Chronic kidney disease among adult participants of the ELSA-Brasil cohort: association with race and socioeconomic position

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ABSTRACT

Background There is increased interest in understanding why chronic kidney disease (CKD) rates vary across races and socioeconomic groups. We investigated the distribution of estimated glomerular filtration rate (eGFR), urinary albumin–creatinine ratio (ACR) and CKD according to these factors in Brazilian adults.

Methods Using baseline data (2008–2010) of 14 636 public sector employees (35–74 years) enrolled in the Brazilian Longitudinal Study of Adult Health (ELSA)-Brasil multicentre cohort, we estimated the prevalence of CKD by sex, age, race and socioeconomic factors. CKD was defined as ACR≥30 mg/g and/or eGFR<60 mL/min/1.73 m². GFR was estimated by CKD epidemiology collaboration without correction for race. We used logistic regression to estimate the association of race and socioeconomic position (education, income, social class and occupational nature) with CKD after adjusting for sex, age and several health-related factors.

Results The prevalence of high ACR or low eGFR, in isolation and combined, increased with age, and was higher in individuals with lower socioeconomic position and among black individuals and indigenous individuals. The overall prevalence of CKD was 8.9%. After full adjustments, it was similar in men and women (OR=0.90; 95% CI 0.79 to 1.02) and increased with age (OR=1.07; 95% CI 1.06 to 1.08). Compared to white individuals, black individuals (OR=1.23; 95% CI 1.03 to 1.47), 'pardos' (OR=1.16; 95% CI 1.00 to 1.35) and Indigenous (OR=1.72; 95% CI 1.07 to 2.76) people had higher odds for CKD. Having high school (OR=1.15; 95% CI 1.00 to 1.34) or elementary education (OR=1.23; 95% CI 1.03 to 1.47) increased the odds for CKD compared to those having a university degree.

Conclusions There were marked discrepancies in the increases in reduced eGFR and high ACR with age and race. The higher prevalences of CKD in individuals with lower educational status and in non-whites were not explained by differences in health-related factors.

INTRODUCTION

Chronic kidney disease (CKD) is one of the major public health problems of the 21st century due to its high morbidity and associated mortality, elevated social and individual costs and increasing prevalence in most countries.[1–5] It is a complex and progressive disease defined by persistent kidney damage, generally marked by urinary albumin–creatinine ratio (ACR) equal or superior to 30 mg/g, or a glomerular filtration rate (GFR) lower than 60 mL/min/1.73 m².[6]

CKD affects 10–16% of the adults living in Asia, Europe, Australia and the USA,[7–10] but data on the incidence and prevalence of CKD, considering its full spectrum, in the general population of Latin America, including Brazil, are very sparse.[11] Most of the available data on the incidence and prevalence of CKD refer to estimates of people under renal replacement therapy (RRT), that is, maintenance dialysis or kidney transplants, and these figures show steady increases in recent years.[12–14] According to a review study, 1.9 million patients are undergoing RRT worldwide, with an annual initiation rate at 73 per million population (pmp).[15] Existing data indicate that the prevalence of patients under RRT in Latin America increased from 119 patients pmp in 1991 to 568 pmp in 2008, with a wide variation between countries.[16]

In Brazil, CKD is estimated to cause 4500–6000 deaths/year.[17] Between 2000 and 2012, the number of patients with CKD receiving publicly financed maintenance dialysis increased by 3.6% per year, reaching a total number of 104 433 in 2012.[18] In 2011, 31.2% of the patients under RRT were on the waiting list for renal transplant.[19] However, there is no information regarding the prevalence of early stages of CKD in Brazilian adults.

