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ASSOCIATION BETWEEN SOCIOECONOMIC INDICATORS AND CHRONIC KIDNEY DISEASE IN RURAL-URBAN GHANA-THE RODAM STUDY

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ASSOCIATION BETWEEN SOCIOECONOMIC INDICATORS AND CHRONIC KIDNEY DISEASE IN RURAL-URBAN GHANA-THE RODAM STUDY

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Abstract

Objectives Studies from high income countries suggest higher prevalence of Chronic Kidney Disease (CKD) among individuals in low socio economic groups. However, some studies from low and middleincome countries (LMICs) show the reverse pattern among those in high socioeconomic groups. It is unknown which pattern applies to individuals living in rural and urban Ghana. We therefore assessed the association between Socio-Economic Status (SES) indicators and CKD in rural and urban Ghana and to what extent the higher SES of people in urban areas of Ghana could account for differences in CKD between rural and urban populations.

Setting: We used baseline data from multi-centre Research on Obesity and Diabetes among African Migrants (RODAM) study.

Participants: A sample of 2492 adults (Rural Ghana, 1043, Urban Ghana, 1,449 aged 25 to 70 years living in Ghana.

Outcomes & Measurements Three CKD outcomes were considered using the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) severity of CKD classification: albuminuria (albumin-creatinine ratio \geq 3 mg/mmol (category \geq A2)); reduced glomerular filtration rate (eGFR < 60 mL/min/1.73 m2 (category \geq G3)) and high to very high CKD risk based on the combination of these two.

Results All three SES indicators were not associated with CKD in both rural and urban Ghana after age and sex adjustment except for rural Ghana where high wealth index was significantly associated with higher odds of reduced eGFR (AOR, 2.38; 95% C.I. 1.03-5.47). The higher rate of CKD observed in urban Ghana was not explained by the higher SES of that population.

Conclusion SES indicators were not associated with prevalence of CKD except for wealth index and reduced eGFR in rural Ghana. Consequently, the higher SES did not account for the increased rate of CKD among urban dwellers suggesting the need to identify other factors that may be driving this.

Index Words: Chronic kidney disease; socioeconomic status; health inequalities; risk factor; ethnic minority groups; migrants; RODAM study, Ghana

Strengths and limitation of the study

- The use of well-standardized study protocols across rural and urban Ghana eliminated intra protocol variability.
- Our study is also the first in Africa to use all three categories of CKD definition (albuminuria, reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of SES with CKD in rural and urban setting, this provides a more detailed information on CKD outcomes.
- The limitation of intra laboratory variability in earlier studies was eliminated using the same standard operating procedures in the same laboratory for running all samples for both rural and urban Ghana.
- The use of three constructs of SES (educational level, occupational level and wealth index) in this study also provides a much better holistic approach to assessing SES association with CKD. Also, the distribution of SES in our study reflect on the national data allowing for generalization of our findings.
- Our study was limited by the use of cross sectional design which prevented us from determining causality between predictors and CKD progression.

Introduction

In general, individuals in lower socio-economic status (SES) groups have been shown to suffer more frequently from Chronic Kidney Disease (CKD), often progressing to End Stage Renal Disease (ESRD), and associated with inadequate dialysis treatment, reduced access to kidney transplantation and poor health outcomes ¹. Recent studies have consistently found low SES to be associated with higher risk of CKD among people of African origin ²⁻⁵.

However, in some settings the well-known inverse association between SES and CKD seems to be absent, or even reversed. For example, Bryne et al. did not find an association between SES and End Stage Renal Disease ⁶. Invariably, others studies have consistently found a positive association between SES and CKD ^{7 8}. Specifically, as SES improved, unhealthful lifestyle (unhealthy diet, physical inactivity, smoking and alcohol consumption) increased in China while that of the United States decreased with improved SES ⁹. People with higher incomes, in these contexts, can afford a western lifestyle, which is more readily available in the urban areas than in the rural areas. There is therefore an interaction between individual SES and environmental factors, such as food and sedentary life style in such populations ¹⁰⁻¹². Consequently, in those settings, people with a higher SES might have higher CKD risk.

In urban areas, the population in general has a higher SES than in rural areas ¹³. For example, individuals with higher educational level migrate from rural areas to find higher occupations matching their higher education to improve on their wealth. If indeed a positive association between SES and CKD is observed in LMICs, this might underlie the well-known health differences between urban and rural areas, with urban areas having an increased risk of CKD ¹⁴. So far, it is unknown whether the reversed SES gradient (higher risk in high SES group) might explain the higher burden of CKD in urban areas as compared to rural areas in Africa.

In view of this, we assessed the association of SES with CKD in rural and urban Ghana and studied what extent the higher SES of people in urban areas could account for differences in CKD between rural and urban populations.

Methods

Study population and study design

In the present analyses, data used were from the RODAM (Research on Obesity & Diabetes among African Migrants) study, a multi-centre cross-sectional study, were used. The rationale, conceptual framework, design and methodology of the RODAM study have been described in detail elsewhere ^{15 16}. As the Healthy Life in an Urban Setting (HELIUS) study conducted among Ghanaian migrants living in Amsterdam did not find any associations between SES and CKD ¹⁷ the current study focused on rural and urban Ghana (Ashanti region of Ghana). The RODAM study was conducted from 2012 to 2015 and it comprised of individuals aged 25-70 years living in rural and urban Ghana and Ghanaian migrants in Europe. All participants below 25 and above 70 years were excluded in the present analyses. The present analysis was restricted to the rural and urban sites (n=2492) RODAM participants. Specifically, 1043 participants from rural Ghana and 1449 from urban Ghana were used in this study.

Data collection for the study was standardized across the sites. Written informed consent was obtained from each participant prior to enrolment in the study. The respective ethics committees in Ghana and the three European countries approved the study protocols before data collection began. The response rate was 76% in rural Ghana and 74% in urban Ghana. In Ghana, participants were randomly drawn from a list of 30 enumeration areas in the Ashanti region based on the 2010 population census using the multistage random sampling. These enumeration areas came from two purposively selected urban cities (Kumasi and Obuasi) and 15 randomly selected rural communities in the Ashanti region. Selected health and community authorities were first identified, notified of the study and letters were sent giving detailed explanation of the study. We sent team members to stay among the communities to familiarize with them and organize mini clinics in the field. This lasted between 1-2 weeks depending on the sampled population and responsiveness of respondents.

In Ghana, questionnaires administration and physical examination were done at the same day/time. The participants were instructed to fast from 10.00 pm the night before the physical examination. For the current study, 2566 participants with data available on both questionnaire data and physical measurements were used. We excluded (n=74) individuals outside the RODAM age range of 25-70 years resulting in a data set of 2492 for analysis. These comprised 1,449 Urban Ghana and 1043 Rural Ghana. For the final analysis, individuals with no data on CKD status (n=42) were excluded.

Measurements

Demographic and lifestyle factors

Information on demographics, educational level, occupational level, wealth index and lifestyle factors (smoking and physical activity) were obtained by questionnaire. Physical examinations were performed with validated devices per standardized operational procedures across all study sites. Weight was measured in light clothing and without shoes with SECA 877 scales to the nearest 0.1 kg. Height was measured without shoes with a portable stadiometer (SECA 217) to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m²). Overweight was defined as BMI of \geq 25 to <30 kg/m² and obesity as BMI \geq 30 kg/m^{2 18}. Waist circumference was measured in cm at the midpoint between the lower rib and the upper margin of the iliac crest. Per participant all anthropometrics were measured twice by the same assessor and the average of the two measurements were used for analyses.

Covariates

Socioeconomic indicators used in this study were educational level, occupational status and level of wealth index. Educational level was determined based on self-reported highest educational qualification accomplished based on the Ghanaian educational system. Occupational level was determined based on self-reported current occupation if still employed or/and last occupation before retirement or student. The reported occupations were further coded according to the International Standard Classification of Occupations scheme (ISCO-08). Wealth index was determined using the World Health Organization (WHO) standard of wealth index classification. Wealth index was based on data collected in the Household Questionnaire. The questionnaire comprised of questions on household's ownership of several consumer items such as television, car, flooring material, toilet facilities etc. Each household was assigned a standard score for each asset. Wealth index was then expressed in five quintiles. The five quintiles were further categorized into three quintiles by combining the second and third quintiles due to small numbers ¹⁹. All three SES constructs were further classified as low, medium and high SES and their relationship to each other tested.

Outcome: CKD prevalence

Participants were asked to bring an early morning urine sample for the analyses of albuminuria and creatinine levels. Urinary albumin concentration (in mg/L) was measured by an immunochemical turbidimetric method (Roche Diagnostics). Urinary creatinine concentration (in umol/L) was measured by a kinetic spectrophotometric method (Roche Diagnostics). Estimated glomerular filtration rate (eGFR)

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was calculated using the CKDEPI (CKD Epidemiology Collaboration) creatinine equation ²⁰. Urinary albumin-creatinine ratio (ACR; expressed in mg/g) was calculated by taking the ratio between urinary albumin and urinary creatinine. eGFR and albuminuria were categorized according to the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) classification ²¹. eGFR was categorized as follows: $G_{1,2} \ge 1$ 90 mL/min/1.73 m² (normal kidney function); G2, 60 to 89 mL/min/1.73 m² (mildly decreased); G3a, 45 to 59 mL/min/1.73 m² (mildly to moderately decreased); G3b, 30 to 44 mL/min/1.73 m² (moderately to severely decreased); G4, 15 to 29 mL/min/1.73 m² (severely decreased); and G5, < 15 mL/min/1.73 m² (kidney failure). Albuminuria categories were derived from ACR and were as follows: A1, < 3mg/mmol (normal to mildly increased); A2, 3 to 30 mg/mmol (moderately increased); and A3, > 30mg/mmol (severely increased). CKD status was categorized according to severity of kidney disease (green, low risk; vellow, moderately increased risk; orange, high risk; and red, very high risk) using the combination of eGFR (G1-G5) and albuminuria (A1-A3) levels defined by the 2012 KDIGO guideline ²². Due to the small number of participants in the very high risk category of CKD, high and very high risk groups were combined. Reduced eGFR was defined as $eGFR < 60 \text{ mL/min}/1.73 \text{ m}^2$. Because of the small number of participants in the severely increased albuminuria category, we defined albuminuria as ACR \geq 3 mg/mmol by combining the moderately increased (A2) and severely increased (A3) categories.

Other variables

Blood pressure (BP) was measured three times using a validated semi-automated device (The Microlife WatchBP home) with appropriate cuffs in a sitting position after at least 5 min rest. The mean of the last two BP measurements was used in the analyses. Hypertension was defined as systolic BP \geq 140 mmHg, and/or diastolic BP \geq 90 mmHg, and/or being on antihypertensive medication treatment, and/or selfreported hypertension. Trained research assistants in the two sites collected fasting venous blood samples. All the blood samples were processed and aliquoted immediately (within one hour to maximum three hours of the vena puncture) after collection per standard operation procedures, and then temporarily stored at the local research location at -20° C. The separated samples were then transported to the local research centres laboratories, where they were checked, registered and stored at -80°C. To avoid intralaboratory variability, the stored blood samples from the local research centres were transported to Berlin, Germany for biochemical analyses. Fasting plasma glucose concentration was measured using an enzymatic method (hexokinase). Type 2 diabetes was defined according to the WHO diagnostic criteria (fasting glucose \geq 7.0 mmol/L, and/or current use of medication prescribed to treat diabetes, and/or selfreported diabetes)²³. Concentration of total cholesterol was assessed using colorimetric test kits. All biochemical analyses were performed using an ABX Pentra 400 chemistry analyzer (ABX Pentra; Horiba ABX, Germany). Hypercholesterolemia was defined as total cholesterol level ≥ 6.22 mmol/L. Serum

creatinine concentration (in umol/L) was determined by a kinetic colorimetric spectrophotometric isotope dilution mass spectrometry–calibrated method (Roche Diagnostics). Biochemical analyses were subject to extensive quality checks including blinded serial measurements.

Patient and Public Involvement

Community leaders were involved in the recruitment of patients. These comprised of religious communities (churches and mosques), endorsement from local key leaders and establishing relationships with healthcare organizations. We also provided information on the study by involving the local media (radio and television stations). We sent letters to all selected health and community authorities to notify participants of the study. Team members were sent to the various community to stay among the community and organize mini clinics for a period of 1-2 weeks. Results of the study were disseminated through seminars, durbars and via radio and television stations.

Statistical methods

Participants' characteristics were expressed as absolute numbers and percentages for categorical variables and as means and standard deviations (SD) for continuous variables. CKD prevalence with 5% error bars were presented as bar graphs for each SES construct across rural and urban Ghana. Spearman's rank correlation was used to determine correlations between the three SES constructs. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were estimated by means of logistic regression analyses to study the odds of albuminuria (ACR>3 mg/mmol, A2-A3, moderately to severely increased albuminuria), reduced kidney function (eGFR< 60 mL/min/1.73 m², G3-G5 moderately to severely decreased kidney function) and increased CKD risk (high and very high CKD risk), with adjustments for potential covariates (age and sex). These covariates were adjusted for to account for their impact in the pathway of CKD incidence, prevalence and progression ²⁴. Model 1 was age and sex adjusted. The analyses were performed for the total population (using low educational level, low occupational status and low level of wealth index as reference categories). Further analysis was conducted using rural Ghana as reference. Model 1 was adjusted for age and sex while model 2 was adjusted for age, sex and educational level. Model 3 was adjusted for age, sex and occupational status while model 4 was adjusted for age, sex and level of wealth index (p < 0.05). Tolerance test and variance inflation factor (VIF) showed very small degree of collinearity among SES predictors thus we adjusted for each of SES variables separately. Complete case analysis approach was used. All data available were included in the ageadjusted models. All analyses were performed using STATA, version 14.0 (StataCorp LP).

Results

Table 1 shows characteristics of study participants. Participants in rural Ghana were slightly older than those in urban Ghana. Female preponderance was observed in both rural and urban Ghana, though higher proportions were observed in urban Ghana. Individuals living in rural Ghana were generally less educated compared with those living in urban Ghana. There were slightly more individuals with low occupational status in urban Ghana compared with their peers in rural Ghana. People in urban Ghana were wealthier than their rural counterparts. Rural Ghanaians were more physically active compared with their urban peers. Smoking was low among Ghanaians though rural Ghanaians were more likely to smoke compared with their urban peers. Hypercholesterolemia was more prevalent in urban Ghana than in rural Ghana. Hypertension and type 2 diabetes were more prevalent in urban Ghanaians compared with those living in rural Ghana. Urban Ghanaians were markedly more obese compared with their rural peers. Except for eGFR, albuminuria and CKD risk prevalence rates were higher in urban Ghana compared with rural Ghana.

<u> </u>	Rural Ghana	Urban Ghana
	10.10 (11.0)	1 4 40 (50 1)
Number of participants, N (%)	1043 (41.9)	1449 (58.1)
Mean age, years (SD)	46.5 (12.6)	45.2 (11.4)
Females, N (%)	638 (61.2)	1034 (71.4)
Educational level n (%)		
Low	555 (56.9)	614 (43.9)
Middle	311 (31.9)	547 (39.1)
High	108 (11.8)	239 (17.0)
Occupational status, n (%)		
Low	250 (25.7)	374 (26.7)
Middle	628 (64.5)	818 (58.4)
High	96 (9.8)	209 (14.9)
Wealth index, n (%)		
Low	449 (46.5)	368 (26.6)
Middle	276 (28.6)	416 (30.0)
High	241 (24.9)	602 (43.4)
Low physical activity, n (%)	663 (47.22)	592 (60.7)
Smoking, n (%)	22 (2.3)	14 (1.0)
Hypercholesterolemia, n (%)	78 (7.6)	270 (18.7)
Hypertension, n (%)	306 (29.3)	531 (36.7)
Diabetes, n (%)	53 (5.1)	153 (10.6)

Table 1: Baseline characteristics by location

Albuminuria, n (%) A1, Normal to mildly increased (ACR <3 mg/mmol)	930 (91.6)	1285 (89.1)
A2-A3, moderately to severely increased (ACR \geq 3 mg/mmol)	85 (8.4)	158 (10.9)
eGFR, n (%)		
G1-G2 ($\geq 60 \text{ mL/min}/1.73 \text{m}^2$)	989 (96.3)	1388 (96.3)
$G3-G5 (<60 \text{ mL/min}/1.73 \text{ m}^2)$	38 (3.7)	54 (3.7)
CKD risk, n (%)		
Low risk (green)	916 (90.5)	1281 (88.9)
Moderately increased to very high risk (yellow to red)	96 (9.5)	160 (11.1)

Abbreviations: N, number of respondents; SD, standard deviation; eGFR, estimated glomerular filtration rate; ACR, albumin creatinine ratio; CKD, Chronic kidney disease

Figure 1 shows prevalence of CKD by level of education in urban and rural Ghana. Prevalence of CKD decreased with increasing levels of education in rural Ghana. Higher prevalence of CKD was observed among individuals with low educational level compared with those with middle and high educational level. However, those with high educational level in urban Ghana had higher prevalence of CKD compared with those with middle level education. For occupational status, prevalence of CKD was higher among individuals with low occupational status in urban Ghana. Similar patterns were observed in rural Ghana, however, those with higher occupational status had higher prevalence of CKD compared with those with middle occupational status (Figure 2). Figure 3 shows prevalence of CKD by level of wealth index. CKD prevalence among the levels of wealth index varied between urban and rural Ghana. Those with middle level wealth index had higher prevalence of CKD compared with those with low or high CKD prevalence in both rural and urban Ghana. CKD prevalence rate for low and high level wealth index in urban Ghana was the same while that of rural Ghana was slightly different.

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In urban Ghana, high educational level was positively associated with high wealth index but inversely associated with occupation. In rural Ghana, high education was positively associated with high wealth index, but there was no significant association between education and occupation. High wealth index was inversely associated with high occupational status in both rural and urban Ghana (Table 2).

Table 2: Relationship between SES constructs (educational, occupational level and wealth index) by urban rural Ghana

Correlation matrix	Educational level	Occupational level	Wealth index	SES
Urban Ghana		604		
Educational level	1.000			
Occupational status	-0.115*	1.000		
Wealth Index	0.294*	-0.126*	1.000	
Composite SES	0.576*	-0.024	0.937*	1.000
Rural Ghana				
Educational level	1.000			
Occupational status	0.017	1.000		
Wealth Index	0.219*	-0.135*	1.000	
SES	0.504*	0.029	0.934*	1.000

Significant at 1%, Spearman's correlation

Table 3 shows association between level of education, occupational status, level of wealth index and prevalence of CKD. After adjusting for age and sex, we observed no significant association between SES indicators (educational level, occupational status and wealth index) and CKD in urban Ghana. In rural Ghana, whereas educational level and occupational status were not associated with CKD prevalence, high wealth index was significantly associated with higher odds of reduced eGFR.

