index, total cholesterol, gamma-glutamyltransferase, and physical activity as covariables. Variables that did not enter the models were gender, urban/rural locality, systolic blood pressure, estimated creatinine clearance, fasting glucose, tobacco use, and antihypertensive medication. Hazard ratios are given with 95% confidence intervals.
and hypertensives,6 as well as in the general population28 where albuminuria was predictive of stroke. However, coronary artery disease is less common in Africans, as shown by Sliwa et al.15 in 1,593 newly diagnosed patients with cardiovascular disease as part of the Heart of Soweto Study. One could speculate that the possible less direct association between albuminuria and heart failure and the lower probability of coronary events in Africans may explain the observed absence of the albuminuria—cardiac mortality relationship.

Urinary albumin excretion prediction of stroke in Africans is clinically important, especially since stroke is common in South Africa.37 In 2010, stroke was the fifth ranked cause of death (4.5% of total deaths) after various infectious diseases (5.0%–11.6% of total deaths).38 Establishing the prognostic significance of albumin excretion from spot urine samples could prove especially beneficial for use in low-resource settings due to the ease of collection and low cost of the analysis (55 ZAR ≈ 5 USD). Clinicians can therefore use this as an effective screening tool for increased vascular risk, which is in line with the current South African Hypertension Guidelines.39 Indeed, recent clinical trials indicate that lowering urinary albumin excretion, especially in hypertensives,40 decreases risk41 and is therefore gaining popularity as a potential therapeutic target.42 Inhibitors of the renin-angiotensin system lower albuminuria and improve outcome,41 but these drugs seem to be less effective in Africans.43,44 African-Americans also demonstrate impaired vasodilation when resistant to the microalbuminuric-lowering effects of angiotensin-converting enzyme inhibitors.45 A need therefore exists for randomized clinical trials to unravel the benefit from pharmacological intervention in Africans. The current hypertension guidelines suggest testing for microalbuminuria in those with diabetes mellitus and selective hypertensives only.46 However, our study excluded diabetic patients, and our findings were independent of blood pressure, suggesting that albuminuria is a sensitive and strong risk indicator and that the current guidelines should recommend earlier testing for albuminuria in cardiovascular risk stratification.

The current study must be interpreted within the context of its potential limitations. Even though our results were multivariable adjusted and consistent in sensitivity analyses after excluding those participants with macroalbuminuria and those on antihypertensive drugs, we cannot exclude the possibility of residual confounding. Results should also be interpreted with caution, as the numbers of stroke and cardiac deaths were low. Nonetheless, the number of events of these two outcome measures was similar. Death was established with death certificates and verbal autopsies that could have caused inaccuracies, possibly resulting in dilution of the result. Also, we excluded 949 participants. This could have resulted in selection bias; however, the albumin-to-creatinine ratio did not differ between the included and excluded participants ($P = 0.13$; Supplementary Table S1). Last, our measurements of urinary albumin excretion were restricted to a single urine specimen, while several measurements on consecutive days are preferable. However, the urinary albumin excretion as reflected by the albumin-to-creatinine ratio determined from a single morning spot urine sample is comparable to 24-hour urinary albumin excretion.8,10

In conclusion, in nondiabetic HIV-uninfected Africans, urinary albumin excretion in spot urine samples predicts all-cause and stroke mortality. This easily obtainable and inexpensive screening tool may prove invaluable in risk stratification in primary healthcare settings and may curb the increasing trend of death and disability from vascular disease in Africans.

**SUPPLEMENTARY MATERIALS**

Supplementary materials are available at American Journal of Hypertension (http://ajh.oxfordjournals.org).

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**DISCLOSURE**

The authors declared no conflict of interest.

**DISCLAIMER**

Any opinion, findings and conclusions or recommendations expressed in this material are those of the author(s) and therefore the NRF do not accept any liability in regard thereto.

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