Owing to the difficulty in direct measurement, the GFR is estimated by equations that take into consideration the serum creatinine, sex, age and a correction factor for black individuals because the concentration of serum creatinine is affected by muscle mass, which is generally greater in African-Americans.[20] The most widely used equations estimated glomerular filtration rate (eGFR) are the modified diet in renal disease (MDRD) and the CKD epidemiology collaboration (CKD-EPI).[21 22] However, there is evidence that the CKD-EPI equation is better for estimating GFR and for predicting prognosis,[23 24] though the CKD-EPI proposing study developed in the USA included a limited number of elders and people of racial and ethnic minorities.[22]

In Brazil, two studies validated the CKD-EPI equation. One used the plasma clearance of Iohexol[25] as a gold standard and the other 51Cr-EDTA.[26] The first study showed that CKD-EPI was better than MDRD at detecting a

reduction in GFR, and that applying the correction term for race did not contribute to more accurate results. The second study found that CKD-EPI with race correction overestimated GFR in participants with GFR≤ 60 mL/min/1.73 m² and underestimate it in those with GFR over this value.[26]

Studies developed in several countries reported results about socioeconomic and racial/ethnic disparities in the prevalence, incidence and treatment of CKD. The data from US studies indicate that black and Hispanic individuals present worse indicators related to CKD than their white counterparts.[27 28] A survey in England found that high albuminuria, but not low eGFR, remained associated with low socioeconomic indicators, after adjustment for ethnicity, lifestyle and clinical variables (obesity, diabetes, hypertension and smoking).[29] Greater prevalence of obesity and uncontrolled hypertension and diabetes among non-white individuals are the most common reasons appointed for racial differences in ACR.[30–33] The CARDIA study found faster rates of decline in the estimated GFR among young black individuals than among their white counterparts.[30]

Social and health inequities remain important problems in Brazil, despite the improvements in access to healthcare and quality of care observed in recent years.[34] Of note, the prevalence of diabetes and hypertension is generally higher among non-white and low socioeconomic groups in the country.[35–37] These conditions may lead to the social inequality in CKD occurrence and progression, as diabetes and hypertension[38 39] are common underlying causal factors of CKD. However, very little is known regarding social and racial/skin colour differences in CKD prevalence based on GFR and/or albuminuria in Brazil. The present study describes the prevalence of CKD in adult participants of the Brazilian Longitudinal Study of Adult Health (ELSA)-Brasil cohort by means of the CKD-EPI equation and ACR level by sex, age and race/skin colour. It also estimates the association of education and race/skin colour with CKD prevalence after considering the effect of known health-related risk factors for CKD.

METHODS
Study participants
The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) is a multicentre prospective cohort study designed primarily to identify risk factors and the natural history of diabetes and cardiovascular disease (CVD). The cohort comprises 15 105 active or retired employees, 35–74 years of age at baseline (2008–2010), from universities or research institutions located in six Brazilian capitals (Belo Horizonte, Porto Alegre, Rio de Janeiro, Salvador, Sao Paulo, Vitoria). ELSA-Brasil includes volunteers (76% of the final sample) and actively recruited participants (24%), the latter being recruited from listings of civil servants. Efforts were made to recruit similar proportions of men and women, as well as predefined proportions of age groups and occupational categories. Exclusion criteria were current or recent (<4 months prior to the first interview) pregnancy, intention to quit working at the institution in the near future, severe cognitive or communication impairment, and, if retired, residence outside of a study centre's corresponding metropolitan area. The details of the study methodology, including design and eligibility criteria and the cohort's profile, have been previously described.[40 41]

The strategy to recruit civil servants was motivated to ensure a minimal dropout rate during follow-up. Since an appreciable proportion of manual and semi-skilled workers are hired as regular employees of universities and research institutions in Brazil, this permits a wide gradient of socioeconomic position across the sample.

The ethics committee of each institution approved the research protocol, and volunteers gave written consent to participate.

For the current cross-sectional analyses, we excluded participants if they were missing information for serum creatinine (n=8) or ACR (n=461). Our final analytic sample comprised 14 636 individuals (96.9% of the cohort).

Data collection
Outcome assessment
ACR was calculated from the 12 h urine samples obtained from urine albumin and creatinine concentrations[42 43] The kinetic Jaffe method (Advia 1200 Siemens, USA) was used to measure urine creatinine, and the immunochemical assay (BN II Nephelometer Siemens Dade Behring, USA) to measure urine albumin.