Table 3: Association of SES indicators (educational level, occupational status and wealth index level) with albuminuria, reduced eGFR and CKD risk

	Albuminuria	a (ACR≥3 mg/mmol)	eGFR < 60 m	eGFR < 60 mL/min/1.73 m2		High to very high CKD risk (KDIGO, 2012)	
		OR (95% CI)		OR (95% CI)		OR (95% CI)	
	n (%)	Model 1	n (%)	Model 1	n cases (%)	Model 1	
Education							
Urban Ghana							
Low	612 (14.7)	1.00 (Reference)	612 (4.1)	1.00 (Reference)	612 (14.1)	1.00 (Reference)	
Middle	546 (7.8)	0.51 (0.34-0.76)	546 (3.7)	1.12 (0.59-2.12)	545 (8.1)	0.59 (0.39-0.89)	
High	238 (8.4)	0.53 (0.31-0.91)	238 (3.4)	0.91 (0.37-2.19)	238 (10.9)	0.83 (0.51-1.38)	
Rural Ghana							
Low	540 (8.7)	1.00 (Reference)	548 (3.8)	1.00 (Reference)	538 (9.5)	1.00 (Reference)	
Middle	301 (6.3)	0.89 (0.51-1.59)	303 (3.9)	1.69 (0.77-3.66)	300 (8.7)	1.33 (0.79-2.25)	
High	105 (3.8)	0.66 (0.23-1.95)	107 (2.8)	1.28 (0.35-4.71)	105 (3.8)	0.69 (0.23-2.02)	
Occupational status							
Urban Ghana							
Low	207 (10.1)	1.00 (Reference)	207 (6.8)	1.00 (Reference)	207 (12.1)	1.00 (Reference)	
Middle	817 (11.1)	1.50 (0.88-2.83)	817 (3.6)	1.15 (0.56-2.35)	816 (11.6)	1.37 (0.84-2.56)	
High	373 (11.0)	1.57 (0.89-2.53)	373 (2.7)	1.02 (0.41-2.52)	373 (9.7)	1.21 (0.68-2.14)	
Rural Ghana							

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Low	95 (10.5)	1.00 (Reference)	96 (10.4)	1.00 (Reference)	95 (14.7)	1.00 (Reference)
Middle	610 (6.7)	0.65 (0.31-1.37)	619 (3.1)	0.37 (0.16-0.85)	608 (7.6)	0.55 (0.28-1.08)
High	241 (8.3)	0.99 (0.43-2.28)	243 (2.9)	0.51 (0.18-1.44)	240 (9.2)	0.94 (0.44-2.01)
Wealth index						
Urban Ghana						
Low	367 (11.2)	1.00 (Reference)	367 (3.5)	1.00 (Reference)	367 (10.1)	1.00 (Reference)
Middle	414 (12.3)	1.12 (0.73-1.74)	414 (3.9)	1.30 (0.61-2.80)	413 (13.1)	1.45 (0.93-2.27)
High	601 (9.8)	0.82 (0.55-1.25)	600 (3.8)	1.13 (0.55-2.31)	600 (10.8)	1.11 (0.72-1.71)
Rural Ghana						
Low	441 (7.9)	1.00 (Reference)	446 (3.1)	1.00 (Reference)	441 (8.4)	1.00 (Reference)
Middle	264 (8.7)	1.13 (0.65-1.98)	269 (3.7)	1.22 (0.52-2.84)	262 (10.3)	1.31 (0.77-2.25)
High	234 (5.6)	0.78 (0.40-1.53)	235 (5.1)	2.38 (1.03-5.47)	233 (7.7)	1.16 (0.63-2.14)

Model 1, adjusted for age and sex; Abbreviations: CI, confidence interval; ACR, albumin creatinine ration; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; OR, odds ratio, n= total number of individuals in rural and urban Ghana among the various levels of SES constructs; %, proportion of individuals with CKD among the various levels of SES constructs in rural and urban Ghana.

Table 4 shows the contribution of all three SES constructs to rural and urban CKD prevalence differences. The odds of albuminuria and CKD risk was significantly higher in urban Ghana compared with rural Ghana. The higher rate of CKD observed in urban Ghana was not explained by the higher SES of that population as compared to their rural counterparts.

Table 4: Contribution of SES indicators to rural-urban differences in albuminuria, reduced eGFR and CKD risk

		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
	0h	Model 1	Model 2	Model 3	Model 4
Albuminuria (ACR≥3 mg/mmol					
Sites	n cases (%)				
Urban Ghana	1,443 (10.9)	1.37 (1.03-1.81)	1.70 (1.25-2.31)	1.55 (1.15-2.10)	1.62 (1.18-2.19)
Rural Ghana	1,015 (8.4)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
eGFR < 60 mL/min/1.73 m2					
Sites	n cases (%)				
Urban Ghana	1,442 (3.7)	1.27 (0.82-1.97)	1.20 (0.76-1.89)	1.18 (0.79-1.86)	1.12 (0.70-1.78)
Rural Ghana	1,027 (3.7)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
High to very high CKD risk					
Sites	n cases (%)				
Urban Ghana	1,441 (11.1)	1.23 (1.01-1.62)	1.44 (1.07-1.93)	1.38 (1.03-1.84)	1.36 (1.01-1.83)
Rural Ghana	1,012 (9.46)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)

Model 1: adjusted for age and sex; Model 2: adjusted for age, sex and education level; Model 3: adjusted for age, sex and occupational status; Model 4: adjusted for age, sex and wealth index; Abbreviations: CI, confidence interval; ACR, albumin creatinine ratio; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; OR, odds ratio, n=number of participants. n= total number of individuals in rural and urban Ghana; %, proportion of individuals with CKD among urban and rural Ghana.

Discussion

Key findings

Our study findings show no association between all three SES constructs and the prevalence of CKD in both rural and urban Ghana except for wealth index in rural Ghana, with the risk of CKD being higher in the wealthier populations. The higher rate of CKD observed in urban Ghana could not be attributed to the higher SES of that population compared to their rural counterparts.

Discussion of key findings

Association of SES with CKD in rural and urban Ghana

Our study did not find any significant associations between all three SES constructs and CKD among rural and urban Ghana except for wealth index in rural Ghana. The positive association observed between wealth index in rural Ghana may be due to a number of reasons. A comparison of the three SES constructs showed higher educational level to be associated with wealth index in both rural and urban Ghana but not occupational level. This seems to suggest that occupational level may not be adequately capturing the SES status of individuals living in these settings in relation to CKD. For example, Masthi et al, compared different SES scales in rural and urban India and concluded that Standard of Living Index (SLI) scale was more accurate for classification of SES in urban and rural setting ²⁵. Our finding is consistent with other studies ^{6 26} which reported no association between SES and CKD in high-income countries and LMICs, but in contrast with other studies ^{2-4 27} that found positive associations between SES and CKD. The reasons for our current finding are unclear. However, it has been suggested that these inconsistent associations may be due to the varying pathways through which the effect of SES on health status is mediated. For example, at a given educational level marked ethnic differences have been reported. Additionally, similar differences were observed for wealth status at a given income level ²⁸⁻³⁰.

Contribution of SES to observed CKD risk differences between rural and urban Ghana

We observed higher rates of CKD in urban Ghana compared with rural Ghana, as expected. The observed higher rates of CKD in our study were not explained by the higher SES of that population as compared to their rural counterparts. Our results indicate that this is due to the lack of a clear difference in the SES distribution of rural and urban Ghana observed in this study, as well as to the lack of associations between SES and CKD. Consistent with our findings, in a study conducted in Northern Tanzania SES did not explain increased risk of CKD in urban Tanzania ²⁶. The lack of associations between SES and CKD

could probably partly be explained by the process of epidemiological transition in relation to the "diffusion theory" of ischemic heart disease mortality. This theory attributes the commencement of ischemic heart disease to individuals in the high SES group due to their ability to afford behaviours (smoking, alcohol and sedentary lifestyles) which increased risk of ischemic heart disease. The lower SES groups were later affected partially because of improved living standards, imitation and urbanization. The higher SES groups were the first to embrace behavioural changes required to decrease the risk of ischemic heart disease and this resulted in reversing the gradient ³¹. The rapid urbanization of some rural communities in the Ashanti region of Ghana and the imitation of urban lifestyle could account for our finding. Also, it could be that whereas the high SES group in urban Ghana has already embraced favourable behavioural changes, those in rural Ghana are vet to do so ³². This explains the observed association of wealth index with CKD in rural Ghana but not in urban Ghana. The complexities of influence of SES on prevalence and progression of CKD and the differential prevalence of established risk factors (diabetes, obesity and hypertension) in rural and urban Ghana may also contribute to the different associations of SES with CKD prevalence observed in rural and urban Ghana. In our study, the prevalence rates of hypercholesterolemia, hypertension and type 2 diabetes were substantially higher in urban Ghana compared with that of rural Ghana. Also, the interplay of other less understood or researched factors (e.g., exposure to nephrotoxins, herbal medications, sepsis) may be influencing the pathway in which SES influences CKD prevalence and progression.

Strength and limitation

 Our study presents several strengths. First, we used well-standardized study protocols across rural and urban Ghana. Our study is also the first in Africa to use all three categories of CKD definition (albuminuria, reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of SES with CKD in rural and urban setting, this provides a more detailed information on CKD outcomes. The limitation of intra laboratory variability in earlier studies was eliminated using the same standard operating procedures in the same laboratory for running all samples for both rural and urban Ghana. The use of three constructs of SES in this study also provides a much better holistic approach to assessing SES. Also, the distribution of SES in our study reflect on the national data allowing for generalization of our findings. Our study was limited by the use of cross sectional design which prevented us from determining causality between predictors and CKD progression.

Conclusion

All three SES constructs appear not to be associated with prevalence of CKD in urban and rural Ghana except for wealth index in rural Ghana. The observed higher prevalence of CKD in urban Ghana was not explained by the higher SES in urban Ghana. Our study seems to suggest that other non-traditional factors such as nephrotoxins, herbal medications and misuse of over the counter drugs may play a role and underscores the need to further explore these factors.

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Contributors

My co-authors have all contributed substantially to this manuscript and approve of this submission. Research idea and study design: DNA, CA, KS, DA, EB, KM, JA; data acquisition and curation: DNA, CA, EB, KM, data analysis/interpretation: DNA, CA, KS, DA, EB, KM, LS, JA, EOD, KKB, FPM, ID, JS, SB, ADA; statistical analysis: DNA, CA, KS. DNA, CA, KS, DA, EB, KM, LS, JA, EOD, KKB, FPM, ID, JS, SB, ADA contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. DNA and CA takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Competing interest: I have communicated with all my co-authors and obtained their full disclosures. My co-authors and I declare no conflicts of interest.

Patient Consent: None declared

Ethics approval: IRBs at each participating site.

Data sharing statement: Data are available from the RODAM research cohort, a third party. Dr. Eric Beune affiliated with the RODAM research cohort and a co-author of this paper in accordance with the RODAM requirements for collaboration. Dr. Beune is the Data Collection Coordinator of RODAM and may be contacted with further questions (e.j.beune@amc.uva.nl). Additionally, researchers interested in further collaboration with RODAM may see the following URL: <u>http://www.rod-am.eu/</u>

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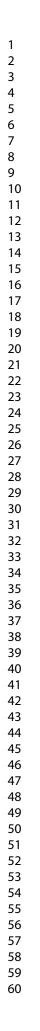
Legend for figures

Figure 1: Prevalence of chronic kidney disease (CKD) across level of education among urban and rural participants Definitions according to 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups.

Figure 2: Prevalence of chronic kidney disease (CKD) across occupational status among urban and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups.

Figure 3: Prevalence of chronic kidney disease (CKD) across wealth index categories among urban and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups.

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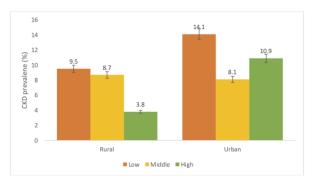


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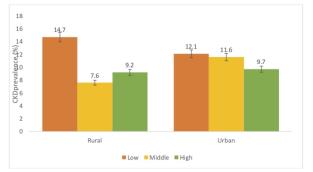
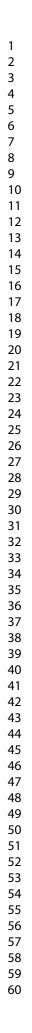


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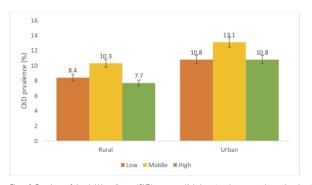


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A CROSS-SECTIONAL STUDY OF ASSOCIATION BETWEEN SOCIOECONOMIC INDICATORS AND CHRONIC KIDNEY DISEASE IN RURAL-URBAN GHANA-THE RODAM STUDY

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Keywords:	Chronic Kidney Disease, Socioeconomic status, Health inequalities, RODAM study, rural, urban

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39 Abstract

4 40 5 41

Objectives: Studies from high income countries suggest higher prevalence of Chronic Kidney Disease 42 (CKD) among individuals in low socio economic groups. However, some studies from low and middle-43 income countries (LMICs) show the reverse pattern among those in high socioeconomic groups. It is 44 unknown which pattern applies to individuals living in rural and urban Ghana. We therefore assessed the 45 association between Socio-Economic Status (SES) indicators and CKD in rural and urban Ghana and to 46 what extent the higher SES of people in urban areas of Ghana could account for differences in CKD 47 between rural and urban populations.

Methods: We used baseline data from multi-centre Research on Obesity and Diabetes among African 50 Migrants (RODAM) study. A sample of 2492 adults (Rural Ghana, 1043, Urban Ghana, 1,449) aged 25 to 51 70 years living in Ghana. Three CKD outcomes were considered using the 2012 KDIGO (Kidney 52 Disease: Improving Global Outcomes) severity of CKD classification: albuminuria (albumin-creatinine 53 ratio \geq 3 mg/mmol (category \geq A2)); reduced glomerular filtration rate (eGFR < 60 mL/min/1.73 m2 54 (category \geq G3)) and high to very high CKD risk based on the combination of these two.

56 Results: All three SES indicators were not associated with CKD in both rural and urban Ghana after age 57 and sex adjustment except for rural Ghana where high wealth index was significantly associated with 58 higher odds of reduced eGFR (AOR, 2.38; 95% C.I. 1.03-5.47). The higher rate of CKD observed in 59 urban Ghana was not explained by the higher SES of that population.

Conclusion: SES indicators were not associated with prevalence of CKD except for wealth index and reduced eGFR in rural Ghana. Consequently, the higher SES did not account for the increased rate of CKD among urban dwellers suggesting the need to identify other factors that may be driving this.

Index Words: Chronic kidney disease; socioeconomic status; health inequalities; risk factor; ethnic minority groups; migrants; RODAM study, Ghana

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2 3	88	Strengths and limitation of the study
4	89	Strengths and minitation of the study
5 6	90	• The use of well-standardized study protocols across rural and urban Ghana eliminated intra
7	91	protocol variability.
8 9	92	
10 11	93	• Our study is also the first in Africa to use all three categories of CKD definition
12	94	(albuminuria, reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of
13 14	95	SES with CKD in rural and urban setting. This provides a more detailed information on
15	96	CKD outcomes.
16 17	97	
18	98	• The limitation of intra laboratory variability in earlier studies was eliminated using the same
19 20	99	standard operating procedures in the same laboratory for running all samples for both rural and
21 22	100	urban Ghana.
23	101	
24 25	102	• The use of three constructs of SES (educational level, occupational level and wealth index) in this
26	103	study also provides a much better holistic approach to assessing SES association with CKD.
27 28	104	
29	105	• Our study was limited by the use of cross sectional design which prevented us from determining
30 31	106	causality between predictors and CKD progression.
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3 4	128	Introduction
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	130	
	131	In general, individuals in lower socio-economic status (SES) groups have been shown to suffer more
	132	frequently from Chronic Kidney Disease (CKD), often progressing to End Stage Renal Disease (ESRD),
	133	and associated with inadequate dialysis treatment, reduced access to kidney transplantation and poor
	134	health outcomes ¹ . Recent studies have consistently found low SES to be associated with higher risk of
	135	CKD among people of African origin ²⁻⁵ .
	136	However, in some settings the well-known inverse association between SES and CKD seems to be absent,
	137	or even reversed. For example, Bryne et al. did not find an association between SES and End Stage Renal
	138	Disease 6 . Other studies have found a positive association between SES and CKD 78 . Specifically, as
	139	SES improved, unhealthful lifestyle (unhealthy diet, physical inactivity, smoking and alcohol
	140	consumption) increased in China while that of the United States decreased with improved SES ⁹ . People
24 25	141	with higher incomes, in these contexts, can afford a western lifestyle, which is more readily available in
25 26	142	the urban areas than in the rural areas. There is therefore an interaction between individual SES and
27 28	143	environmental factors, such as food and sedentary life style in such populations ¹⁰⁻¹² . Consequently, in
29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47	144	those settings, people with a higher SES might have higher CKD risk.
	145	In urban areas, the population in general has a higher SES than in rural areas ¹³ . For example, individuals
	146	with higher educational level migrate from rural areas to find higher occupations matching their higher
	147	education to improve on their wealth. If indeed a positive association between SES and CKD is observed
	148	in LMICs, this might underlie the well-known health differences between urban and rural areas, with
	149	urban areas having an increased risk of CKD ¹⁴ . So far, it is unknown whether the reversed SES gradient
	150	(higher risk in high SES group) might explain the higher burden of CKD in urban areas as compared to
	151	rural areas in Africa.
	152	
	153	In view of this, we assessed the association of SES with CKD in rural and urban Ghana and studied what
	154	extent the higher SES of people in urban areas could account for differences in CKD between rural and
	155	urban populations.
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2 3 4 5 6	162 163 164 165	Methods Study population and study design
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24	165	In the present analyses, data from the RODAM (Research on Obesity & Diabetes among African
	167	Migrants) study, a multi-centre cross-sectional study were used. The rationale, conceptual framework,
	168	design and methodology of the RODAM study have been described in detail elsewhere $^{15 16}$. As the
	169	Healthy Life in an Urban Setting (HELIUS) study conducted among Ghanaian migrants living
	170	in Amsterdam did not find any associations between SES and CKD ¹⁷ the current study focused on
	171	rural and urban Ghana (Ashanti region of Ghana). The RODAM study was conducted from 2012 to 2015
	172	and it comprised of individuals aged 25-70 years living in rural and urban Ghana and Ghanaian migrants
	173	in Europe. All participants below 25 and above 70 years were excluded in the present analyses. The
	174	present analysis was restricted to the rural and urban sites (n=2492) RODAM participants. Specifically,
	175	1043 participants from rural Ghana and 1449 from urban Ghana were used in this study.
25	176 177	Data collection for the study was standardized across the sites. Written informed consent was obtained
26 27	177	from each participant prior to enrolment in the study. The respective ethics committees in Ghana and the
28 29	178	three European countries approved the study protocols before data collection began. Specifically, we
30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	179	obtained ethical clearance in Ghana from (School of Medical Sciences/Komfo Anokye Teaching Hospital
	180	
		Committee on Human Research, Publication & Ethical Review Board, in the Netherlands, (Institutional Review Board of the AMC, University of Amsterdam) in Committee of Charita
	182 183	Review Board of the AMC, University of Amsterdam), in Germany, (Ethics Committee of Charite-
		Universitätsmedizin) and the UK (London School of Hygiene and Tropical Medicine Research Ethics
	184	Committee) before data collection began in each country.
	185	The response rate was 76% in rural Ghana and 74% in urban Ghana. In Ghana, participants were
	186	randomly drawn from a list of 30 enumeration areas in the Ashanti region based on the 2010 population
	187	census using the multistage random sampling. These enumeration areas came from two purposively
	188	selected urban cities (Kumasi and Obuasi) and 15 randomly selected rural communities in the Ashanti
45 46	189	region. Selected health and community authorities were first identified, notified of the study and letters
47 48 49 50 51 52 53 54	190	were sent giving detailed explanation of the study. We sent team members to stay among the communities
	191	to familiarize with them and organize mini clinics in the field. This lasted between 1-2 weeks depending
	192	on the sampled population and responsiveness of respondents.
	193	In Ghana, questionnaires administration and physical examination were done at the same day/time. The
	194	participants were instructed to fast from 10.00 pm the night before the physical examination. For the
55 56 57	195	current study, 2566 participants with data available on both questionnaire data and physical measurements

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196 were used. We excluded (n=74) individuals outside the RODAM age range of 25-70 years resulting in a 197 data set of 2492 for analysis. These comprised 1,449 Urban Ghana and 1043 Rural Ghana. For the final 198 analysis, individuals with no data on CKD status (n=42) were excluded.

199 Measurements

11 200 **Covariates**

201 Demographic and lifestyle factors

Information on demographics, educational level, occupational level, wealth index and lifestyle factors (smoking and physical activity) were obtained by questionnaire. Physical examinations were performed with validated devices per standardized operational procedures across all study sites. Weight was measured in light clothing and without shoes with SECA 877 scales to the nearest 0.1 kg. Height was measured without shoes with a portable stadiometer (SECA 217) to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) . Overweight was defined as BMI of \geq 25 to <30 kg/m² and obesity as BMI \geq 30 kg/m²¹⁸. Per participant all anthropometrics were measured twice by the same assessor and the average of the two measurements were used for analyses.

210 Predictor: SES

Socioeconomic indicators used in this study were educational level, occupational status and level of wealth index. Educational level was determined based on self-reported highest educational qualification accomplished based on the Ghanaian educational system. Occupational level was determined based on self-reported current occupation if still employed and/or last occupation before retirement or student. The reported occupations were further coded according to the International Standard Classification of Occupations scheme (ISCO-08). Where 'high' (professionals, managers, clerical support staff, higher grade routine non-manual employees service and sales-related occupations) and 'low' (craft and related trades workers, elementary occupations and farmers) and the rest were categorize into the 'middle'. Wealth index was determined using the World Health Organization (WHO) standard of wealth index classification. Wealth index was based on data collected in the Household Questionnaire. The questionnaire comprised of questions on household's ownership of several consumer items such as television, car, flooring material, toilet facilities etc. Each household was assigned a standard score for each asset. Wealth index was then expressed in five categories. The five categories were further categorized into three categories by combining the second and third category due to small numbers ¹⁹. All three SES constructs were further classified as low, medium and high SES and their relationship to each

other tested. A composite SES variable (SES) was generated based on the three SES constructs using the
 EGEN group command in STATA. This was also categorized into 3 categories (low, medium and high).

228 Co-morbidity factors

Blood pressure (BP) was measured three times using a validated semi-automated device (The Microlife WatchBP home) with appropriate cuffs in a sitting position after at least 5 min rest. The mean of the last two BP measurements was used in the analyses. Hypertension was defined as systolic BP > 140 mmHg. and/or diastolic BP \geq 90 mmHg, and/or being on antihypertensive medication treatment, and/or self-reported hypertension. Trained research assistants in the two sites collected fasting venous blood samples. All the blood samples were processed and aliquoted immediately (within one hour to maximum three hours of the vena puncture) after collection per standard operation procedures, and then temporarily stored at the local research location at -20° C. The separated samples were then transported to the local research centres laboratories, where they were checked, registered and stored at -80°C. To avoid intra-laboratory variability, the stored blood samples from the local research centres were transported to Berlin, Germany for biochemical analyses. Fasting plasma glucose concentration was measured using an enzymatic method (hexokinase). Type 2 diabetes was defined according to the WHO diagnostic criteria (fasting glucose \geq 7.0 mmol/L, and/or current use of medication prescribed to treat diabetes, and/or self-reported diabetes)²⁰. Concentration of total cholesterol was assessed using colorimetric test kits. All biochemical analyses were performed using an ABX Pentra 400 chemistry analyzer (ABX Pentra: Horiba ABX, Germany). Hypercholesterolemia was defined as total cholesterol level ≥ 6.22 mmol/L. Serum creatinine concentration (in umol/L) was determined by a kinetic colorimetric spectrophotometric isotope dilution mass spectrometry-calibrated method (Roche Diagnostics). Biochemical analyses were subject to extensive quality checks including blinded serial measurements.

40248Outcome: CKD prevalence

Participants were asked to bring an early morning urine sample for the analyses of albuminuria and creatinine levels. Urinary albumin concentration (in mg/L) was measured by an immunochemical turbidimetric method (Roche Diagnostics). Urinary creatinine concentration (in umol/L) was measured by a kinetic spectrophotometric method (Roche Diagnostics). Estimated glomerular filtration rate (eGFR) was calculated using the CKDEPI (CKD Epidemiology Collaboration) creatinine equation ²¹. Urinary albumin-creatinine ratio (ACR; expressed in mg/g) was calculated by taking the ratio between urinary albumin and urinary creatinine. eGFR and albuminuria were categorized according to the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) classification ²². eGFR was categorized as follows: $G_{1,2} \ge 1$ 90 mL/min/1.73 m² (normal kidney function); G2, 60 to 89 mL/min/1.73 m² (mildly decreased); G3a, 45

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to 59 mL/min/1.73 m² (mildly to moderately decreased); G3b, 30 to 44 mL/min/1.73 m² (moderately to severely decreased); G4, 15 to 29 mL/min/1.73 m² (severely decreased); and G5, < 15 mL/min/1.73 m² (kidney failure). Albuminuria categories were derived from ACR and were as follows: A1, < 3mg/mmol (normal to mildly increased); A2, 3 to 30 mg/mmol (moderately increased); and A3, > 30 mg/mmol (severely increased). CKD status was categorized according to severity of kidney disease (green, low risk; vellow, moderately increased risk; orange, high risk; and red, very high risk) using the combination of eGFR (G1-G5) and albuminuria (A1-A3) levels defined by the 2012 KDIGO guideline ²³. Due to the small number of participants in the very high risk category of CKD, high and very high risk groups were combined. Reduced eGFR was defined as eGFR < 60 mL/min/1.73 m². Because of the small number of participants in the severely increased albuminuria category, we defined albuminuria as ACR \geq 3 mg/mmol by combining the moderately increased (A2) and severely increased (A3) categories.

Patient and Public Involvement

Community leaders were involved in the recruitment of patients. These comprised of religious communities (churches and mosques), endorsement from local key leaders and establishing relationships with healthcare organizations. We also provided information on the study by involving the local media (radio and television stations). We sent letters to all selected health and community authorities to notify participants of the study. Team members were sent to the various community to stay among the community and organize mini clinics for a period of 1-2 weeks. Results of the study were disseminated through seminars, durbars and via radio and television stations.

Statistical methods

Participants' characteristics were expressed as absolute numbers and percentages for categorical variables and as means and standard deviations (SD) for continuous variables. CKD prevalence with 5% error bars were presented as bar graphs for each SES construct across rural and urban Ghana. Spearman's rank correlation was used to determine correlations between the three SES constructs. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were estimated by means of logistic regression analyses to study the odds of albuminuria (ACR>3 mg/mmol, A2-A3, moderately to severely increased albuminuria), reduced kidney function (eGFR< 60 mL/min/1.73 m^2 , G3-G5 moderately to severely decreased kidney function) and increased CKD risk (high and very high CKD risk) by SES, with adjustments for potential covariates (age and sex). These covariates were adjusted for to account for their impact in the pathway of CKD incidence, prevalence and progression²⁴. The analyses were performed for the total population (using low educational level, low occupational status and low level of wealth index as reference categories). Further analysis was conducted using rural Ghana as reference. Model 1

was adjusted for age and sex while model 2 was adjusted for age, sex and educational level. Model 3 was adjusted for age, sex and occupational status while model 4 was adjusted for age, sex and level of wealth index. Model 5 was adjusted for age, sex, educational level, occupational level and wealth index (p<0.05). Tolerance test and variance inflation factor (VIF) showed very small degree of collinearity among SES predictors thus we adjusted for each of SES variables separately. Complete case analysis approach was used. All data available were included in the age-adjusted models. All analyses were performed using STATA, version 14.0 (StataCorp LP).

297 Results

 Table 1 shows characteristics of study participants. Participants in rural Ghana were slightly older than those in urban Ghana. Female preponderance was observed in both rural and urban Ghana, though higher proportions were observed in urban Ghana. Individuals living in rural Ghana were generally less educated compared with those living in urban Ghana. There were slightly more individuals with low occupational status in urban Ghana compared with their peers in rural Ghana. People in urban Ghana were wealthier than their rural counterparts. Rural Ghanaians were more physically active compared with their urban peers. Smoking was low among Ghanaians though rural Ghanaians were more likely to smoke compared with their urban peers. Hypercholesterolemia was more prevalent in urban Ghana than in rural Ghana. Hypertension and type 2 diabetes were more prevalent in urban Ghanaians compared with those living in rural Ghana. Urban Ghanaians were markedly more obese compared with their rural peers. Except for eGFR, albuminuria and CKD risk prevalence rates were higher in urban Ghana compared with rural Ghana.

Table 1: Baseline characteristics by location

	Rural Ghana	Urban Ghana
Number of participants, N (%)	1043 (41.9)	1449 (58.1)
Mean age, years (SD)	46.5 (12.6)	45.2 (11.4)
Females, N (%)	638 (61.2)	1034 (71.4)
Educational level n (%)		
Low	555 (56.9)	614 (43.9)
Middle	311 (31.9)	547 (39.1)
High	108 (11.2)	239 (17.0)
Occupational status, n (%)		
Low	250 (25.7)	374 (26.7)
Middle	628 (64.5)	818 (58.4)

~				
3 4		High	96 (9.8)	209 (14.9)
4 5		Wealth index, n (%)		
6		Low	449 (46.5)	368 (26.6)
7		Middle	276 (28.6)	416 (30.0)
8 9		High	241 (24.9)	602 (43.4)
10		BMI (kg/m ²	()	
11		< 25	794 (76.3)	579 (39.9)
12 13		25-29.9	189 (18.2)	495 (34.2)
14		≥ 30	58 (5.5)	374 (25.9)
15		Low physical activity, n (%)	663 (47.22)	592 (60.7)
16 17		Smoking, n (%)	22 (2.3)	14 (1.0)
18				
19		Hypercholesterolemia, n (%)	78 (7.6)	270 (18.7)
20		Hypertension, n (%)	306 (29.3)	531 (36.7)
21 22		Diabetes, n (%)	53 (5.1)	153 (10.6)
22		Albuminuria, n (%)		
24		A1, Normal to mildly increased (ACR <3 mg/mmol)	930 (91.6)	1285 (89.1)
25		A2-A3, moderately to severely increased (ACR \geq 3 mg/mmol)	85 (8.4)	158 (10.9)
26		eGFR, n (%)		
27 28		$G1-G2 (\geq 60 \text{ mL/min}/1.73 \text{ m}^2)$	989 (96.3)	1388 (96.3)
29		$G3-G5 (<60 \text{ mL/min}/1.73 \text{ m}^2)$	38 (3.7)	54 (3.7)
30		CKD risk, n (%)		
31 32		Low risk (green)	916 (90.5)	1281 (88.9)
32 33		Moderately increased to very high risk (yellow to red)	96 (9.5)	160 (11.1)
34	313	The defaulty mercused to very mgn fisk (genew to red)	<i>y</i> (<i>yy</i>)	100 (11.1)
35	314	Abbreviations: N, number of respondents; SD, standard deviation; eGFR, estimat	ed glomerular filtration rat	e; ACR, albumin
36	315	creatinine ratio; CKD, Chronic kidney disease	-	
37	316			

Figure 1 shows prevalence of CKD by level of education in urban and rural Ghana. Prevalence of CKD decreased with increasing levels of education in rural Ghana. Higher prevalence of CKD was observed among individuals with low educational level compared with those with middle and high educational level. However, those with high educational level in urban Ghana had higher prevalence of CKD compared with those with middle level education. For occupational status, prevalence of CKD was higher among individuals with low occupational status in urban Ghana. Similar patterns were observed in rural Ghana, however, those with higher occupational status had higher prevalence of CKD compared with those with middle occupational status (Figure 2). Figure 3 shows prevalence of CKD by level of wealth index. CKD prevalence among the levels of wealth index varied between urban and rural Ghana. Those with middle level wealth index had higher prevalence of CKD compared with those with low or high CKD prevalence in both rural and urban Ghana. CKD prevalence rate for low and high level wealth index same while that of rural Ghana was urban Ghana was the slightly different. in

Among the whole group, educational level was positively associated with wealth index (p<0.01) and composite SES (P<0.01). Occupational level was also inversely associated with educational level (p<0.01) and wealth index (p<0.01). In urban Ghana, high educational level was positively associated with high wealth index but inversely associated with occupation (p<0.01). In rural Ghana, high education was positively associated with high wealth index (p<0.01), but there was no significant association between education and occupation. High wealth index was inversely associated with high occupational status in both rural and urban Ghana (p<0.01) (Table 2).

334 Table 2: Relationship between SES constructs (educational, occupational level and wealth index) by urban rural Ghana

Correlation matrix	Educational level	Occupational level	Wealth index S
Whole group		Co Co	
Educational level	1.000		
Occupational status	-0.060	1.000	
	0.004		
Wealth Index	0.282	-0.121	1.000
	0.001	0.001	
SES	1.000	-0.059	0.282 1.0
	0.003	0.006	0.001
Urban Ghana			
Educational level	1.000		
Occupational status	-0.115	1.000	
	0.001		
Wealth Index	0.294	-0.126	1.000

1 2					
3 4		0.001	0.001		
5	SES	1.000	-0.024	0.937	1.000
7 8		0.002	0.001	0.001	
9	Rural Ghana				
10 11	Educational level	1.000			
12 13	Occupational status	0.017	1.000		
14 15		0.589			
16 17	Wealth Index	0.219	-0.135	1.000	
18		0.001	0.001		
19 20	SES	0.504	0.017	0.934	1.000
21 22		0.001	0.587	0.001	
23 337 24 338 25 338 26 339 27 340 28 341 30 342 31 343 32 343 33 344 34 345 36 346 37 348 41 349 42 43 44 45 46 46		For peer review only - h	12 http://bmjopen.bmj.com/		lelines.xhtml

Table 3 shows association between level of education, occupational status, level of wealth index and prevalence of CKD. After adjusting for age and sex for the whole group, albuminuria was associated with middle level education (p<0.01). After adjusting for age and sex, we observed no significant association between SES indicators (educational level, occupational status and wealth index) and CKD in urban Ghana. However, middle and higher level education was associated with reduced albuminuria in urban Ghana (p<0.01). Whereas educational level and occupational status were not associated with CKD prevalence, high wealth index was significantly associated with higher odds of reduced eGFR (p<0.01).

Table 3: Association of SES indicators (educational level, occupational status and wealth index level) with albuminuria, reduced eGFR and CKD risk

	Albuminuria	(ACR≥3 mg/mmol)	eGFR < 60 mL	/min/1.73 m2	High to very high CKD risk (K 2012)	
		OR (95% CI)		OR (95% CI)		OR (95% CI)
	n (%)	Model 1	n (%)	Model 1	n cases (%)	Model 1
Education						
Whole group						
Low	1,152 (11.89)	1.00 (Reference)	1,160 (3.97)	1.00 (Reference)	1.150 (11.91)	1.00 (Reference
Middle	847 (7.32)	0.66 (0.48-0.91)	849 (3.77)	1.36 (0.83-2.22)	845 (8.28)	0.82 (0.59-1.12
High	343 (7.00)	0.67 (0.42-1.07)	345 (3.19)	1.11 (0.55-2.29)	343 (8.75)	0.96 (0.62-1.49
Urban Ghana						
Low	612 (14.7)	1.00 (Reference)	612 (4.1)	1.00 (Reference)	612 (14.1)	1.00 (Reference
Middle	546 (7.8)	0.51 (0.34-0.76)	546 (3.7)	1.12 (0.59-2.12)	545 (8.1)	0.59 (0.39-0.89
High	238 (8.4)	0.53 (0.31-0.91)	238 (3.4)	0.91 (0.37-2.19)	238 (10.9)	0.83 (0.51-1.38
Rural Ghana						
Low	540 (8.7)	1.00 (Reference)	548 (3.8)	1.00 (Reference)	538 (9.5)	1.00 (Reference
Middle	301 (6.3)	0.89 (0.51-1.59)	303 (3.9)	1.69 (0.77-3.66)	300 (8.7)	1.33 (0.79-2.25
High	105 (3.8)	0.66 (0.23-1.95)	107 (2.8)	1.28 (0.35-4.71)	105 (3.8)	0.69 (0.23-2.02
Occupational st	tatus					
Whole group						
Low	614 (9.93)	1.00 (Reference)	616 (2.76)	1.00 (Reference)	613 (9.46)	1.00 (Reference

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Middle	1,427 (9.25)	0.82 (0.59-1.14)	1,436 (3.34)	0.93 (0.52-1.66)	1,424 (9.90)	0.89 (0.65-1.2
High	302 (10.26)	0.76 (0.47-1.22)	303 (7.92)	1.33 (0.67-2.62)	302 (12.91)	0.90 (0.57-1.4
Urban Ghana						
Low	207 (10.1)	1.00 (Reference)	207 (6.8)	1.00 (Reference)	207 (12.1)	1.00 (Reference
Middle	817 (11.1)	1.50 (0.88-2.83)	817 (3.6)	1.15 (0.56-2.35)	816 (11.6)	1.37 (0.84-2.5
High	373 (11.0)	1.57 (0.89-2.53)	373 (2.7)	1.02 (0.41-2.52)	373 (9.7)	1.21 (0.68-2.1
Rural Ghana						
Low	95 (10.5)	1.00 (Reference)	96 (10.4)	1.00 (Reference)	95 (14.7)	1.00 (Reference
Middle	610 (6.7)	0.65 (0.31-1.37)	619 (3.1)	0.37 (0.16-0.85)	608 (7.6)	0.55 (0.28-1.0
High	241 (8.3)	0.99 (0.43-2.28)	243 (2.9)	0.51 (0.18-1.44)	240 (9.2)	0.94 (0.44-2.0
Wealth index						
Whole group						
Low	808 (9.65)	1.00 (Reference)	813 (3.32)	1.00 (Reference)	808 (9.16)	1.00 (Reference
Middle	678 (10.91)	1.18 (0.84-1.66)	683 (3.81)	1.30 (0.74-2.28)	675 (12.0)	1.43 (1.02-2.0
High	835 (8.62)	0.93 (0.66-1.31)	835 (4.19)	1.55 (0.91-2.64)	833 (9.96)	1.21 (0.86-1.
Urban Ghana						
Low	367 (11.2)	1.00 (Reference)	367 (3.5)	1.00 (Reference)	367 (10.1)	1.00 (Referen
Middle	414 (12.3)	1.12 (0.73-1.74)	414 (3.9)	1.30 (0.61-2.80)	413 (13.1)	1.45 (0.93-2.2
High	601 (9.8)	0.82 (0.55-1.25)	600 (3.8)	1.13 (0.55-2.31)	600 (10.8)	1.11 (0.72-1.)
Rural Ghana						
Low	441 (7.9)	1.00 (Reference)	446 (3.1)	1.00 (Reference)	441 (8.4)	1.00 (Referen
Middle	264 (8.7)	1.13 (0.65-1.98)	269 (3.7)	1.22 (0.52-2.84)	262 (10.3)	1.31 (0.77-2.2
High	234 (5.6)	0.78 (0.40-1.53)	235 (5.1)	2.38 (1.03-5.47)	233 (7.7)	1.16 (0.63-2.1

Table 4 shows the contribution of all three SES constructs to rural and urban CKD prevalence differences. The odds of albuminuria and CKD risk was significantly higher in urban Ghana compared with rural Ghana. The higher rate of CKD observed in urban Ghana was not explained by the higher SES of that population as compared to their rural counterparts.

368 Table 4: Contribution of SES indicators to rural-urban differences in albuminuria, reduced eGFR and CKD risk

				ŕ		
		OR (95% CI)				
		Model 1	Model 2	Model 3	Model 4	Model 5
Albuminuria (ACR≥3 mg/mmol		5				
Sites	n cases (%)					
Urban Ghana	1,443 (10.9)	1.37 (1.03-1.81)	1.70 (1.25-2.31)	1.55 (1.15-2.10)	1.62 (1.18-2.19)	1.74 (1.27-2.38)
Rural Ghana	1,015 (8.4)	1.00 (Reference)				
eGFR < 60 mL/min/1.73 m2						
Sites	n cases (%)					
Urban Ghana	1,442 (3.7)	1.27 (0.82-1.97)	1.20 (0.76-1.89)	1.18 (0.79-1.86)	1.12 (0.70-1.78)	1.07 (0.67-1.72)
Rural Ghana	1,027 (3.7)	1.00 (Reference)				
High to very high CKD risk						
Sites	n cases (%)					
Urban Ghana	1,441 (11.1)	1.23 (1.01-1.62)	1.44 (1.07-1.93)	1.38 (1.03-1.84)	1.36 (1.01-1.83)	1.40 (1.04-1.91)
Rural Ghana	1,012 (9.46)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference

Model 1: adjusted for age and sex; Model 2: adjusted for age, sex and education level; Model 3: adjusted for age, sex and occupational status; Model 4: adjusted for age, sex and wealth index; Model 5: adjusted for age, sex, educational level, occupational status and wealth index; Abbreviations: CI, confidence interval; ACR, albumin creatinine ration; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; OR, odds ratio, n=number of participants. n= total number of individuals in rural and urban Ghana; %,

proportion of individuals with CKD among urban and rural Ghana.