A 12 h fasting blood sample was drawn by venipuncture soon after the patient arrived at the baseline clinic visit.[42 43] Baseline creatinine was measured in serum specimens by the kinetic Jaffé method (Advia 1200 Siemens, USA), after applying a conversion factor derived from calibration samples traceable to isotopedilution mass[23] spectrometry.

eGFR using the CKD-EPI equation[22] was calculated as follows:

$$eGFRcreatinine = 141 \times \min(SCr/k, 1)a \times \max(SCr/k, 1)$$
$$- 1.209 \times 0.993 Age \times 1.018 \text{ [if female]}$$
$$\times 1.159 \text{ [if black]}.$$

Where SCr is serum creatinine (mg/dL), k is 0.7 if female and 0.9 if male and a is −0.329 if female and −0.411 if male, and min indicates the minimum of SCr/k or 1, and max indicates the maximum of SCr/k or 1.

On the basis of the results of the two Brazilian validation studies of the CKD-EPI equation,[25 26] we decided to apply the equation with the correction factor for race. Thus, the eGFR shown is without correction for race. Individuals with eGFR <60 mL/min/1.73 m² (yes/no) and/or ACR ≥30 mg/g (yes/no) were classified as having CKD (yes/no).

Exposure assessment
The main predictor variables were sex, age in years (continuous), self-declared skin colour/race (white, black, 'pardo', indigenous and Asian descent), formal educational level achieved (elementary, high school or university), social class of the current occupation (high, middle, low) and occupational nature of the present job (manual, not manual but routine work, not manual and not routine work). 'Pardo' in our sample reflects mainly the admixture of white individuals and black individuals.

The following health covariates were included as adjusting factors in the analysis: hypertension, diabetes, CVD, body mass index, smoking status and total/HDL (high-density lipoprotein) cholesterol. Adjustments were made by these covariates because they are associated with both CKD and the socioeconomic factors assessed as the main predictor variables.[44 45]

Hypertension (no/yes) was defined as systolic blood pressure=140 mm Hg or diastolic blood pressure =90 mm Hg or verified treatment with antihypertensive medication. Diabetes status (no/yes) was classified using blood glucose and glycated haemoglobin (A1c) measurements and self-reported information. A participant was considered to have previously diagnosed

diabetes when answering 'yes' to either "Have you been previously told by a physician that you had diabetes (sugar in the blood)?" or "Have you used medication for diabetes in the past 2 weeks?" The remaining ones were evaluated for undiagnosed diabetes based on their laboratory values and then classified as having diabetes if they reached the threshold for fasting plasma glucose (=126 mg/dL), 2 h postload plasma glucose (=200 mg/dL) or % A1c (≥6.5%). Presence of CVD (no/yes) was defined on the basis of the report of coronary revascularisation, or of a medical diagnosis of myocardial infarct and/or) and/or stroke and/or heart failure.

Obesity (no/yes) was defined by body mass index (BMI) >30 kg/m². Current cigarette smoking (no/yes) was determined by self-report during the interview. Total and HDL-cholesterol were determined by the enzymatic colorimetric method. The strategies for the collection, processing, transportation and quality control of blood and urine tests in the ELSA-Brasil cohort are described in detail elsewhere.[42 43]

Statistical analysis

First, we present the sociodemographic and health characteristics of participants of the ELSA Brasil cohort. We show the relative (%) contribution of eGFR and ACR cut-off levels to define the presence of CKD by sex and according to skin colour. Then we show the distribution of participants according to combined KDIGO6 classes based on eGFR and ACR levels.

Multivariable logistic regression analysis was used to investigate the association of each socioeconomic indicator and skin colour with the presence of CKD, before and after adjusting for age, sex and CKD common risk factors (smoking, obesity, diabetes, hypertension and total/HDL cholesterol). The magnitude of the associations was estimated by the OR and 95% CI. We retained in the full adjusted model only the variables that remained statistically associated with CKD at a level 5% (p<0.05). The analysis was run using STATA, V.12.0.