2		
3 4	375	Discussion
5	376	Key findings
6 7	377	Our study findings show no association between all three SES constructs and the prevalence of CKD in
8	378	both rural and urban Ghana except for wealth index in rural Ghana, with the risk of CKD being higher in
9 10	379	the wealthier populations. The higher rate of CKD observed in urban Ghana could not be attributed to the
11	380	higher SES of that population compared to their rural counterparts.
12 13	381	
14 15	382	Discussion of key findings
15 16	383	
17 18 19	384 385	Association of SES with CKD in rural and urban Ghana
20	386	Our study did not find any significant associations between all three SES constructs and CKD among
21 22	387	rural and urban Ghana except for wealth index in rural Ghana. The positive association observed between
23	388	wealth index in rural Ghana may be due to a number of reasons. A comparison of the three SES
24 25	389	constructs showed higher educational level to be associated with wealth index in both rural and urban
26	390	Ghana but not occupational level. This seems to suggest that occupational level may not be adequately
27 28	391	capturing the SES status of individuals living in these settings in relation to CKD. For example, Masthi et
29 30	392	al, compared different SES scales in rural and urban India and concluded that Standard of Living Index
31	393	(SLI) scale was more accurate for classification of SES in urban and rural setting ²⁵ . Our finding is
32 33	394	consistent with other studies, ^{6 26} which reported no association between SES and CKD in high-income
34 35	395	countries and LMICs, but in contrast with other studies ²⁻⁴ ²⁷ that found positive associations between
36 37	396	SES and CKD. The reasons for our current finding are unclear. However, it has been suggested that these
38	397	inconsistent associations may be due to the varying pathways through which the effect of SES on health
39 40	398	status is mediated. For example, at a given educational level marked ethnic differences have been
41 42	399	reported. Additionally, similar differences were observed for wealth status at a given income level ²⁸⁻³⁰ .
43 44 45	400 401 402	Contribution of SES to observed CKD risk differences between rural and urban Ghana
46	402	We observed higher rates of CKD in urban Ghana compared with rural Ghana, as expected. The observed
47 48	404	higher rates of CKD in our study were not explained by the higher SES of that population as compared to
49 50	405	their rural counterparts. Our results indicate that this is due to the lack of a clear difference in the SES
50 51	406	distribution of rural and urban Ghana observed in this study, as well as to the lack of associations between
52 53	407	SES and CKD. Consistent with our findings, in a study conducted in Northern Tanzania SES did not
54	408	explain increased risk of CKD in urban Tanzania ²⁶ . The lack of associations between SES and CKD
55 56 57	409	could probably partly be explained by the process of epidemiological transition in relation to the

"diffusion theory" of ischemic heart disease mortality. This theory attributes the commencement of ischemic heart disease to individuals in the high SES group due to their ability to afford behaviours (smoking, alcohol and sedentary lifestyles) which increased risk of ischemic heart disease. The lower SES groups were later affected partially because of improved living standards, imitation and urbanization. The higher SES groups were the first to embrace behavioural changes required to decrease the risk of ischemic heart disease and this resulted in reversing the gradient ³¹. The rapid urbanization of some rural communities in the Ashanti region of Ghana and the imitation of urban lifestyle could account for our finding. Also, it could be that whereas the high SES group in urban Ghana has already embraced favourable behavioural changes, those in rural Ghana are vet to do so ³². This explains the observed association of wealth index with CKD in rural Ghana but not in urban Ghana. The complexities of influence of SES on prevalence and progression of CKD and the differential prevalence of established risk factors (diabetes, obesity and hypertension) in rural and urban Ghana may also contribute to the different associations of SES with CKD prevalence observed in rural and urban Ghana. In our study, the prevalence rates of hypercholesterolemia, hypertension and type 2 diabetes were substantially higher in urban Ghana compared with that of rural Ghana. Also, the interplay of other less understood or researched factors (e.g., exposure to nephrotoxins, herbal medications, sepsis) may be influencing the pathway in which SES influences CKD prevalence and progression.

Strength and limitation

Our study presents several strengths. First, we used well-standardized study protocols across rural and urban Ghana. Our study is also the first in Africa to use all three categories of CKD definition (albuminuria, reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of SES with CKD in rural and urban setting, this provides a more detailed information on CKD outcomes. The limitation of intra laboratory variability in earlier studies was eliminated using the same standard operating procedures in the same laboratory for running all samples for both rural and urban Ghana. The use of three constructs of SES in this study also provides a much better holistic approach to assessing SES. Also, the distribution of SES in our study reflect on the national data allowing for generalization of our findings. Our study was limited by the use of cross sectional design, which prevented us from determining causality between predictors and CKD progression. Furthermore, there were more women than men in our study due to the higher response rate in women compared with men. However, this applied to both rural and urban Ghana. We therefore do not expect this to influence our results in a significant way.

Conclusion

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All three SES constructs appear not to be associated with prevalence of CKD in urban and rural Ghana except for wealth index in rural Ghana. The observed higher prevalence of CKD in urban Ghana was not explained by the higher SES in urban Ghana. Our study seems to suggest that other non-traditional factors such as nephrotoxins, herbal medications and misuse of over the counter drugs may play a role and underscores the need to further explore these factors.

Acknowledgement

The authors are very grateful to the research assistants, interviewers and other staff of the five research locations who took part in gathering the data and the Ghanaian volunteers in all the participating RODAM sites. We gratefully acknowledge the advisory board members for their valuable support in shaping the RODAM study methods and the Academic Medical Centre Biobank for their support in biobank management and high-quality storage of collected samples.

Contributors

My co-authors have all contributed substantially to this manuscript and approve of this submission. Research idea and study design: DNA, CA, KS, DA, EB, KM, JA; data acquisition and curation: DNA, CA, EB, KM, data analysis/interpretation: DNA, CA, KS, DA, EB, KM, LS, JA, EOD, KKB, FPM, ID, JS, SB, ADA; statistical analysis: DNA, CA, KS, DNA, CA, KS, DA, EB, KM, LS, JA, EOD, KKB, FPM, ID, JS, SB, ADA contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. DNA and CA takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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 Gompeting interest: I have communicated with all my co-authors and obtained their full disclosures. My co-authors and I declare no conflicts of interest. Patient Consent: None declared Ethics approval: IRBs at each participating site. Data sharing statement: Data are available from the RODAM research cohort, a third party. Dr. Eric Beune affiliated with the RODAM research cohort and a co-author of this paper in accordance with the RODAM requirements for collaboration. Dr. Beune is the Data Collection Coordinator of RODAM and may be contacted with further questions (c.j.beune@ame.uva.nl). Additionally, researchers interested in further collaboration with RODAM may see the following URL: http://www.rod-am.eu/ URL: http://www.rod-am.eu/ Wassing and the statement of the	1		
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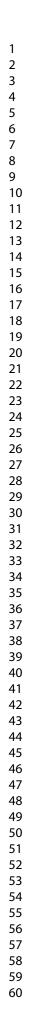
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Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups.

Figure 2: Prevalence of chronic kidney disease (CKD) across occupational status among urban and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups.

Figure 3: Prevalence of chronic kidney disease (CKD) across wealth index categories among urban and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, js. or very high-risk groups.

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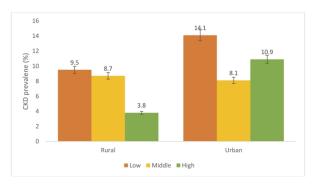


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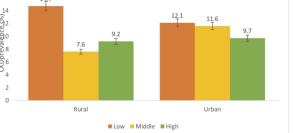
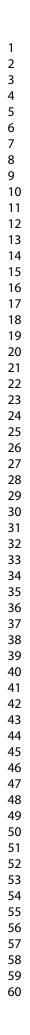


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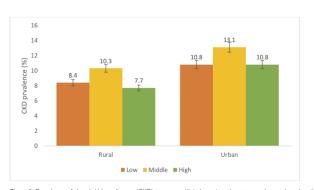


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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation		Page No.	Relevant text from manuscript
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1,2		We have included a commonly used term in the title and abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2		Our study did not find an associations between SE indicators and CKD in bot rural and urban Ghana after ag and sex adjustment except i rural Ghana where wealth inde was associated with prevalenc of CKD. Consequently, th higher SES did not account fo the increased rate of CKI among urban dweller suggesting the need to identif other factors that may be drivin this.
Introduction					
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4		The theoretical and scientifi background as well as th rationale for conducting th study have been provided in th introduction section.
Objectives	3	State specific objectives, including any prespecified hypotheses	4		We assessed the association of SES with CKD in rural an urban Ghana and studied wha extent the higher SES of peopl in urban areas could account for differences in CKD betwee rural and urban populations
Methods					
Study design	4	Present key elements of study design early in the paper	5-6		Details given in the methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6		Rural or urban Ghana.
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Participants	6	 (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls 		A multi-centre cross-sectional study was conducted among Ghanaian adults (n=2492) aged 25-70 years residing in rural and urban Ghana.
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6-8	
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per		
		case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8	The main outcomes have been clearly defined.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8	We defined each variable of interest in the methods accordingly
Bias	9	Describe any efforts to address potential sources of bias	18	Potential sources of bias have discussed in the discussion section
Study size	10	Explain how the study size was arrived at	5	Given in the methods section and we have also referred to the RODAM study methods paper
Continued on next page				
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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9	Please see methods
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	8-9	Please see methods
methods		(b) Describe any methods used to examine subgroups and interactions	8-9	Please see methods
		(c) Explain how missing data were addressed	8-9	
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	NA	We have reported non-response
		Case-control study—If applicable, explain how matching of cases and controls was addressed		across sites
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling		
		strategy		
		(<u>e</u>) Describe any sensitivity analyses	NA	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially eligible, examined	5	Non-response analysis was done to
		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		shed light on the differential response rates across sites
		(b) Give reasons for non-participation at each stage	5	response rates across sites
		(c) Consider use of a flow diagram	5	We have also referred to RODAM
				methods paper
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on	5	We have also referred to RODAM
		exposures and potential confounders		methods paper
		(b) Indicate number of participants with missing data for each variable of interest	5	We have also referred to RODAM
				methods paper
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	NA	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	NA	
		Case-control study-Report numbers in each exposure category, or summary measures of exposure	NA	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9-10	Summary measures are given in the results section and in tables and figures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	12-16	Unadjusted and adjusted estimates
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were		are given in the results section and
		included		in figures
		(b) Report category boundaries when continuous variables were categorized	12-16	We have provided mean and corresponding standard deviations for the continuous variables.
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		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	NA	
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Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	NA	
Discussion				
Key results	18	Summarise key results with reference to study objectives	8	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18	Key limitations regarding stud methods including differentia response rates and samplin methods in the various study site have been provided
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-18	Cautious overall interpretation o the key findings have been provided.
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18	
Other informati	on			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	19	The funders had no role in stud design, data collection and analysis
*Give informatio	on sep	original study on which the present article is based	in cohort and	decision to publish, or preparation of the manuscript
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A CROSS-SECTIONAL STUDY OF ASSOCIATION BETWEEN SOCIOECONOMIC INDICATORS AND CHRONIC KIDNEY DISEASE IN RURAL-URBAN GHANA-THE RODAM STUDY

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7 8	3	RURAL-URBAN GHANA-THE RODAM STUDY			
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7 8	40	Abstract
9	41	Obiectives. Studies from high income countries success higher provelance of Chronic Kidney Disease
10	42 43	Objectives: Studies from high income countries suggest higher prevalence of Chronic Kidney Disease (CKD) among individuals in low socio-economic groups. However, some studies from low and middle-
11 12	43 44	income countries (LMICs) show the reverse pattern among those in high socioeconomic groups. It is
12	44	unknown which pattern applies to individuals living in rural and urban Ghana. We therefore assessed the
14	46	association between Socio-Economic Status (SES) indicators and CKD in rural and urban Ghana and to
15	47	what extent the higher SES of people in urban areas of Ghana could account for differences in CKD
16	48	between rural and urban populations.
17	49	
18 19	50	Methods: We used baseline data from multi-centre Research on Obesity and Diabetes among
20	51	African Migrants (RODAM) study. The sample consisted of 2492 adults (Rural Ghana, 1043, Urban
21	52	Ghana, 1,449) aged 25 to 70 years living in Ghana. Three CKD outcomes were considered using the 2012
22	53	KDIGO (Kidney Disease: Improving Global Outcomes) severity of CKD classification: albuminuria
23 24	54	(albumin-creatinine ratio \geq 3 mg/mmol (category \geq A2)); reduced glomerular filtration rate (eGFR < 60
25	55	mL/min/1.73 m2 (category \geq G3)) and high to very high CKD risk based on the combination of these two.
26	56	
27	57	Results: All three SES indicators were not associated with CKD in both rural and urban Ghana after age
28	58 59	and sex adjustment except for rural Ghana where high wealth index was significantly associated with higher odds of reduced eGFR (AOR, 2.38; 95% C.I. 1.03-5.47). The higher rate of CKD observed in
29	60	urban Ghana was not explained by the higher SES of that population.
30 21	61	urban Ghana was not explained by the higher SES of that population.
31 32	62	Conclusion: SES indicators were not associated with prevalence of CKD except for wealth index and
33	63	reduced eGFR in rural Ghana. Consequently, the higher SES of did not account for the increased rate of
34	64	CKD among urban dwellers suggesting the need to identify other factors that may be driving this.
35	65	
36	66	
37	67	Index Words: Chronic kidney disease; socioeconomic status; health inequalities; risk factor; ethnic
38 39	68	minority groups; migrants; RODAM study, Ghana
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12	84	
13 14	85	Strengths and limitation of the study
15 16	86	
17	87	• The use of well-standardized study protocols across rural and urban Ghana eliminated intra
18 19	88	protocol variability.
20	89	
21 22	90	• Our study is also the first in Africa to use all three categories of CKD definitions (albuminuria,
23 24	91	reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of SES with CKD in rural
24 25	92	and urban setting. This provides more detailed information on CKD outcomes.
26 27	93	and urban setting. This provides more detailed information on exploateomes.
28	94	• The limitation of intra laboratory variability in earlier studies was eliminated using the same
29 30	94 95	standard operating procedures in the same laboratory for running all samples for both rural and
31	95 96	urban Ghana.
32 33	90 97	
34 35		
35 36	98 00	• The use of three constructs of SES (educational level, occupational level and wealth index) in this
37 38	99 100	study also provides a much better holistic approach to assessing SES associations with CKD.
39	100	
40 41	101	• Our study was limited because of the use of cross sectional design which prevented us from
42	102	determining causality between predictors and CKD progression.
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26	124	
27	125	Introduction

127 In general, individuals in lower socio-economic status (SES) groups have been shown to suffer more 128 frequently from Chronic Kidney Disease (CKD), often progressing to End Stage Renal Disease (ESRD), 129 and associated with inadequate dialysis treatment, reduced access to kidney transplantation and poor 130 health outcomes ¹. Recent studies have consistently found low SES to be associated with higher risk of 131 CKD among people of African origin ²⁻⁵.

However, in some settings the well-known inverse association between SES and CKD seems to be absent, or even reversed. For example, Bryne et al. did not find an association between SES and End Stage Renal Disease ⁶. Other studies have found ⁷⁸. Specifically, as SES improved, a positive association between SES and CKD unhealthful lifestyle (unhealthy diet, physical inactivity, smoking and alcohol consumption) increased in China while that of the United States decreased with improved SES ⁹. People with higher incomes, in these contexts, can afford a western

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2 3	139	lifectule which is more readily evailable in the urban areas than in the rural areas			
4 5	139	lifestyle, which is more readily available in the urban areas than in the rural areas.			
6 7	140	There is therefore an interaction between individual SES and environmental factors,			
8 9 10	141	such as food and sedentary life style in such populations ¹⁰⁻¹² . Consequently, in those			
10 11 12	142	settings, people with a higher SES might have higher CKD risk.			
13	143	In urban areas, the population in general has a higher SES than in rural areas ¹³ . For example, individuals			
14 15	144	with higher educational level migrate from rural areas to find higher occupations matching their higher			
16	145	education to improve on their wealth. If indeed a positive association between SES and CKD is observed			
17 18	146	in LMICs, this might underlie the well-known health differences between urban and rural areas, with			
19	147	urban areas having an increased risk of CKD ¹⁴ . So far, it is unknown whether the reversed SES gradient			
20 21	148	(higher risk in high SES group) might explain the higher burden of CKD in urban areas as compared to			
22	149	rural areas in Africa.			
23 24	150				
25	151	In view of this, we assessed the association of SES with CKD in rural and urban Ghana and studied what			
26 27	152	extent the higher SES of people in urban areas could account for differences in CKD between rural and			
28	152				
29 30	155	urban populations.			
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41 42	160				
43 44	161	Methods			
45	162				
46 47	163	Study population and study design			
48 49	164	In the present analyses, data from the RODAM (Research on Obesity & Diabetes			
50 51 52	165	among African Migrants) study, a multi-centre cross-sectional study were used. The			
53 54	166	rationale, conceptual framework, design and methodology of the RODAM study have			
55 56 57 58	167	been described in detail elsewhere ^{15 16} . As the Healthy Life in an Urban Setting			
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168 (HELIUS) study conducted among Ghanaian migrants living in Amsterdam did not find any 169 associations between SES and CKD ¹⁷ the current study focused on rural and urban Ghana (Ashanti 170 region of Ghana). The RODAM study was conducted from 2012 to 2015 and it comprised 171 of individuals aged 25-70 years living in rural and urban Ghana and Ghanaian 172 migrants in Europe. All participants below 25 and above 70 years were excluded in 173 the present analyses. The present analysis was restricted to the rural and urban sites 174 (n=2492) RODAM participants. Specifically, 1043 participants from rural Ghana and 175 1449 from urban Ghana were used in this study.

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177 Data collection for the study was standardized across all sites. Written informed 178 consent was obtained from each participant prior to enrolment in the study. The 179 respective ethics committees in Ghana and the three European countries approved the 180 study protocols before data collection began. Specifically, we obtained ethical clearance 181 in Ghana from School of Medical Sciences/Komfo Anokye Teaching Hospital 182 Committee on Human Research, Publication & Ethical Review Board. In the 183 Netherlands the Institutional Review Board of the AMC, University of Amsterdam gave 184 approval for the study. In Germany, approval for the study was obtained from the 185 Ethics Committee of Charite-Universitäts medizin. The London School of Hygiene and 186 Tropical Medicine Research Ethics Committee gave approval for the study in the UK.

The response rate was 76% in rural Ghana and 74% in urban Ghana. In Ghana, participants were randomly drawn from a list of 30 enumeration areas in the Ashanti region based on the 2010 population census using the multistage random sampling. These enumeration areas came from two purposively selected urban cities (Kumasi and Obuasi) and 15 randomly selected rural communities in the Ashanti region.

192 Selected health and community authorities were first identified, notified of the study 193 and letters were sent giving detailed explanation of the study. We sent team members 194 to stay among the communities to familiarize with them and organize mini clinics in 195 the field. This lasted between 1-2 weeks depending on the sampled population and 196 responsiveness of respondents.

In Ghana, questionnaires administration and physical examination were done at the same day/time. The participants were instructed to fast from 10.00 pm the night before the physical examination. For the current study, 2566 participants with data available on both questionnaire data and physical measurements were used. We excluded (n=74) individuals outside the RODAM age range of 25-70 years resulting in a data set of 2492 for analysis. These comprised 1,449 Urban Ghana and 1043 Rural Ghana. For the final analysis, individuals with no data on CKD status (n=42) were excluded.