RESULTS

The mean age of 14 636 participants in this study was 52.2 (SD: 9.1) years (median=51.0 years). There was a slight predominance of female participants (54.1%); 52.4% self-declared themselves as white, 28.1% as 'pardo', 16.0% as black, 2.5% as

being of Asian descent and 1.1% as indigenous. Over half of the individuals had a university degree. Most participants were middle class and had non-manual, non-routine jobs. Prevalence of hypertension and diabetes was 35.9% and 19.8%, respectively. Most participants with hypertension (28.9%) reported a previous diagnosis of this condition, and less than half (8.8%) of those with diabetes were aware of their status. The prevalence of CVD was 4.9%, 13% smoked and 22.9% had a BMI that exceeded 30 kg/m².

According to the 2012 KDIGO criteria (figure 1), 38.3% of the participants had normal/high eGFR and normal to mildly increased ACR, whereas 52.7% of the participants had mildly decreased (G2) excretory renal function (eGFR: 60–89 mL/min/1.73 m²) with normal to mildly increased ACR (<30 mg/g). About 4.8% of the participants had a substantially reduced eGFR (<60 mL/min/1.73 m²), and 0.6% showed clinically relevant albuminuria (ACR>300 mg/g). Almost 4.0% of the participants presented with increased albuminuria with eGFR above 60 mL/min /1.73 m².

As shown in table 1, almost 9% of the participants had CKD, that is, they had a decrease in eGFR and/or an increase in albuminuria, with the overall prevalence of CKD being greater among men (10.1%) than among women (7.9%). Table 1 also shows that in comparison with participants without CKD, the prevalences of CKD, and of the percentage with high ACR or low eGFR, in isolation and combined, increased with age, were higher in less educated, poorer individuals from a low social class and who had manual or non-manual routine jobs, as CKD was also more frequent among those who smoked or presented with obesity, hypertension, diabetes or CVD at baseline. Mean total/HDL cholesterol ratio was also higher among those with CKD, high ACR and low eGFR than among those without CKD.

Table 2 shows the prevalence of CKD based on the eGFR and ACR by age group and according to sex. The increase in the prevalence of CKD with age was greatest among men in all age groups. In men, CKD prevalence increases from 3.8% among 35–44-year-olds to 31.6% among 70–74-year-olds. The increase is less steep among women, from 3.5% among the youngest group to 21.4% among the oldest one. As age increases, the contribution of eGFR to CKD increases. A marked disparity

				Persistent albuminuria categories Description and rang			
				A1	**A2**	**A3**	
				Normal to mildly increased	Moderately increased	Severely increased	
				< 30 mg/g	30-300 mg/g	> 300 mg/g	**All**
GFR stages, description and range (ml/min/1.73m²)	**G1**	Normal or high	≥ 90	5609(38.3%)	208(1.4%)	15(0.1%)	5832(39.8%)
	G2	Mildly decreased	60 - 89	7719(52.7%)	359(2.4%)	27(0.2%)	8105(55.3%)
	G3a	Mildly to moderately decreased	45 - 59	521(3.5%)	55(0.4%)	17(0.1%)	593(4.0%)
	G3b	Moderately to severely decreased	30 - 44	48 (0.3%)	19(0.1%)	14(0.1%)	81(0.6%)
	G4	Severely decreased	15 - 29	4(0.1%)	3(0.0%)	10(0.1%)	17(0.1%)
	G5	Kidney Failure	< 15	1(0.0%)	0(0.0%)	7(0.0%)	8(0.1%)
All				13902(95.0%)	644(4.4%)	90(0.6)%	14636(100.0%)

Figure 1 Percentage of ELSA participants by eGFR (CKD-EPI without correction for race) and albuminuria category—KDIGO, 2012[6] (N=14 636). CKD-EPI, chronic kidney disease epidemiology collaboration; eGFR: estimated glomerular filtration rate; ELSA, The Brazilian Longitudinal Study of Adult Health.

Table 1 Sociodemographic and health characteristics of participants of the ELSA-Brasil cohort according to the presence of CKD and criteria for CKD: 2008–2010 (N=14 636)

	CKD		Criteria for CKD		
	No	Yes	ACR≥30 alone	eGFR<60 alone	Both
Variables	N (%)	N (%)	N (%)	N (%)	N (%)
All	13 328 (91.1)	1308 (8.9)	609 (4.1)	574 (3.9)	125 (0.9)
Gender					
Male	6038 (89.9)	680 (10.1)	316 (4.7)	274 (4.1)	90 (1.3)
Female	7290 (92.1)	628 (7.9)	293 (3.7)	300 (3.8)	35 (0.4)
Age group (years)					
35–44	3090 (96.4)	116 (3.6)	93 (2.9)	20 (0.6)	3 (0.1)
45–54	5406 (94.3)	329 (5.7)	225 (3.9)	80 (1.4)	24 (0.4)
55–64	3680 (88.9)	459 (11.1)	204 (4.9)	218 (5.3)	37 (0.9)
65–74	1152 (74.0)	404 (26.0)	87 (5.6)	256 (16.5)	61 (3.9)
Race/skin colour					
White	6974 (92.1)	601 (7.9)	245 (3.2)	304 (4.0)	52 (0.7)
Black	2061 (88.9)	258 (11.1)	128 (5.5)	103 (4.4)	27 (1.2)
'Pardo'	3683 (90.8)	374 (9.2)	197 (4.8)	138 (3.4)	39 (1.0)
Asian descent	331 (91.9)	29 (8.1)	14 (3.9)	11 (3.1)	4 (1.1)
Indigenous	129 (84.3)	24 (15.7)	13 (8.5)	9 (5.9)	2 (1.3)
Educational level					
University	7136 (92.7)	565 (7.3)	229 (3.0)	291 (3.8)	45 (0.5)
High school	4614 (91.1)	450 (8.9)	253 (5.0)	160 (3.2)	37 (0.7)
Elementary	1578 (84.3)	293 (15.7)	127 (6.8)	123 (6.6)	43 (2.3)
Income (quintile)					
1—Highest	2158 (89.9)	242 (10.1)	74 (3.1)	145 (6.0)	23 (1.0)
2	3025 (92.1)	260 (7.9)	117 (3.6)	123 (3.7)	20 (0.6)
3	2761 (91.5)	258 (8.5)	122 (4.0)	107 (3.5)	29 (1.0)
4	2694 (91.7)	243 (8.3)	128 (4.4)	101 (3.4)	14 (0.5)
5—Lowest	2630 (89.8)	300 (10.2)	167 (5.7)	94 (3.2)	39 (1.3)
Social class					
High	4408 (91.8)	395 (8.2)	147 (3.1)	212 (4.4)	36 (0.7)
Middle	5532 (91.9)	487 (8.1)	257 (4.3)	196 (3.3)	34 (0.5)
Low	3174 (88.7)	404 (11.3)	194 (5.4)	160 (4.5)	50 (1.4)
Occupational nature					
Non-manual/non-routine	7030 (92.2)	598 (7.8)	246 (3.2)	304 (4.0)	48 (0.6)
Non-manual/routine	3759 (90.7)	385 (9.3)	196 (4.8)	160 (3.9)	29 (0.6)
Manual	2303 (88.7)	294 (11.3)	152 (5.8)	100 (3.8)	42 (1.6)
Current smoking					
No	11 600 (91.2)	1126 (8.8)	492 (3.8)	524 (4.1)	110 (0.9)
Yes	1727 (90.5)	182 (9.5)	117 (6.1)	50 (2.6)	15 (0.8)
Cardiovascular disease					
No	12 749 (91.7)	1148 (8.3)	548 (4.0)	495 (3.6)	105 (0.7)
Yes	560 (78.5)	153 (21.5)	57 (8.0)	76 (10.7)	20 (2.8)
Diabetes					
No	10 981 (93.5)	764 (6.5)	343 (2.9)	380 (3.2)	41 (0.4)
Yes	2346 (81.2)	544 (18.8)	266 (9.2)	194 (6.7)	84 (2.9)
Hypertension					
No	8918 (95.2)	453 (4.8)	237 (2.5)	200 (2.1)	16 (0.2)
Yes	4400 (83.8)	852 (16.2)	372 (7.1)	372 (7.1)	108 (2.0)
Obesity					
BMI <30 kg/m²	10 395 (92.1)	891 (7.9)	393 (3.5)	412 (3.7)	86 (0.7)
BMI >30 kg/m²	2928 (87.5)	417 (12.5)	216 (6.5)	162 (4.9)	39 (1.1)
Total/HDL cholesterol ratio					
Mean (SD)	3.94 (1.02)	4.17 (1.36)	4.24 (1.62)	4.05 (1.07)	4.37 (1.06)