204 Measurements

205 Covariates

206 Demographic and lifestyle factors

Information on demographics, educational level, occupational level, wealth index and lifestyle factors (smoking and physical activity) were obtained by questionnaire. Physical examinations were performed with validated devices per standardized operational procedures across all study sites. Weight was measured in light clothing and without shoes with SECA 877 scales to the nearest 0.1 kg. Height was measured without shoes with a portable stadiometer (SECA 217) to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Overweight was defined as BMI of \geq 25 to <30 kg/m² and obesity as BMI \geq 30 kg/m² ¹⁸. Per participant, all anthropometrics were measured twice by the same assessor and the average of the two measurements were used for analyses.

215 Predictor: SES

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Socioeconomic indicators used in this study were educational level, occupational status and level of wealth index. Educational level was determined based on self-reported highest educational qualification accomplished based on the Ghanaian educational system. Occupational level was determined based on self-reported current occupation if still employed and/or last occupation before retirement or student. The reported occupations were further coded according to the International Standard Classification of Occupations scheme (ISCO-08). Where 'high' (professionals, managers, clerical support staff, higher grade routine non-manual employees service and sales-related occupations) and 'low' (craft and related trades workers, elementary occupations and farmers) and the rest were categorized into the 'middle'. Wealth index was determined using the World Health Organization (WHO) standard of wealth index classification. Wealth index was based on data collected in the Household Questionnaire. The questionnaire comprised of questions on household's ownership of several consumer items such as television, car, flooring material, toilet facilities etc. Each household was assigned a standard score for each asset. Wealth index was then expressed in five categories. The five categories were further categorized into three categories by combining the second and third category due to small numbers ¹⁹. All three SES constructs were further classified as low, medium and high SES and their relationship to each other tested. A composite SES variable (SES) was generated based on the three SES constructs (education, occupation and wealth index) using the EGEN group command in STATA. The codes were combined into numerical variables and their averages computed. The resultant values were recoded into three categories (low, medium and high).

Co-morbidity factors

Blood pressure (BP) was measured three times using a validated semi-automated device (The Microlife WatchBP home) with appropriate cuffs in a sitting position after at least 5 min rest. The mean of the last two BP measurements was used in the analyses. Hypertension was defined as systolic BP \geq 140 mmHg, and/or diastolic BP \geq 90 mmHg, and/or being on antihypertensive medication treatment, and/or self-reported hypertension. Trained research assistants in the two sites collected fasting venous blood samples. All the blood samples were processed and aliquoted immediately (within one hour to maximum three hours of the vena puncture) after collection per standard operation procedures, and then temporarily stored at the local research location at -20° C. The separated samples were then transported to the local research centres laboratories, where they were checked, registered and stored at -80°C. To avoid intra-laboratory variability, the stored blood samples from the local research centres were transported to Berlin, Germany for biochemical analyses. Fasting plasma glucose concentration was measured using an enzymatic method (hexokinase). Type 2 diabetes was defined according to the WHO diagnostic criteria (fasting glucose \geq 7.0 mmol/L, and/or current use of medication prescribed to treat diabetes, and/or self-

reported diabetes) ²⁰. Concentration of total cholesterol was assessed using colorimetric test kits. All biochemical analyses were performed using an ABX Pentra 400 chemistry analyzer (ABX Pentra; Horiba ABX, Germany). Hypercholesterolemia was defined as total cholesterol level \geq 6.22 mmol/L. Serum creatinine concentration (in umol/L) was determined by a kinetic colorimetric spectrophotometric isotope dilution mass spectrometry–calibrated method (Roche Diagnostics). Biochemical analyses were subject to extensive quality checks including blinded serial measurements.

Outcome: CKD prevalence

Participants were asked to bring an early morning urine sample for the analyses of albuminuria and creatinine levels. Urinary albumin concentration (in mg/L) was measured by an immunochemical turbidimetric method (Roche Diagnostics). Urinary creatinine concentration (in umol/L) was measured by a kinetic spectrophotometric method (Roche Diagnostics). Estimated glomerular filtration rate (eGFR) was calculated using the CKDEPI (CKD Epidemiology Collaboration) creatinine equation ²¹. Urinary albumin-creatinine ratio (ACR; expressed in mg/g) was calculated by taking the ratio between urinary albumin and urinary creatinine. eGFR and albuminuria were categorized according to the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) classification ²². eGFR was categorized as follows: $G_{1,2} \ge 1$ 90 mL/min/1.73 m² (normal kidney function); G2, 60 to 89 mL/min/1.73 m² (mildly decreased); G3a, 45 to 59 mL/min/1.73 m² (mildly to moderately decreased); G3b, 30 to 44 mL/min/1.73 m² (moderately to severely decreased); G4, 15 to 29 mL/min/1.73 m² (severely decreased); and G5, < 15 mL/min/1.73 m² (kidney failure). Albuminuria categories were derived from ACR and were as follows: A1, < 3mg/mmol (normal to mildly increased); A2, 3 to 30 mg/mmol (moderately increased); and A3, > 30mg/mmol (severely increased). CKD status was categorized according to severity of kidney disease (green, low risk; yellow, moderately increased risk; orange, high risk; and red, very high risk) using the combination of eGFR (G1-G5) and albuminuria (A1-A3) levels defined by the 2012 KDIGO guideline ²³. Due to the small number of participants in the very high risk category of CKD, high and very high risk groups were combined. Reduced eGFR was defined as $eGFR < 60 \text{ mL/min}/1.73 \text{ m}^2$. Because of the small number of participants in the severely increased albuminuria category, we defined albuminuria as ACR \geq 3 mg/mmol by combining the moderately increased (A2) and severely increased (A3) categories.

Patient and Public Involvement

Community leaders were involved in the recruitment of patients. These comprised of religious communities (churches and mosques), endorsement from local key leaders and establishing relationships with healthcare organizations. We also provided information on the study by involving the local media (radio and television stations). We sent letters to all selected health and community authorities to notify

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281 participants of the study. Team members were sent to the various communities to stay among the 282 community and organize mini clinics for a period of 1-2 weeks. Results of the study were disseminated 283 through seminars, durbars and via radio and television stations.

284 Statistical methods

Participants' characteristics were expressed as absolute numbers and percentages for categorical variables and as means and standard deviations (SD) for continuous variables. CKD prevalence with 5% error bars were presented as bar graphs for each SES construct across rural and urban Ghana. Spearman's rank correlation was used to determine correlations between the three SES constructs. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were estimated by means of logistic regression analyses to study the odds of albuminuria (ACR>3 mg/mmol, A2-A3, moderately to severely increased albuminuria), reduced kidney function (eGFR< 60 mL/min/1.73 m², G3-G5 moderately to severely decreased kidney function) and increased CKD risk (high and very high CKD risk) by SES, with adjustments for potential confounders (age and sex).²⁴ In addition, the analyses were performed for the total population (using low educational level, low occupational status and low level of wealth index as reference categories). Further analysis was conducted to assess the contribution of SES indicators to rural-urban differences in albuminuria, reduced eGFR and CKD risk using rural Ghana as reference. Tolerance test and variance inflation factor (VIF) showed very small degree of collinearity among SES predictors thus we therefore adjusted for each of SES variables separately. Complete case analysis approach was used. All data available were included in the age-adjusted models. All analyses were performed using STATA, version 14.0 (StataCorp LP).

302 Results

46 303

Table 1 shows characteristics of study participants. Participants in rural Ghana were slightly older than those in urban Ghana. Female preponderance was observed in both rural and urban Ghana, though higher proportions were observed in urban Ghana. Individuals living in rural Ghana were generally less educated compared with those

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308	living in urban Ghana. There were slightly more individuals with low occupational
309	status in urban Ghana compared with their peers in rural Ghana. People in urban
310	Ghana were wealthier than their rural counterparts. Rural Ghanaians were more
311	physically active compared with their urban peers. Smoking was low among Ghanaians
312	though rural Ghanaians were more likely to smoke compared with their urban peers.
313	Hypercholesterolemia was more prevalent in urban Ghana than in rural Ghana.
314	Hypertension and type 2 diabetes were more prevalent in urban Ghanaians compared
315	with those living in rural Ghana. Urban Ghanaians were markedly more obese
316	compared with their rural peers. Except for eGFR, albuminuria and CKD risk
317	prevalence rates were higher in urban Ghana compared with rural Ghana.

318

Table 1: Baseline characteristics by location

	Rural Ghana	Urban Ghana
Number of participants, N (%)	1043 (41.9)	1449 (58.1)
Mean age, years (SD)	46.5 (12.6)	45.2 (11.4)
Females, N (%)	638 (61.2)	1034 (71.4)
Educational level n (%)		
Low	555 (56.9)	614 (43.9)
Middle	311 (31.9)	547 (39.1)
High	108 (11.2)	239 (17.0)
Occupational status, n (%)		
Low	250 (25.7)	374 (26.7)
Middle	628 (64.5)	818 (58.4)
High	96 (9.8)	209 (14.9)
Wealth index, n (%)		
Low	449 (46.5)	368 (26.6)
Middle	276 (28.6)	416 (30.0)

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2 3 4		High	241 (24.9)	602 (43.4)
5		BMI (kg/m²	, , , , , , , , , , , , , , , , , , ,	· · · · ·
6 7		< 25	794 (76.3)	579 (39.9)
8 9		25-29.9	189 (18.2)	495 (34.2)
10 11		≥ 30	58 (5.5)	374 (25.9)
12		Low physical activity, n (%)	663 (47.22)	592 (60.7)
13 14		Smoking, n (%)	22 (2.3)	14 (1.0)
15 16		Hypercholesterolemia, n (%)	78 (7.6)	270 (18.7)
17		Hypertension, n (%)	306 (29.3)	531 (36.7)
18 19			53	
20 21		Diabetes, n (%)	(5.1)	153 (10.6)
22		Albuminuria, n (%)		
23 24			930 (91.6)	
25 26		A1, Normal to mildly increased (ACR <3 mg/mmol)	85	1285 (89.1)
27		A2-A3, moderately to severely increased (ACR≥ 3 i	mg/ (8.4)	158 (10.9)
28 29		eGFR, n (%)		
30 31		G1-G2 (≥ 60 mL/min/1.73m²)	989 (96.3)	1388 (96.3)
32		G3-G5 (<60 mL/min/1.73m ²)	38 (3.7)	54 (3.7)
33 34		CKD risk, n (%)		
35 36		Low risk (green)	916 (90.5)	1281 (88.9)
37		Moderately increased to very high risk		
38 39		(yellow to red)	96 (9.5)	160 (11.1)
40 41	320			
42	321	Abbreviations: N, number of respondents; SD, standard deviation; eGFR, estim	ated glomerular filtration	rate; ACR, albumin

Abbreviations: N, number of respondents; SD, standard deviation; eGFR, estimated glomerular filtration rate; ACR, albumin creatinine ratio; CKD, Chronic kidney disease

Figure 1 shows prevalence of CKD by level of education in urban and rural Ghana. Prevalence of CKD decreased with increasing levels of education in rural Ghana. Higher prevalence of CKD was observed among individuals with low educational level compared with those with middle and high educational level. However, those with high educational level in urban Ghana had higher prevalence of CKD compared with those

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with middle level education. For occupational status, prevalence of CKD was higher among individuals with low occupational status in urban Ghana. Similar patterns were observed in rural Ghana; however, those with higher occupational status had higher prevalence of CKD compared with those with middle occupational status (Figure 2). Figure 3 shows prevalence of CKD by level of wealth index. CKD prevalence among the levels of wealth index varied between urban and rural Ghana. Those with middle level wealth index had higher prevalence of CKD compared with those with low or high CKD prevalence in both rural and urban Ghana. CKD prevalence rate for low and high level wealth index in urban Ghana was the same while that of rural Ghana was slightly different.

339	Among the whole g	group, educational le	vel was positively ass	ociated with we	alth index (p<0.01) and composite SES
340	(P<0.01). Occupation	nal level was also in	versely associated with	educational leve	el (p<0.01) and wealth index (p<0.01). In
341	urban Ghana, high	educational level w	as positively associate	d with high wea	alth index but inversely associated with
342	occupation (p<0.01).	In rural Ghana, higi	n education was positiv	ely associated w	rith high wealth index (p<0.01), but there
343	was no significant a	ssociation between e	education and occupation	on. High wealth	index was inversely associated with high
344	occupational status i	in both rural and urb	an Ghana (p<0.01) (Ta	ble 2).	
345					
346	Table 2: Relations	hip between SES	constructs (education	nal, occupation	al level and wealth index) by urban
347	rural Ghana				
348 349					
515	Correlation matrix	Educational level	Occupational level	Wealth index	SES
	Whole group			6	
	Educational level	1.000			
	Occupational status	-0.060	1.000		
		0.004			
	Wealth Index	0.282	-0.121	1.000	
		0.001	0.001		
1	SES	1.000	-0.059	0.282	1.000
)		0.003	0.006	0.001	
			14		

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Educational level	1.000

Occu	pational status	-0.115	1.000		
		0.001			
Wea	lth Index	0.294	-0.126	1.000	
		0.001	0.001		
SES		1.000	-0.024	0.937	1.000
		0.002	0.001	0.001	
Rura	l Ghana				
Educ	ational level	1.000			
Occu	ipational status	0.017	1.000		
		0.589			
Wea	lth Index	0.219	-0.135	1.000	
		0.001	0.001		
SES		0.504	0.017	0.934	1.000
		0.001	0.587	0.001	
350					

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57 58 59	Table 3: Association of SES indi	cators (educational level, o	occupational sta	tus and wealth index le	vel) with albun	ninuria, reduced eGFR and CH
57 58	Table 3. Association of SES indi	entars (adjugational lavel of	accumentional ete	tus and wealth index la	val) with album	inuria reduced of FD and CL
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	ouus of founded off (p (0.01).					
65 66	educational level and occupationa odds of reduced eGFR (p<0.01).	n status were not associa	acu with CKD	prevalence, nigh wea	ini index was	significantly associated with
64 65	urban Ghana. However, middle	C				· · · ·
63	age and sex, we observed no sign				•	,
62	CKD. After adjusting for age and					
61	Table 3 shows association					
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Education						
Whole group						
Low	1,152 (11.89)	1.00 (Reference)	1,160 (3.97)	1.00 (Reference)	1.150 (11.91)	1.00 (Reference
Middle	847 (7.32)	0.66 (0.48-0.91)	849 (3.77)	1.36 (0.83-2.22)	845 (8.28)	0.82 (0.59-1.12
High	343 (7.00)	0.67 (0.42-1.07)	345 (3.19)	1.11 (0.55-2.29)	343 (8.75)	0.96 (0.62-1.49
Urban Ghana						X
Low	612 (14.7)	1.00 (Reference)	612 (4.1)	1.00 (Reference)	612 (14.1)	1.00 (Reference)
Middle	546 (7.8)	0.51 (0.34-0.76)	546 (3.7)	1.12 (0.59-2.12)	545 (8.1)	0.59 (0.39-0.89)
High	238 (8.4)	0.53 (0.31-0.91)	238 (3.4)	0.91 (0.37-2.19)	238 (10.9)	0.83 (0.51-1.38)
Rural Ghana						
Low	540 (8.7)	1.00 (Reference)	548 (3.8)	1.00 (Reference)	538 (9.5)	1.00 (Reference)
Middle	301 (6.3)	0.89 (0.51-1.59)	303 (3.9)	1.69 (0.77-3.66)	300 (8.7)	1.33 (0.79-2.25)
High	105 (3.8)	0.66 (0.23-1.95)	107 (2.8)	1.28 (0.35-4.71)	105 (3.8)	0.69 (0.23-2.02)
Occupational	status					
Whole group						
Low	614 (9.93)	1.00 (Reference)	616 (2.76)	1.00 (Reference)	613 (9.46)	1.00 (Reference)
Middle	1,427 (9.25)	0.82 (0.59-1.14)	1,436 (3.34)	0.93 (0.52-1.66)	1,424 (9.90)	0.89 (0.65-1.24)
High	302 (10.26)	0.76 (0.47-1.22)	303 (7.92)	1.33 (0.67-2.62)	302 (12.91)	0.90 (0.57-1.42)
Urban Ghana				Ň Ň		
Low	207 (10.1)	1.00 (Reference)	207 (6.8)	1.00 (Reference)	207 (12.1)	1.00 (Reference)
Middle	817 (11.1)	1.50 (0.88-2.83)	817 (3.6)	1.15 (0.56-2.35)	816 (11.6)	1.37 (0.84-2.56)
High	373 (11.0)	1.57 (0.89-2.53)	373 (2.7)	1.02 (0.41-2.52)	373 (9.7)	1.21 (0.68-2.14)
Rural Ghana						
Low	95 (10.5)	1.00 (Reference)	96 (10.4)	1.00 (Reference)	95 (14.7)	1.00 (Reference)
Middle	610 (6.7)	0.65 (0.31-1.37)	619 (3.1)	0.37 (0.16-0.85)	608 (7.6)	0.55 (0.28-1.08)
High	241 (8.3)	0.99 (0.43-2.28)	243 (2.9)	0.51 (0.18-1.44)	240 (9.2)	0.94 (0.44-2.01)
Wealth index						
Whole group						

	Low	808 (9.65)	1.00 (Reference)	813 (3.32)	1.00 (Reference)	808 (9.16)	1.00 (Reference)
	Middle	678 (10.91)	1.18 (0.84-1.66)	683 (3.81)	1.30 (0.74-2.28)	675 (12.0)	1.43 (1.02-2.01)
	High	835 (8.62)	0.93 (0.66-1.31)	835 (4.19)	1.55 (0.91-2.64)	833 (9.96)	1.21 (0.86-1.69)
	Urban Ghana						
	Low	367 (11.2)	1.00 (Reference)	367 (3.5)	1.00 (Reference)	367 (10.1)	1.00 (Reference)
	Middle	414 (12.3)	1.12 (0.73-1.74)	414 (3.9)	1.30 (0.61-2.80)	413 (13.1)	1.45 (0.93-2.27)
	High	601 (9.8)	0.82 (0.55-1.25)	600 (3.8)	1.13 (0.55-2.31)	600 (10.8)	1.11 (0.72-1.71)
	Rural Ghana						
	Low	441 (7.9)	1.00 (Reference)	446 (3.1)	1.00 (Reference)	441 (8.4)	1.00 (Reference)
	Middle	264 (8.7)	1.13 (0.65-1.98)	269 (3.7)	1.22 (0.52-2.84)	262 (10.3)	1.31 (0.77-2.25)
	High	234 (5.6)	0.78 (0.40-1.53)	235 (5.1)	2.38 (1.03-5.47)	233 (7.7)	1.16 (0.63-2.14)
73 74	total number of individua rural and urban Ghana.	ils in the whole group, r	ural and urban Ghana among tl		ion; eGFR, estimated glomerular constructs; %, proportion of indi	viduals with CKD among	the various levels of SES const
73 74 75 76	rural and urban Ghana. Table 4 shows the	contribution of a	ll three SES constructs	to rural and urba	constructs; %, proportion of indi n CKD prevalence diffe	viduals with CKD among rences. The od	ds of albuminuria
73 74 75 76	rural and urban Ghana. Table 4 shows the	contribution of a	ll three SES constructs	to rural and urba	constructs; %, proportion of indi	viduals with CKD among rences. The od	ds of albuminuria
70 71 72 73 74 75 76 77 78	rural and urban Ghana. Table 4 shows the CKD risk was	contribution of a significantly	ll three SES constructs higher in urban C	to rural and urba	constructs; %, proportion of indi n CKD prevalence diffe	viduals with CKD among rences. The od na. The higher rat	ds of albuminuria
73 74 75 76 77 78	rural and urban Ghana. Table 4 shows the CKD risk was	contribution of a significantly	ll three SES constructs higher in urban C	to rural and urba	constructs; %, proportion of indi n CKD prevalence diffe red with rural Gha	viduals with CKD among rences. The od na. The higher rat	ds of albuminuria
73 74 75 76 77	rural and urban Ghana. Table 4 shows the CKD risk was Ghana was not exp	contribution of a significantly plained by the hig	ll three SES constructs higher in urban C her SES of that popula	to rural and urba Chana compared	constructs; %, proportion of indi n CKD prevalence diffe red with rural Gha	viduals with CKD among rences. The ode na. The higher rat	ds of albuminuria te of CKD observed in t
73 74 75 76 77 78 79 80	rural and urban Ghana. Table 4 shows the CKD risk was Ghana was not exp	contribution of a significantly plained by the hig	ll three SES constructs higher in urban C her SES of that popula	to rural and urba Chana compared	constructs; %, proportion of indi n CKD prevalence diffe red with rural Gha to their rural counterpar	viduals with CKD among rences. The ode na. The higher rat	ds of albuminuria te of CKD observed in t
73 74 75 76 77 78 79	rural and urban Ghana. Table 4 shows the CKD risk was Ghana was not exp Table 4: Cont	contribution of a significantly plained by the hig	ll three SES constructs higher in urban C her SES of that popula	to rural and urba Chana compared	constructs; %, proportion of indi n CKD prevalence diffe red with rural Gha to their rural counterpar	viduals with CKD among rences. The ode na. The higher rat	ds of albuminuria te of CKD observed in t

n cases (%) 1,443 (10.9)	1.37 (1.03- 1.81)	1.70 (1.25-	4 66 /4 46		
(%) 1,443	-	1.70 (1.25-	4 66 /4 46		
(%) 1,443	-	1.70 (1.25-	4 FE /4 4F		
1,443	-	1.70 (1.25-	4 66 /4 46		
	-	1.70 (1.25-	4 66 /4 46		
(10.9)	1 81)		1.55 (1.15-	1.62 (1.18-	1.74 (1.27-
		2.31)	2.10)	2.19)	2.38)
	1.00	1.00	1.00	1.00	1.00
1,015 (8.4)	(Reference)	(Reference)	(Reference)	(Reference)	(Reference)
n cases					
(%)					
	1.27 (0.82-	1.20 (0.76-	1.18 (0.79-	1.12 (0.70-	1.07 (0.67-
1,442 (3.7)	1.97)	1.89)	1.86)	1.78)	1.72)
	1.00	1.00	1.00	1.00	1.00
1,027 (3.7)	(Reference)	(Reference)	(Reference)	(Reference)	(Reference)
n cases					
(%)					
1,441	1.23 (1.01-	1.44 (1.07-	1.38 (1.03-	1.36 (1.01-	1.40 (1.04-
(11.1)	1.62)	1.93)	1.84)	1.83)	1.91)
1,012	1.00	1.00	1.00	1.00	1.00 (Reference
(9.46)	(Reference)	(Reference)	(Reference)	(Reference)	
_		. 19	/ I . / . I II		
-	n cases (%) 1,442 (3.7) 1,027 (3.7) n cases (%) 1,441 (11.1) 1,012 (9.46)	n cases (%) 1.27 (0.82- 1,442 (3.7) 1.97) 1.00 1,027 (3.7) (Reference) n cases (%) 1,441 1.23 (1.01- (11.1) 1.62) 1,012 1.00 (9.46) (Reference)	n cases (%) 1.27 (0.82- 1.20 (0.76-1.442 (3.7) 1.97) 1.89) 1.00 1.00 1,027 (3.7) (Reference) (Reference) n cases (%) 1,441 1.23 (1.01- 1.44 (1.07-(11.1) 1.62) 1.93) 1,012 1.00 1.00 (9.46) (Reference) (Reference)	n cases (%) 1.27 (0.82- 1.20 (0.76- 1.18 (0.79- 1.442 (3.7) 1.97) 1.89) 1.86) 1.00 1.00 1.00 1.00 1,027 (3.7) (Reference) (Reference) (Reference) n cases (%) 1,441 1.23 (1.01- 1.44 (1.07- 1.38 (1.03- (11.1) 1.62) 1.93) 1.84) 1,012 1.00 1.00 1.00 (9.46) (Reference) (Reference) (Reference)	n cases (%) 1.27 (0.82- $1.20 (0.76- 1.18 (0.79- 1.12 (0.70- 1.442 (3.7) 1.97) 1.89) 1.86) 1.78)$ 1.00 1.00 1.00 1.00 1.00 1,027 (3.7) (Reference) (Reference) (Reference) (Reference) n cases (%) 1,441 1.23 (1.01- 1.44 (1.07- 1.38 (1.03- 1.36 (1.01- (11.1) 1.62) 1.93) 1.84) 1.83) 1,012 1.00 1.00 1.00 1.00

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, e.g. sex ar. del 5: adjusted fo. artic cGFR, estimated glomes .dividuals with CKD among urban and. Model 1#: adjusted for age and sex; Model 2: adjusted for age, sex and education level; Model 3: adjusted for age, sex and occupational status; Model 4: adjusted for age, sex and wealth index; Model 5: adjusted for age, sex, educational level, occupational status and wealth index; Abbreviations: CI, confidence interval; ACR, albumin creatinine ratio; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; OR, odds ratio, n= total number of individuals in rural and urban Ghana; %, proportion of individuals with CKD among urban and rural Ghana.

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1 2		
2 3 4	388	Discussion
5 6	389	Key findings
7 8 9	390	Our study findings show no association between all three SES constructs and the
10 11	391	prevalence of CKD in both rural and urban Ghana except for wealth index in rural
12 13	392	Ghana, with the risk of CKD being higher in the wealthier populations. The higher rate
14 15 16	393	of CKD observed in urban Ghana could not be attributed to the higher SES of that
17 18	394	population compared to their rural counterparts.
19 20	395	
21 22 23	396	Discussion of key findings
24 25	397	
26 27	398	Association of SES with CKD in rural and urban Ghana
28 29	399	
30 31	400	Our study did not find any significant associations between all three SES constructs
32 33	401	and CKD among rural and urban Ghana except for wealth index in rural Ghana. The
34 35	402	positive association observed between wealth index in rural Ghana may be due to
36 37 38	403	several reasons. A comparison of the three SES constructs showed higher educational
39 40	404	level to be associated with wealth index in both rural and urban Ghana but not
41 42	405	occupational level. This seems to suggest that occupational level may not be
43 44 45	406	adequately capturing the SES status of individuals living in these settings in relation to
45 46 47	407	CKD. For example, Masthi et al, compared different SES scales in rural and urban
48 49	408	India and concluded that Standard of Living Index (SLI) scale was more accurate for classification
50 51	409	of SES in urban and rural settings ²⁵ . Our finding is consistent with other studies, ^{6 26} which
52 53 54	410	reported no association between SES and CKD in high-income countries and LMICs,
55 56 57 58	411	but in contrast with other studies $^{2-4}$ 27 that found positive associations between SES

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and CKD. The reasons for our current finding are unclear. However, it has been suggested that these inconsistent associations may be due to the varying pathways through which the effect of SES on health status is mediated. For example, at a given educational level marked ethnic differences have been reported. Additionally, similar differences were observed for wealth status at a given income level ²⁸⁻³⁰.

Contribution of SES to observed CKD risk differences between rural and urban Ghana

We observed higher rates of CKD in urban Ghana compared with rural Ghana, as expected. The observed higher rates of CKD in our study were not explained by the higher SES of that population as compared to their rural counterparts. Our results indicate that this is due to the lack of a clear difference in the SES distribution of rural and urban Ghana observed in this study, as well as to the lack of associations between SES and CKD. Consistent with our findings, in a study conducted in Northern Tanzania SES did not explain increased risk of CKD in urban Tanzania²⁶. The lack of associations between SES and CKD could probably partly be explained by the process of epidemiological transition in relation to the "diffusion theory" of ischemic heart disease mortality. This theory attributes the commencement of ischemic heart disease to individuals in the high SES group due to their ability to afford behaviours (smoking, alcohol and sedentary lifestyles) which increased risk of ischemic heart disease. The lower SES groups were later affected partially because of improved living standards, imitation and urbanization. The higher SES groups were the first to embrace behavioural changes required to decrease the risk of ischemic heart disease and this resulted in reversing the gradient ³¹. The rapid urbanization of some rural communities in the Ashanti region of Ghana and the imitation of urban lifestyle could account for our finding. Also, it could be that whereas the high SES group in urban Ghana has already embraced favourable behavioural changes, those in rural Ghana are yet to do so ³². This explains the observed association of wealth index with CKD in rural Ghana but not in urban Ghana. Also, the interplay of other less understood or researched factors

(e.g., exposure to nephrotoxins, herbal medications, sepsis, psychosocial factors) may

be influencing the pathway in which SES influences CKD prevalence and progression.

Strength and limitation

Our study presents several strengths. First, we used well-standardized study protocols across rural and urban Ghana. Our study is also the first in Africa to use all three categories of CKD definition (albuminuria, reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of SES with CKD in rural and urban setting, this provided more detailed information on CKD outcomes. The limitation of intra laboratory variability in earlier studies was eliminated using the same standard operating procedures in the same laboratory for running all samples for both rural and urban Ghana. The use of three constructs of SES in this study also provides a much better holistic approach to assessing SES. Also, the distribution of SES in our study reflects on the national data allowing for generalization of our findings. Our study was limited by the use of cross sectional design, which prevented us from determining causality between predictors and CKD progression. Furthermore, there were more women than men in our study due to the higher response rate in women compared with men. However, this applied to both rural and urban Ghana. We therefore do not expect this to influence our results in a significant way.

Conclusion

All three SES constructs appear not to be associated with prevalence of CKD in urban and rural Ghana except for wealth index in rural Ghana. The observed higher prevalence of CKD in urban Ghana was not explained by the higher SES in urban Ghana. Our study seems to suggest that other non-traditional factors such as nephrotoxins, herbal medications, psychosocial stressors and misuse of over the counter drugs may play a role and underscores the need to further explore these factors.

Acknowledgement

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Contributors

My co-authors have all contributed substantially to this manuscript and approve of this submission. Research idea and study design: DNA, CA, KS, DA, EB, KM, JA; data acquisition and curation: DNA, CA, EB, KM, data analysis/interpretation: DNA, CA, KS, DA, EB, KM, LS, JA, EOD, KKG, FPM, ID, JS, SB, ADA; statistical analysis: DNA, CA, KS, DNA, CA, KS, DA, EB, KM, LS, JA, EOD, KKG, FPM, ID, JS, SB, ADA contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. DNA and CA take responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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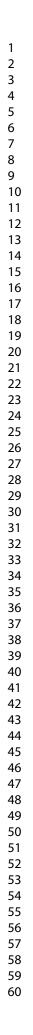
Competing interest: I have communicated with all my co-authors and obtained their full disclosures. My co-authors and I declare no conflicts of interest.

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3 4	498	Patient Consent: None declared
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7	500	Ethics approval: IRBs at each participating site.
8 9	501	
10 11	502	Data sharing statement: Data are available from the RODAM research cohort, a third
12 13	503	party. Dr. Eric Beune affiliated with the RODAM research cohort and a co-author of this paper
14 15	504	in accordance with the RODAM requirements for collaboration. Dr. Beune is the Data Collection
16	505	Coordinator of RODAM and may be contacted with further questions (e.j.beune@amc.uva.nl).
17 18	506	Additionally, researchers interested in further collaboration with RODAM may see the following
19 20	507	URL: <u>http://www.rod-am.eu/</u>
21 22	508	Additionally, researchers interested in further collaboration with RODAM may see the following URL: http://www.rod-am.eu/
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24	630	Legend for figures
25	631 632	Figure 1: Prevalence of chronic kidney disease (CKD) across level of education among urban
26 27	633	and rural participants Definitions according to 2012 KDIGO (Kidney Disease: Improving Global
28	634	Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very
29	635	high-risk groups.
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33	638	Figure 2: Prevalence of chronic kidney disease (CKD) across occupational status among urban
34 25	639	and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving
35 36	640	Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk,
37	641	or very high-risk groups.
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42	646	urban and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving
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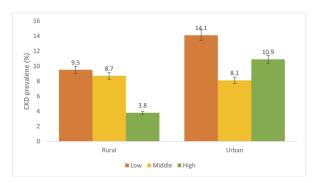


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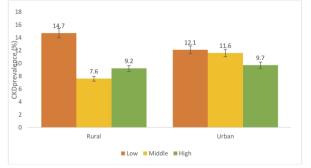
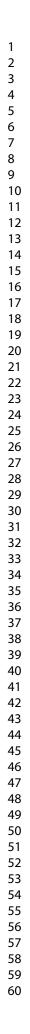


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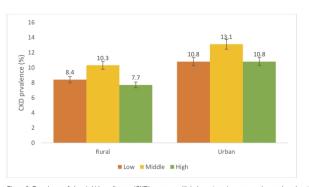


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STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No.	Recommendation		Page No.	Relevant text from manuscript
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1,2		We have included a commonly used term in the title and abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2		Our study did not find any associations between SES indicators and CKD in both rural and urban Ghana after age and sex adjustment except in rural Ghana where wealth index was associated with prevalence of CKD. Consequently, the higher SES did not account for the increased rate of CKD among urban dwellers suggesting the need to identify other factors that may be driving this.
Introduction					
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4		The theoretical and scientific background as well as the rationale for conducting the study have been provided in the introduction section.
Objectives	3	State specific objectives, including any prespecified hypotheses	4		We assessed the association o SES with CKD in rural and urban Ghana and studied wha extent the higher SES of peopl- in urban areas could account fo differences in CKD between rural and urban populations
Methods					
Study design	4	Present key elements of study design early in the paper	5-6		Details given in the methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6		Rural or urban Ghana.
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Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of 6-8 6-8 participants (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed 6-8 Case-control study—For matched studies, give matching criteria and the number of controls per case 7 Variables 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable 6-8 The main outcomes have clearly defined. Data sources/ 8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group 6-8 We defined each variable interest in the me accordingly Bias 9 Describe any efforts to address potential sources of bias 18 Potential sources of bias discussed in the methods se and we have also referred RODAM study methods perfored RODAM study methods perfored RODAM study methods perfored RODAM study methods se and we have also referred RODAM study methods perfored RODAM study methods performed RODAM	6	 (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls 		A multi-centre cross-sectional study was conducted among Ghanaian adults (n=2492) aged 25-70 years residing in rural and urban Ghana.
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Continued on next page	9	Describe any efforts to address potential sources of bias	18	
Continued on next page	10	Explain how the study size was arrived at	5	Given in the methods section and we have also referred to the RODAM study methods paper
		7 8* 9	participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable 8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group 9 Describe any efforts to address potential sources of bias 10 Explain how the study size was arrived at	participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. 6-8 Give diagnostic criteria, if applicable 8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group 9 Describe any efforts to address potential sources of bias

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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9	Please see methods
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	8-9	Please see methods
methods		(b) Describe any methods used to examine subgroups and interactions	8-9	Please see methods
		(c) Explain how missing data were addressed	8-9	
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	NA	We have reported non-response
		Case-control study—If applicable, explain how matching of cases and controls was addressed		across sites
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling		
		strategy		
		(<u>e</u>) Describe any sensitivity analyses	NA	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially eligible, examined	5	Non-response analysis was done to
		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		shed light on the differential response rates across sites
		(b) Give reasons for non-participation at each stage	5	response rates across sites
		(c) Consider use of a flow diagram	5	We have also referred to RODAM
				methods paper
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on	5	We have also referred to RODAM
		exposures and potential confounders		methods paper
		(b) Indicate number of participants with missing data for each variable of interest	5	We have also referred to RODAM
				methods paper
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	NA	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	NA	
		Case-control study-Report numbers in each exposure category, or summary measures of exposure	NA	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9-10	Summary measures are given in the results section and in tables and figures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	12-16	Unadjusted and adjusted estimates
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were		are given in the results section and
		included		in figures
		(b) Report category boundaries when continuous variables were categorized	12-16	We have provided mean and corresponding standard deviations for the continuous variables.
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		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	NA	
Continued on next pa	ige			
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	NA	
Discussion				
Key results	18	Summarise key results with reference to study objectives	8	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18	Key limitations regarding stuc methods including differenti response rates and samplir methods in the various study site have been provided
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-18	Cautious overall interpretation of the key findings have been provided.
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18	
Other informati	ion			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	19	The funders had no role in stud design, data collection and analysi
*Give informatio	on sep	original study on which the present article is based	in cohort and	decision to publish, or preparation of the manuscript
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A CROSS-SECTIONAL STUDY OF ASSOCIATION BETWEEN SOCIOECONOMIC INDICATORS AND CHRONIC KIDNEY DISEASE IN RURAL-URBAN GHANA: THE RODAM STUDY

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4	1	A CROSS-SECTIONAL STUDY OF ASSOCIATION BETWEEN
5 6	2	SOCIOECONOMIC INDICATORS AND CHRONIC KIDNEY DISEASE IN
7	3	RURAL-URBAN GHANA: THE RODAM STUDY
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85 Abstract

Objectives: Studies from high income countries suggest higher prevalence of Chronic Kidney Disease (CKD) among individuals in low socio-economic groups. However, some studies from low and middleincome countries (LMICs) show the reverse pattern among those in high socioeconomic groups. It is unknown which pattern applies to individuals living in rural and urban Ghana. We assessed the association between Socio-Economic Status (SES) indicators and CKD in rural and urban Ghana and to what extent the higher SES of people in urban areas of Ghana could account for differences in CKD between rural and urban populations.

95 Setting: The study was conducted in Ghana (Ashanti region). We used baseline data from a
96 multi-centre Research on Obesity and Diabetes among African Migrants (RODAM)
97 study.

99 Participants: The sample consisted of 2492 adults (Rural Ghana, 1043, Urban Ghana, 1,449) aged 25 to
70 years living in Ghana.

102 Exposure: Educational level, occupational level and wealth index.103

104 Outcome: Three CKD outcomes were considered using the 2012 KDIGO (Kidney Disease: Improving
 105 Global Outcomes) severity of CKD classification: albuminuria, reduced glomerular filtration rate and
 106 high to very high CKD risk based on the combination of these two.

Results: All three SES indicators were not associated with CKD in both rural and urban Ghana after age and sex adjustment except for rural Ghana where high wealth index was significantly associated with higher odds of reduced eGFR (AOR, 2.38; 95% C.I. 1.03-5.47). The higher rate of CKD observed in urban Ghana was not explained by the higher SES of that population.

Conclusion: SES indicators were not associated with prevalence of CKD except for wealth index and
 reduced eGFR in rural Ghana. Consequently, the higher SES of urban Ghana did not account for the
 increased rate of CKD among urban dwellers suggesting the need to identify other factors that may be
 driving this.

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 119 Index Words: Chronic kidney disease; socioeconomic status; health inequalities; risk factor; ethnic
 120 minority groups; migrants; RODAM study, Ghana

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14 15	136	Strengths and limitation of the study
16 17	130	Chenguis and miniation of the study
18	137	> The use of well-standardized study protocols across rural and urban Ghana eliminated intra
19 20	139	protocol variability.
21 22	140	
23 24	141	> Our study is also the first in Africa to use all three categories of CKD definitions (albuminuria,
25	142	reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of SES with CKD in rural
26 27	143	and urban setting. This provides more detailed information on CKD outcomes.
28	144	
29 30	145	> The limitation of intra laboratory variability in earlier studies was eliminated using the same
31 32	146	standard operating procedures in the same laboratory for running all samples for both rural and
33	147	urban Ghana.
34 35	148	
36 37	149	> The use of three constructs of SES (educational level, occupational level and wealth index) in this
38	150	study also provides a much better holistic approach to assessing SES associations with CKD.
39 40	151	
41 42	152	> Our study was limited because of the use of cross sectional design which prevented us from
43	153	determining causality between predictors and CKD progression.
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176 Introduction

rc str In general, individuals in lower socio-economic status (SES) groups have been shown to suffer more 178 179 frequently from Chronic Kidney Disease (CKD), often progressing to End Stage Renal Disease (ESRD), 180 and associated with inadequate dialysis treatment, reduced access to kidney transplantation and poor 181 health outcomes ¹. Recent studies have consistently found low SES to be associated with higher risk of 182 CKD among people of African origin ²⁻⁵.