ACR, albumin–creatinine ratio (mg/g); BMI, body mass index; CKD, chronic kidney disease; CKD-EPI, chronic kidney disease epidemiology collaboration; ELSA, The Brazilian Longitudinal Study of Adult Health; eGFR, glomerular filtration rate estimated by CKD-EPI without correction for race/skin colour black (mL/min/1.73 m²); HDL, high-density lipoprotein.

was seen between the increases in eGFR and ACR by age, the latter, in isolated form, detecting, in absolute terms, 50% more CKD in the 65–74-year-olds compared to the 35–44-year-olds.

On the other hand, isolated eGFR detected, in absolute terms, a 20-fold increase in CKD prevalence. The prevalence of isolated high ACR increased with age among men, but there was no

Table 2 Distribution of participants according to eGFR (mL/min/1.73 m^2) estimated by CKD-EPI equation and ACR (mg/g) cut-offs used to define the presence of CKD by sex and age group; ELSA Brasil, 2008–2010 (N=14 636)

		Age group (%)			
Male (n=6718)	**All**	**35–44**	**45–54**	**55–64**	**65–74**
Without CKD					
eGFR≥60 and ACR<30	89.9	96.2	93.5	88.0	69.4
With CKD (overall)	**10.1**	**3.8**	**6.5**	**12.0**	**31.6**
eGFR≥60 and ACR≥30	4.7	2.9	4.4	5.7	7.1
eGFR<60 and ACR<30	4.1	0.8	1.5	5.1	16.9
eGFR<60 and ACR≥30	1.3	0.1	0.6	1.2	6.6
		Age group (%)			
Female (n=7918)	**All**	**35–44**	**45–54**	**55–64**	**65–74**
Without CKD					
eGFR≥60 and ACR<30	92.1	96.5	94.9	89.6	78.6
With CKD (overall)	**7.9**	**3.5**	**5.1**	**10.4**	**21.4**
eGFR≥60 and ACR≥30	3.7	2.9	3.5	4.4	4.1
eGFR<60 and ACR<30	3.8	0.5	1,3	5,4	16.0
eGFR<60 and ACR≥30	0.4	0.1	0.3	0.6	1.3

Bold indicates results that are statistically significant at p<0.05.
ACR, albumin–creatinine ratio (mg/g); CKD, chronic kidney disease; CKD-EPI, CKD epidemiology collaboration; eGFR, glomerular filtration rate (mL/min/1.73 m^2) estimated by CKD-EPI without correction for race/skin colour black; ELSA, The Brazilian Longitudinal Study of Adult Health.

clear trend among women, and it was higher among older men than among women. In the age group 65–74 years, the prevalence of ACR≥30 mg/g in persons with eGFR<60 mL/min/1.73 m^2 was approximately 70% higher in men than in women.