183 However, in some settings the well-known inverse association between SES and CKD 184 seems to be absent, or even reversed. For example, Bryne et al. did not find any association between SES and End Stage Renal Disease ⁶. Other studies have found 185 ⁷⁸. Specifically, as SES improved, 186 a positive association between SES and CKD 187 (unhealthy unhealthful physical lifestyle diet, inactivity, smoking and alcohol 188 consumption) increased in China while that of the United States decreased with

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Methods

Study population and study design

improved SES ⁹. People with higher incomes, in these contexts, can afford a western 39 90 lifestyle, which is more readily available in the urban areas than in the rural areas. There is therefore an interaction between individual SES and environmental factors, 91 such as food, alcohol, smoking and sedentary life style in such populations ¹⁰⁻¹². 92 93 Consequently, in those settings, people with a higher SES might have higher CKD 94 risk.

95 In urban areas, the population in general has higher SES than in rural areas ¹³. For example, individuals 96 with higher educational level migrate from rural areas to find higher occupations matching their higher 97 education to improve on their wealth. If indeed a positive association between SES and CKD is observed 98 in LMICs, this might underlie the well-known health differences between urban and rural areas, with 99 urban areas having an increased risk of CKD¹⁴. So far, it is unknown whether the reversed SES gradient 00 (higher risk in high SES group) might explain the higher burden of CKD in urban areas as compared to 01 rural areas in Africa.

03 In view of this, we assessed the association of SES with CKD in rural and urban Ghana and studied the)4 extent to which the higher SES of people in urban areas could account for differences in CKD between)5 rural and urban populations.

In the present analyses, data from the RODAM (Research on Obesity & Diabetes

among African Migrants) study, a multi-centre cross-sectional study were used. The

rationale, conceptual framework, design and methodology of the RODAM study have been described in detail elsewhere ¹⁵ ¹⁶. As the Healthy Life in an Urban Setting (HELIUS) study conducted among Ghanaian migrants living in Amsterdam did not find any associations between SES and CKD ¹⁷ the current study focused on rural and urban Ghana (Ashanti region of Ghana). The RODAM study was conducted from 2012 to 2015 and it comprised of individuals aged 25-70 years living in rural and urban Ghana and Ghanaian migrants in Europe. All participants below 25 and above 70 years were excluded in the present analyses. The present analysis was restricted to the rural and urban sites (n=2492) RODAM participants. Specifically, 1043 participants from rural Ghana and 1449 from urban Ghana were used in this study.

Data collection for the study was standardized across all sites. Written informed consent was obtained from each participant prior to enrolment in the study. The respective ethics committees in Ghana and the three European countries approved the study protocols before data collection began. Specifically, we obtained ethical clearance in Ghana from School of Medical Sciences/Komfo Anokye Teaching Hospital Committee on Human Research, Publication & Ethical Review Board. In the Netherlands, the Institutional Review Board of the AMC, University of Amsterdam gave approval for the study. In Germany, approval for the study was obtained from the Ethics Committee of Charite-Universitäts medizin. The London School of Hygiene and Tropical Medicine Research Ethics Committee gave approval for the study in the UK.

The response rate was 76% in rural Ghana and 74% in urban Ghana. In Ghana,
participants were randomly drawn from a list of 30 enumeration areas in the Ashanti

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region based on the 2010 population census using the multistage random sampling. These enumeration areas came from two purposively selected urban cities (Kumasi and Obuasi) and 15 randomly selected rural communities in the Ashanti region. Selected health and community authorities were first identified, notified of the study and letters were sent giving detailed explanation of the study. We sent team members to stay among the communities to familiarize with them and organize mini clinics in the field. This lasted between 1-2 weeks depending on the sampled population and responsiveness of respondents.

In Ghana, questionnaires administration and physical examination were done at the same day/time. The participants were instructed to fast from 10.00pm the night before the physical examination. For the current study, 2566 participants with data available on both questionnaire data and physical measurements were used. We excluded (n=74) individuals outside the RODAM age range of 25-70 years resulting in a data set of 2492 for analysis. These comprised 1,449 Urban Ghana and 1043 Rural Ghana. For the final analysis, individuals with no data on CKD status (n=42) were excluded.

255 Measurements

256 Covariates

257 Demographic and lifestyle factors

Information on demographics, educational level, occupational level, wealth index and lifestyle factors (smoking and physical activity) were obtained by questionnaire. Physical examinations were performed with validated devices per standardized operational procedures across all study sites. Weight was measured in light clothing and without shoes with SECA 877 scales to the nearest 0.1 kg. Height was measured without shoes with a portable stadiometer (SECA 217) to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m²). Overweight was defined as BMI of ≥ 25 to $\leq 30 \text{ kg/m}^2$ and obesity as BMI $\geq 30 \text{ kg/m}^2$ ¹⁸. Per participant, all anthropometrics were measured twice by the same assessor and the average of the two measurements were used for analyses.

266 Predictor: SES

Socioeconomic indicators used in this study were educational level, occupational status and level of wealth index. Educational level was determined based on self-reported highest educational qualification accomplished based on the Ghanaian educational system. Occupational level was determined based on self-reported current occupation if employed and/or last occupation before retirement or student. The reported occupations were further coded according to the International Standard Classification of Occupations scheme (ISCO-08). Where 'high' (professionals, managers, clerical support staff, higher grade routine non-manual employees service and sales-related occupations) and 'low' (craft and related trades workers, elementary occupations and farmers) and the rest were categorized into the 'middle'. Wealth index was determined using the World Health Organization (WHO) standard of wealth index classification. Wealth index was based on data collected in the Household Questionnaire. The questionnaire comprised of questions on household's ownership of several consumer items such as television, car, flooring material, toilet facilities etc. Each household was assigned a standard score for each asset. Wealth index was then expressed in five categories. The five categories were further categorized into three categories by combining the second and third as well as fourth and fifth categories due to small numbers ¹⁹. All three SES constructs were further classified as low, medium and high SES and their relationship to each other tested. A composite SES variable (SES) was generated based on the three SES constructs (education, occupation and wealth index) using the EGEN group command in STATA. The codes were combined into numerical variables and their averages computed. The resultant values were recoded into three categories (low, medium and high).

40
41286Co-morbidity factors

Blood pressure (BP) was measured three times using a validated semi-automated device (The Microlife WatchBP home) with appropriate cuffs in a sitting position after at least 5 min rest. The mean of the last two BP measurements was used in the analyses. Hypertension was defined as systolic BP \geq 140 mmHg, and/or diastolic $BP \ge 90$ mmHg, and/or being on antihypertensive medication treatment, and/or self-reported hypertension. Trained research assistants in the two sites collected fasting venous blood samples. All the blood samples were processed and aliquoted immediately (within one hour to maximum three hours of the vena puncture) after collection per standard operation procedures, and then temporarily stored at the local research location at -20° C. The separated samples were then transported to the local research centres laboratories, where they were checked, registered and stored at -80° C. To avoid intra-

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laboratory variability, the stored blood samples from the local research centres were transported to Berlin, Germany for biochemical analyses. Fasting plasma glucose concentration was measured using an enzymatic method (hexokinase). Type 2 diabetes was defined according to the WHO diagnostic criteria (fasting glucose \geq 7.0 mmol/L, and/or current use of medication prescribed to treat diabetes, and/or self-reported diabetes)²⁰. Concentration of total cholesterol was assessed using colorimetric test kits. All biochemical analyses were performed using an ABX Pentra 400 chemistry analyzer (ABX Pentra; Horiba ABX, Germany). Hypercholesterolemia was defined as total cholesterol level ≥ 6.22 mmol/L. Serum creatinine concentration (in umol/L) was determined by a kinetic colorimetric spectrophotometric isotope dilution mass spectrometry-calibrated method (Roche Diagnostics). Biochemical analyses were subject to extensive quality checks including blinded serial measurements.

20 306 **Outcome: CKD prevalence**

Participants were asked to bring an early morning urine sample for the analyses of albuminuria and creatinine levels. Urinary albumin concentration (in mg/L) was measured by an immunochemical turbidimetric method (Roche Diagnostics). Urinary creatinine concentration (in umol/L) was measured by a kinetic spectrophotometric method (Roche Diagnostics). Estimated glomerular filtration rate (eGFR) was calculated using the CKDEPI (CKD Epidemiology Collaboration) creatinine equation ²¹. Urinary albumin-creatinine ratio (ACR; expressed in mg/g) was calculated by taking the ratio between urinary albumin and urinary creatinine. eGFR and albuminuria were categorized according to the 2012 KDIGO (Kidney Disease: Improving Global Outcomes) classification 22 . eGFR was categorized as follows: G1, > 90 mL/min/1.73 m² (normal kidney function); G2, 60 to 89 mL/min/1.73 m² (mildly decreased); G3a, 45 to 59 mL/min/1.73 m² (mildly to moderately decreased); G3b, 30 to 44 mL/min/1.73 m² (moderately to severely decreased); G4, 15 to 29 mL/min/1.73 m² (severely decreased); and G5, < 15 mL/min/1.73 m² (kidney failure). Albuminuria categories were derived from ACR and were as follows: A1, < 3mg/mmol (normal to mildly increased); A2, 3 to 30 mg/mmol (moderately increased); and A3, > 30mg/mmol (severely increased). CKD status was categorized according to severity of kidney disease (green, low risk; vellow, moderately increased risk; orange, high risk; and red, very high risk) using the combination of eGFR (G1-G5) and albuminuria (A1-A3) levels defined by the 2012 KDIGO guideline ²³. Due to the small number of participants in the very high risk category of CKD, high and very high risk groups were combined. Reduced eGFR was defined as eGFR $< 60 \text{ mL/min}/1.73 \text{ m}^2$. Because of the small number of participants in the severely increased albuminuria category, we defined albuminuria as ACR >3 mg/mmol by combining the moderately increased (A2) and severely increased (A3) categories.

327 Patient and Public Involvement

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Community leaders were involved in the recruitment of patients. These comprised of religious communities (churches and mosques), endorsement from local key leaders and establishing relationships with healthcare organizations. We also provided information on the study by involving the local media (radio and television stations). We sent letters to all selected health and community authorities to notify participants of the study. Team members were sent to the various communities to stay among the community and organize mini clinics for a period of 1-2 weeks. Results of the study were disseminated through seminars, durbars and via radio and television stations.

335 Statistical methods

Participants' characteristics were expressed as absolute numbers and percentages for categorical variables and as means and standard deviations (SD) for continuous variables. CKD prevalence with 5% error bars were presented as bar graphs for each SES construct across rural and urban Ghana. Spearman's rank correlation was used to determine correlations between the three SES constructs. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were estimated by means of logistic regression analyses to study the odds of albuminuria (ACR>3 mg/mmol, A2-A3, moderately to severely increased albuminuria), reduced kidney function (eGFR< 60 mL/min/1.73 m², G3-G5 moderately to severely decreased kidney function) and increased CKD risk (high and very high CKD risk) by SES, with adjustments for potential confounders (age and sex).²⁴ In addition, the analyses were performed for the total population (using low educational level, low occupational status and low level of wealth index as reference categories). Further analysis was conducted to assess the contribution of SES indicators to rural-urban differences in albuminuria, reduced eGFR and CKD risk using rural Ghana as reference. Tolerance test and variance inflation factor (VIF) showed very small degree of collinearity among SES predictors thus we therefore adjusted for each of SES variables separately. Complete case analysis approach was used. All data available were included in the age-adjusted models. All analyses were performed using STATA, version 14.0 (StataCorp LP).

353 Results

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Table 1 shows characteristics of study participants. Participants in rural Ghana were slightly older than those in urban Ghana. Female preponderance was observed in both rural (61.2%) and urban (71.4%) Ghana, though higher proportions were observed in urban Ghana. Individuals living in rural Ghana were generally less educated (56.9%) compared with those living in urban (43.9%) Ghana. There were slightly more individuals with low occupational status in urban Ghana compared with their peers in rural Ghana. People in urban Ghana (43.4%) were wealthier than their rural (24.9%) counterparts. Rural Ghanaians (47.2%) were more physically active compared with their urban peers. Smoking was low among Ghanaians though rural Ghanaians were more likely to smoke compared with their urban peers. Hypercholesterolemia was more prevalent in urban Ghana than in rural Ghana. Hypertension (36.7%) and type 2 diabetes (10.6%) were more prevalent in urban Ghanaians compared with those living in rural Ghana. Urban Ghanaians were markedly more obese compared with their rural peers. Except for eGFR, albuminuria and CKD risk prevalence rates were higher in urban Ghana compared with rural Ghana.

Table 1: Baseline characteristics by loc	ation	
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	Rural Ghana	Urban Ghana
Number of participants, N (%)	1043 (41.9)	1449 (58.1
Mean age, years (SD)	46.5 (12.6)	45.2 (11.4
Females, N (%)	638 (61.2)	1034 (71.4
Educational level n (%)		
Low	555 (56.9)	614 (43.9
Middle	311 (31.9)	547 (39.1
High	108 (11.2)	239 (17.0
Occupational status, n (%)		
Low	250 (25.7)	374 (26.7
Middle	628 (64.5)	818 (58.4
High	96 (9.8)	209 (14.9
Wealth index, n (%)		
Low	449 (46.5)	368 (26.6
Middle	276 (28.6)	416 (30.0
High	241 (24.9)	602 (43.4
BMI (kg/m²		
< 25	794 (76.3)	579 (39.9
25-29.9	189 (18.2)	495 (34.2
≥ 30	58 (5.5)	374 (25.9
Low physical activity, n (%)	663 (47.2)	592 (60.7

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3		Smoking, n (%)	22 (2.3)	14 (1.0)
4			ZZ (Z.J)	14 (1.0)
5 6		Hypercholesterolemia, n (%)	78 (7.6)	270 (18.7)
7		Hypertension, n (%)	306 (29.3)	531 (36.7)
8 9			53	
10 11		Diabetes, n (%)	(5.1)	153 (10.6)
12		Albuminuria, n (%)		
13 14			930 (91.6)	
15 16		A1, Normal to mildly increased (ACR <3 mg/mmol)	85	1285 (89.1)
17		A2-A3, moderately to severely increased (ACR≥ 3 m	ng/ (8.4)	158 (10.9)
18 19		eGFR, n (%)		
20 21		G1-G2 (≥ 60 mL/min/1.73m²)	989 (96.3)	1388 (96.3)
22		G3-G5 (<60 mL/min/1.73m²)	38 (3.7)	54 (3.7)
23 24		CKD risk, n (%)		
25 26		Low risk (green)	916 (90.5)	1281 (88.9)
27		Moderately increased to very high risk		
28 29		(yellow to red)	96 (9.5)	160 (11.1)
30 31	391 392	Abbreviations: N, number of respondents; SD, standard deviation; eGFR, estima creatinine ratio; CKD, Chronic kidney disease	ted glomerular filtration ra	te; ACR, albumin
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Figure 1 shows prevalence of CKD by level of education in urban and rural Ghana. Prevalence of CKD decreased with increasing levels of education in rural Ghana. Higher prevalence of CKD was observed among individuals with low educational level compared with those with middle and high educational level. However, those with high educational level in urban Ghana had higher prevalence of CKD compared with those with middle level education. For occupational status, prevalence of CKD was higher among individuals with low occupational status in urban Ghana. Similar patterns were observed in rural Ghana; however, those with higher occupational status had higher prevalence of CKD compared with those with middle occupational status (Figure 2). Figure 3 shows prevalence of CKD by level of wealth index. CKD prevalence among

404 the levels of wealth index varied between urban and rural Ghana. Those with middle 405 level wealth index had higher prevalence of CKD compared with those with low or 406 high CKD prevalence in both rural and urban Ghana. CKD prevalence rate for low and 407 high level wealth index in urban Ghana was the same while that of rural Ghana was 408 slightly different.

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409	Among the whole group, educational level was positively associated with wealth index (p<0.01) and composite SES
410	(P<0.01). Occupational level was also inversely associated with educational level (p<0.01) and wealth index (p<0.01). In
411	urban Ghana, high educational level was positively associated with high wealth index but inversely associated with
412	occupation (p<0.01). In rural Ghana, high education was positively associated with high wealth index (p<0.01), but there
413	was no significant association between education and occupation. High wealth index was inversely associated with high
414	occupational status in both rural and urban Ghana (p<0.01) (Table 2).
415	
416	Table 2: Relationship between SES constructs (educational, occupational level and wealth index) by urban
417	rural Ghana
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	Correlation matrix Educational level Occupational level Wealth index SES
	Whole group

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	Correlation matrix	Educational level	Occupational level	Wealth index	SES
	Whole group			C	
	Educational level	1.000			
	Occupational status	-0.060	1.000		
		0.004			
	Wealth Index	0.282	-0.121	1.000	
		0.001	0.001		
	SES	1.000	-0.059	0.282	1.000
		0.003	0.006	0.001	

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Educational level	1.000

Occupational status	-0.115	1.000		
	0.001			
Wealth Index	0.294	-0.126	1.000	
	0.001	0.001		
SES	1.000	-0.024	0.937	1.000
	0.002	0.001	0.001	
Rural Ghana				
Educational level	1.000			
Occupational status	0.017	1.000		
	0.589			
Wealth Index	0.219	-0.135	1.000	
	0.001	0.001		
SES	0.504	0.017	0.934	1.000
	0.001	0.587	0.001	

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3 4	424	4								
5 6 7	425	5								
, 8 9	426	6								
10 11	427	7								
12 13 14	428	8								
14 15 16	429	9								
17 18	430	0								
19 20 21	431	1 Table 3 shows association between level of education, occupational status, level of wealth index an	d prevalence of							
22 23	432	2 CKD. After adjusting for age and sex for the whole group, albuminuria was associated with middle level education (AC)R=0.66, 0.48-0.91,							
24	433	3 p<0.01). After adjusting for age and sex, we observed no significant association between SES indicators (educational level, occ	upational status and							
25 26	434	4 wealth index) and CKD in urban Ghana. However, middle (AOR=0.51, 0.34-0.76, <0.01) and higher (AOR=0.53, 0.31-	0.91, p<0.01) level							
27	435	education was associated with reduced albuminuria in urban Ghana. Whereas educational level and occupational status were not associated with								
28 29	436	6 CKD prevalence, high wealth index was significantly associated with higher odds of reduced eGFR in rural Ghana (AC)R=2.38, 1.03-5.47,							
30 31	437	7 P<0.01).								
32 33	438	8								
34 35	439	9 Table 3: Association of SES indicators (educational level, occupational status and wealth index level) with albuminuria, reduced	eGFR and CKD risk							
36 37	440	0								
38 39		Albuminuria (ACR ≥ 3 mg/mmol)eGFR < 60 mL/min/1.73 m2	(KDIGO,							
40 41 42		OR (95% CI) OR (95% CI) OR (95% C	(I)							
43 44 45 46 47		18 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml								

	n (%)	Model 1	n (%)	Model 1	n (%)	Model 1
Education						
Whole group						
Low	1,152 (11.89)	1.00 (Reference)	1,160 (3.97)	1.00 (Reference)	1.150 (11.91)	1.00 (Reference)
Middle	847 (7.32)	0.66 (0.48-0.91)	849 (3.77)	1.36 (0.83-2.22)	845 (8.28)	0.82 (0.59-1.12)
High	343 (7.00)	0.67 (0.42-1.07)	345 (3.19)	1.11 (0.55-2.29)	343 (8.75)	0.96 (0.62-1.49)
Urban Ghana				(0.00 2.2))		0.50 (0.02 1.05)
Low	612 (14.7)	1.00 (Reference)	612 (4.1)	1.00 (Reference)	612 (14.1)	1.00 (Reference)
Middle	546 (7.8)	0.51 (0.34-0.76)	546 (3.7)	1.12 (0.59-2.12)	545 (8.1)	0.59 (0.39-0.89)
High	238 (8.4)	0.53 (0.31-0.91)	238 (3.4)	0.91 (0.37-2.19)	238 (10.9)	0.83 (0.51-1.38)
Rural Ghana						
Low	540 (8.7)	1.00 (Reference)	548 (3.8)	1.00 (Reference)	538 (9.5)	1.00 (Reference)
Middle	301 (6.3)	0.89 (0.51-1.59)	303 (3.9)	1.69 (0.77-3.66)	300 (8.7)	1.33 (0.79-2.25)
High	105 (3.8)	0.66 (0.23-1.95)	107 (2.8)	1.28 (0.35-4.71)	105 (3.8)	0.69 (0.23-2.02)
Occupational st	atus					
Whole group						
Low	614 (9.93)	1.00 (Reference)	616 (2.76)	1.00 (Reference)	613 (9.46)	1.00 (Reference)
Middle	1,427 (9.25)	0.82 (0.59-1.14)	1,436 (3.34)	0.93 (0.52-1.66)	1,424 (9.90)	0.89 (0.65-1.24)
High	302 (10.26)	0.76 (0.47-1.22)	303 (7.92)	1.33 (0.67-2.62)	302 (12.91)	0.90 (0.57-1.42)
Urban Ghana						
Low	207 (10.1)	1.00 (Reference)	207 (6.8)	1.00 (Reference)	207 (12.1)	1.00 (Reference)
Middle	817 (11.1)	1.50 (0.88-2.83)	817 (3.6)	1.15 (0.56-2.35)	816 (11.6)	1.37 (0.84-2.56)
High	373 (11.0)	1.57 (0.89-2.53)	373 (2.7)	1.02 (0.41-2.52)	373 (9.7)	1.21 (0.68-2.14)
Rural Ghana						
Low	95 (10.5)	1.00 (Reference)	96 (10.4)	1.00 (Reference)	95 (14.7)	1.00 (Reference)
Middle	610 (6.7)	0.65 (0.31-1.37)	619 (3.1)	0.37 (0.16-0.85)	608 (7.6)	0.55 (0.28-1.08)
High	241 (8.3)	0.99 (0.43-2.28)	243 (2.9)	0.51 (0.18-1.44)	240 (9.2)	0.94 (0.44-2.01)

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	Whole group						
	Low	808 (9.65)	1.00 (Reference)	813 (3.32)	1.00 (Reference)	808 (9.16)	1.00 (Reference)
	Middle	678 (10.91)	1.18 (0.84-1.66)	683 (3.81)	1.30 (0.74-2.28)	675 (12.0)	1.43 (1.02-2.01)
	High	835 (8.62)	0.93 (0.66-1.31)	835 (4.19)	1.55 (0.91-2.64)	833 (9.96)	1.21 (0.86-1.69)
	Urban Ghana						
	Low	367 (11.2)	1.00 (Reference)	367 (3.5)	1.00 (Reference)	367 (10.1)	1.00 (Reference)
	Middle	414 (12.3)	1.12 (0.73-1.74)	414 (3.9)	1.30 (0.61-2.80)	413 (13.1)	1.45 (0.93-2.27)
	High	601 (9.8)	0.82 (0.55-1.25)	600 (3.8)	1.13 (0.55-2.31)	600 (10.8)	1.11 (0.72-1.71)
	Rural Ghana						
	Low	441 (7.9)	1.00 (Reference)	446 (3.1)	1.00 (Reference)	441 (8.4)	1.00 (Reference)
	Middle	264 (8.7)	1.13 (0.65-1.98)	269 (3.7)	1.22 (0.52-2.84)	262 (10.3)	1.31 (0.77-2.25)
	High	234 (5.6)	0.78 (0.40-1.53)	235 (5.1)	2.38 (1.03-5.47)	233 (7.7)	1.16 (0.63-2.14)
443 446 447 448							
449	observed in urban	n Ghana was not ex	xplained by the higher	SES of that popul	ation as compared to the	eir rural counterpar	ts.
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451	Table 4: Con	tribution of S	ES indicators to	rural-urban d	ifferences in albu	minuria, reduc	ed eGFR and CKD
452	risk						
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							I) OR (95% CI)
	 447 448 449 450 451 	High Urban Ghana Low Middle High Rural Ghana Low Middle High Model 1, adjusted for ag total number of individu rural and urban Ghana. 444 445 446 447 Table 4 shows the 448 CKD risk wa 449 observed in urban 450 451 Table 4: Con 452 risk	Middle $678 (10.91)$ High $835 (8.62)$ Urban GhanaLow $367 (11.2)$ Middle $414 (12.3)$ High $601 (9.8)$ Rural GhanaLow $441 (7.9)$ Middle $264 (8.7)$ High $234 (5.6)$ 441Model 1, adjusted for age and sex; Abbreviations total number of individuals in the whole group, rural and urban Ghana.443444445446447448CKD risk was significantly observed in urban Ghana was not ex 450451Table 4: Contribution of S 452452risk	Middle 678 (10.91) 1.18 (0.84-1.66) High 835 (8.62) 0.93 (0.66-1.31) Urban Ghana Low 367 (11.2) 1.00 (Reference) Middle 414 (12.3) 1.12 (0.73-1.74) High 601 (9.8) 0.82 (0.55-1.25) Rural Ghana Low 441 (7.9) 1.00 (Reference) Middle 264 (8.7) 1.13 (0.65-1.98) High 234 (5.6) 0.78 (0.40-1.53) Model 1, adjusted for age and sex; Abbreviations: CL confidence interval; ACE total number of individuals in the whole group, rural and urban Ghana among the rural and urban Ghana. 444 445 445 446 447 Table 4 shows the contribution of all three SES constructs 448 CKD risk was significantly higher in urban 449 observed in urban Ghana was not explained by the higher in 450 451 Table 4: Contribution of SES indicators to 452 453 453	Middle 678 (10.91) 1.18 (0.84-1.66) 683 (3.81) High 835 (8.62) 0.93 (0.66-1.31) 835 (4.19) Urban Ghana Low 367 (11.2) 1.00 (Reference) 367 (3.5) Middle 414 (12.3) 1.12 (0.73-1.74) 414 (3.9) High 601 (9.8) 0.82 (0.55-1.25) 600 (3.8) Rural Ghana Low 441 (7.9) 1.00 (Reference) 446 (3.1) Middle 264 (8.7) 1.13 (0.65-1.98) 269 (3.7) High 234 (5.6) 0.78 (0.40-1.53) 235 (5.1) Model 1, adjusted for age and sex; Abbreviations: CI, confidence interval; ACR, abbumin creatinine rati 444 Model 1, adjusted for age and sex; Abbreviations: CI, confidence interval; ACR, abbumin creatinine rati 444 Model 1, adjusted for age and sex; Abbreviations: CI, confidence interval; ACR, abbumin creatinine rati 444 444 445 446 444 445 446 445 446 447 446 448 CKD risk was significantly higher in urban Ghana comp 449 observed in urban Ghana was not explained by the higher SES of that popula 450 451	Middle 678 (10.91) 1.18 (0.84-1.66) 683 (3.81) 1.30 (0.74-2.28) High 835 (8.62) 0.93 (0.66-1.31) 835 (4.19) 1.55 (0.91-2.64) Urban Ghana Image: Construct of the state of the	Middle 678 (10.91) 1.18 (0.84-1.66) 683 (3.81) 1.30 (0.74-2.28) 675 (12.0) High 835 (8.62) 0.93 (0.66-1.31) 835 (4.19) 1.55 (0.91-2.64) 833 (9.96) Urban Ghana Image: Construction of the end of the e

		Model 1	Model 2	Model 3	Model 4	Model 5
Albuminuria (ACR ≥ 3						
mg/mmol						
	n cases					
Sites	(%)					
	1,443	1.37 (1.03-	1.70 (1.25-	1.55 (1.15-	1.62 (1.18-	1.74 (1.27-
Jrban Ghana	(10.9)	1.81)	2.31)	2.10)	2.19)	2.38)
		1.00	1.00	1.00	1.00	1.00
Rural Ghana	1,015 (8.4)	(Reference)	(Reference)	(Reference)	(Reference)	(Reference)
eGFR < 60 mL/min/1.73						
m2						
	n cases					
Sites	(%)					
		1.27 (0.82-	1.20 (0.76-	1.18 (0.79-	1.12 (0.70-	1.07 (0.67-
Jrban Ghana	1,442 (3.7)	1.97)	1.89)	1.86)	1.78)	1.72)
		1.00	1.00	1.00	1.00	1.00
Rural Ghana	1,027 (3.7)	(Reference)	(Reference)	(Reference)	(Reference)	(Reference)
High to very high CKD risk						
	n cases					
Sites	(%)					
	1,441	1.23 (1.01-	1.44 (1.07-	1.38 (1.03-	1.36 (1.01-	1.40 (1.04-
Jrban Ghana	(11.1)	1.62)	1.93)	1.84)	1.83)	1.91)
	1,012	1.00	1.00	1.00	1.00	1.00 (Reference
Rural Ghana	(9.46)	(Reference)	(Reference)	(Reference)	(Reference)	
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<text> Model 1#: adjusted for age and sex; Model 2: adjusted for age, sex and education level; Model 3: adjusted for age, sex and occupational status; Model 4: adjusted for age, sex and wealth index; Model 5: adjusted for age, sex, educational level, occupational status and wealth index; Abbreviations: CI, confidence interval; ACR, albumin creatinine ratio; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; OR, odds ratio, n= total number of individuals in rural and urban Ghana; %, proportion of individuals with CKD among urban and rural Ghana.

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2 3 4	459	
5 6 7	460	Discussion
7 8 9	461	Key findings
10 11	462	Our study findings show no association between all three SES constructs and the
12 13	463	prevalence of CKD in both rural and urban Ghana except for wealth index in rural
14 15 16	464	Ghana, with the risk of CKD being higher in the wealthier populations. The higher rate
17 18	465	of CKD observed in urban Ghana could not be attributed to the higher SES of that
19 20	466	population compared to their rural counterparts.
21 22 23	467	
23 24 25	468	Discussion of key findings
26 27	469	
28 29	470	Association of SES with CKD in rural and urban Ghana
30 31	471	
32 33	472	Our study did not find any significant associations between all three SES constructs
34 35	473	and CKD among rural and urban Ghana except for wealth index in rural Ghana. The
36 37 38	474	positive association observed between wealth index in rural Ghana may be due to
39 40	475	several reasons. A comparison of the three SES constructs showed higher educational
41 42	476	level to be associated with wealth index in both rural and urban Ghana but not
43 44	477	occupational level. This seems to suggest that occupational level may not be
45 46 47	478	adequately capturing the SES status of individuals living in these settings in relation to
48 49	479	CKD. For example, Masthi et al, compared different SES scales in rural and urban
50 51	480	India and concluded that Standard of Living Index (SLI) scale was more accurate for classification
52 53 54	481	of SES in urban and rural settings ²⁵ . Our finding is consistent with other studies, ^{6 26} which
54 55 56 57	482	reported no association between SES and CKD in high-income countries and LMICs,
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but in contrast with other studies ²⁻⁴ ²⁷ that found positive associations between SES and CKD. The reasons for our current finding are unclear. However, it has been suggested that these inconsistent associations may be due to the varying pathways through which the effect of SES on health status is mediated. For example, at a given educational level marked ethnic differences have been reported. Additionally, similar differences were observed for wealth status at a given income level ²⁸⁻³⁰.

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490 Contribution of SES to observed CKD risk differences between rural and 491 urban Ghana

We observed higher rates of CKD in urban Ghana compared with rural Ghana, as expected. The observed higher rates of CKD in our study were not explained by the higher SES of that population as compared to their rural counterparts. Our results indicate that this is due to the lack of a clear difference in the SES distribution of rural and urban Ghana observed in this study, as well as to the lack of associations between SES and CKD. Consistent with our findings, in a study conducted in Northern Tanzania SES did not explain increased risk of CKD in urban Tanzania²⁶. The lack of associations between SES and CKD could probably and partly be explained by the process of epidemiological transition in relation to the "diffusion theory" of ischemic heart disease mortality. This theory attributes the commencement of ischemic heart disease to individuals in the high SES group due to their ability to afford behaviours (smoking, alcohol and sedentary lifestyles) which increased risk of ischemic heart disease. The lower SES groups were later affected partially because of improved living standards, unhealthy life style imitation and urbanization. The higher SES groups were the first to embrace behavioural changes required to decrease the risk of ischemic heart disease and this resulted in reversing the gradient ³¹. The rapid urbanization of some rural communities in the Ashanti region of Ghana and the imitation of urban lifestyle could account for our finding. Also, it could be that whereas the high SES group in urban Ghana has already embraced favourable behavioural changes, those in rural Ghana are yet to do so ³². This explains the observed association of wealth index with CKD in rural Ghana but not in urban Ghana. Also, the interplay of other less

understood or researched factors (e.g., exposure to nephrotoxins, herbal medications,
sepsis, psychosocial factors) may be influencing the pathway in which SES influences
CKD prevalence and progression.

515 Strength and limitation

Our study presents several strengths. First, we used well-standardized study protocols across rural and urban Ghana. Our study is also the first in Africa to use all three categories of CKD definition (albuminuria, reduced eGFR and CKD risk) by KDIGO 2012 in assessing association of SES with CKD in rural and urban setting, this provided more detailed information on CKD outcomes. The limitation of intra laboratory variability in earlier studies was eliminated using the same standard operating procedures in the same laboratory for running all samples for both rural and urban Ghana. The use of three constructs of SES in this study also provides a much better holistic approach to assessing SES. Also, the distribution of SES in our study reflects on the national data allowing for generalization of our findings. Our study was limited by the use of cross sectional design, which prevented us from determining causality between predictors and CKD progression. Furthermore, there were more women than men in our study due to the higher response rate in women compared with men. However, this applied to both rural and urban Ghana. We therefore do not expect this to influence our results in a significant way.

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Conclusion

All three SES constructs appear not to be associated with prevalence of CKD in urban and rural Ghana except for wealth index in rural Ghana. The observed higher prevalence of CKD in urban Ghana was not explained by the higher SES in urban Ghana. Our study seems to suggest that other non-traditional factors such as nephrotoxins, herbal medications, psychosocial stressors and misuse of over the counter drugs may play a role and underscores the need to further explore these factors.

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549 **Contributors**

50 My co-authors have all contributed substantially to this manuscript and approve of this 51 submission. Research idea and study design: DNA, CA, KS, DA, EB, KM, JA; data acquisition 52 and curation: DNA, CA, EB, KM, data analysis/interpretation: DNA, CA, KS, DA, EB, KM, LS, 53 JA, EOD, KKG, FPM, ID, JS, SB, ADA; statistical analysis: DNA, CA, KS, DNA, CA, KS, DA, 54 EB, KM, LS, JA, EOD, KKG, FPM, ID, JS, SB, ADA contributed important intellectual content 55 during manuscript drafting or revision and accepts accountability for the overall work by 56 ensuring that questions pertaining to the accuracy or integrity of any portion of the work are 57 appropriately investigated and resolved. DNA and CA take responsibility that this study has been 58 reported honestly, accurately, and transparently; that no important aspects of the study have been 59 omitted; and that any discrepancies from the study as planned have been explained.

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568 **Competing interest:** I have communicated with all my co-authors and obtained their full disclosures. My co-authors and I declare no conflicts of interest.

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0	Patient	Consent:	None	declared
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572 Ethics approval: IRBs at each participating site.

Data sharing statement: Data are available from the RODAM research cohort, a third party. Dr. Eric Beune affiliated with the RODAM research cohort and a co-author of this paper in accordance with the RODAM requirements for collaboration. Dr. Beune is the Data Collection με τ d in furth. Coordinator of RODAM and may be contacted with further questions (e.j.beune@amc.uva.nl). Additionally, researchers interested in further collaboration with RODAM may see the following URL: http://www.rod-am.eu/

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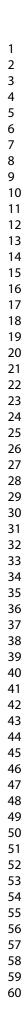
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29	707	Figure 1: Prevalence of chronic kidney disease (CKD) across level of education among urban
30	708	and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving
31 32	709	Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk,
32 33	710	or very high-risk groups.
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36	713	Figure 2: Prevalence of chronic kidney disease (CKD) across occupational status among urban
37	714	and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving
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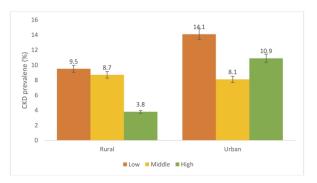


Figure 1: Prevalence of chronic kidney disease (CKD) across level of education among urban and rural participants Definitions according to 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups

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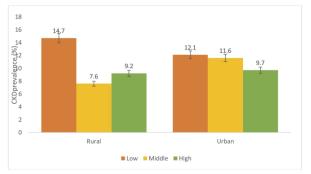
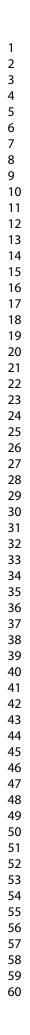


Figure 2: Prevalence of chronic kidney disease (CKD) across occupational status among urban and rural participants. Definitions according to 2012 KDIGO (kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups

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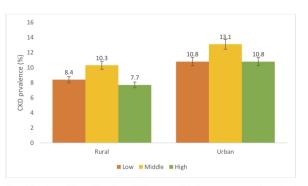


Figure 3: Prevalence of chronic kidney disease (CKD) across wealth index categories among urban and rural participants. Definitions according to 2012 KDIGO (Kidney Disease: Improving Global Outcomes) guideline. CKD was defined as being in moderately increased risk, high-risk, or very high-risk groups

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STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No.	Recommendation		Page No.	Relevant text from manuscript
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1,2		We have included a commonly used term in the title and abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2		Our study did not find any associations between SES indicators and CKD in both rural and urban Ghana after age and sex adjustment except in rural Ghana where wealth index was associated with prevalence of CKD. Consequently, the higher SES did not account for the increased rate of CKD among urban dwellers suggesting the need to identify other factors that may be driving this.
Introduction					
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4		The theoretical and scientific background as well as the rationale for conducting the study have been provided in the introduction section.
Objectives	3	State specific objectives, including any prespecified hypotheses	4		We assessed the association o SES with CKD in rural and urban Ghana and studied wha extent the higher SES of peopl- in urban areas could account fo differences in CKD between rural and urban populations
Methods					
Study design	4	Present key elements of study design early in the paper	5-6		Details given in the methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6		Rural or urban Ghana.
		1			
		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xh	ıtml		

Participants	6	 (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls 		A multi-centre cross-sectional study was conducted among Ghanaian adults (n=2492) aged 25-70 years residing in rural and urban Ghana.
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6-8	
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8	The main outcomes have been clearly defined.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8	We defined each variable of interest in the methods accordingly
Bias	9	Describe any efforts to address potential sources of bias	18	Potential sources of bias have discussed in the discussion section
Study size	10	Explain how the study size was arrived at	5	Given in the methods section and we have also referred to the RODAM study methods paper
		2		
		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xl	ntml	

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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9	Please see methods
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	8-9	Please see methods
methods		(b) Describe any methods used to examine subgroups and interactions	8-9	Please see methods
		(c) Explain how missing data were addressed	8-9	
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	NA	We have reported non-response
		Case-control study—If applicable, explain how matching of cases and controls was addressed		across sites
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling		
		strategy		
		(<u>e</u>) Describe any sensitivity analyses	NA	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially eligible, examined	5	Non-response analysis was done to
		for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		shed light on the differential response rates across sites
		(b) Give reasons for non-participation at each stage	5	response rates across sites
		(c) Consider use of a flow diagram	5	We have also referred to RODAM
				methods paper
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on	5	We have also referred to RODAM
		exposures and potential confounders		methods paper
		(b) Indicate number of participants with missing data for each variable of interest	5	We have also referred to RODAM
				methods paper
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	NA	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	NA	
		Case-control study-Report numbers in each exposure category, or summary measures of exposure	NA	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9-10	Summary measures are given in the results section and in tables and figures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	12-16	Unadjusted and adjusted estimates
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were		are given in the results section and
		included		in figures
		(b) Report category boundaries when continuous variables were categorized	12-16	We have provided mean and corresponding standard deviations for the continuous variables.
		3		
		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xł	tml	

		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	NA	
Continued on next pa	ge			
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	NA	
Discussion				
Key results	18	Summarise key results with reference to study objectives	8	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18	Key limitations regarding stud methods including differentia response rates and samplin methods in the various study site have been provided
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-18	Cautious overall interpretation o the key findings have been provided.
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18	
Other informati	on			
E	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	19	The funders had no role in stud
Funding *Give informatio		original study on which the present article is based		decision to publish, or preparatio of the manuscript
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