Figure 2A–C shows the prevalence of CKD among men and women according to skin colour and the criteria used to define the presence of CKD. Among men, the prevalence of high ACR is greatest among black individuals and of low eGFR among indigenous individuals. Among women, indigenous individuals presented the highest prevalence of high ACR and of low eGFR.

The results of the unadjusted regression analysis in table 3 show that the chances of having CKD are greater among men, increase with age and are higher among participants with lower socioeconomic position for all social markers used (educational status, Income per capita, social class and occupational nature). People who reported their race/skin colour as black, 'pardo' or indigenous also have a greater chance of CKD compared to white individuals. Smoking, obesity, diabetes, hypertension and CVD were all associated with higher chances of CKD. The presence of CKD rose with increasing total/HDL cholesterol ratio.

After adjusting for age and sex (table 3), the chances of CKD did not differ by sex, but remained greater among individuals with lower socioeconomic position (all indicators) or who declared themselves as black, 'pardo' or indigenous. All the other covariates also remained statistically associated with higher chances of CKD in the same direction as the crude analysis. However, after further adjustments for the health related factors included in table 3, the associations with lower income quintile, social class and occupational nature all lost statistical significance. Having high school (p=0.05) or elementary education (p<0.01) and skin colour/race black, 'pardo' or indigenous remained independently associated with greater chances of CKD (table 3).

DISCUSSION
Using the 2012 KDIGO criteria,[6] we found that nearly 1 in every 10 adults enrolled in the ELSA-Brasil cohort has CKD. The estimated prevalence of CKD in this Brazilian cohort is closer to the ones reported in some countries,[7] [9] but lower than that found in England.[46] However, comparing the prevalence of CKD among studies is quite difficult because of differences in sociodemographic characteristics and in the equation used to estimate GFR.[47] For instance, the ELSA-Brasil cohort does not include the oldest age group (≥75 years), which has the highest prevalence of CKD, and over 50% of the cohort have a university degree, a condition associated with lower CKD prevalence, as seen in our study. Also, GFR estimated by CKD-EPI is lower than that estimated by the MDRD equation.[21] In the Whitehall study, which is also a cohort of civil servants, the prevalence of low GFR based on the CKD-EPI equation was 7.8% for men, higher than what we have found (4.6% for men) but the mean age of the Whitehall cohort is 65.5 years, while that of the ELSA cohort is 52.2 years.[48] As in most studies, we found that the prevalence was particularly high for early stages of CKD, that is, the stages represented by a mild decrease in GFR or moderate increases in ACR. Owing to the high prevalence, these early stages of CKD in adults living in different regions of Brazil are likely to play an important role in the population attributable risk for fatal and non-fatal outcomes associated with CKD, particularly CVD.[3] [49]

Our results indicate the greater contribution of ACR than of eGFR to CKD prevalence among younger individuals and of low eGFR among older participants. We also found that the contribution of ACR and eGFR to CKD differed by subgroups of gender and race/skin colour. In women, the role of ACR in defining CKD is lowest among white individuals and greatest among indigenous individuals. In men, the contribution of ACR to CKD prevalence was lowest among those of Asian descent and white individuals and highest among black individuals.

There has been some debate as to whether low eGFR and increased ACR in older people should be viewed as a disease or a natural result of the ageing process.[21] It is important to note that, regardless of the cause of the alteration in kidney damage or function, for all age groups the risk of adverse outcomes (mortality and cardiovascular outcomes) increases with CKD progression. However, the magnitude of the excess risk associated with more advanced CKD stage varies by age groups

Figure 2 (A–C)—Percentage of participants with reduced eGFR and/or elevated ACR by sex and according to race/skin colour. ELSA—Brasil, 2008–2010 (N=14 464). eGFR (given as mL/min/1.73 m^2) estimated by CKD-EPI without correction for race/skin colour black; ACR (given as mg/g). ACR, albumin-creatinin rate; CKD-EPI, chronic kidney disease epidemiology collaboration; eGFR: estimated glomerular filtration rate; ELSA, The Brazilian Longitudinal Study of Adult Health.
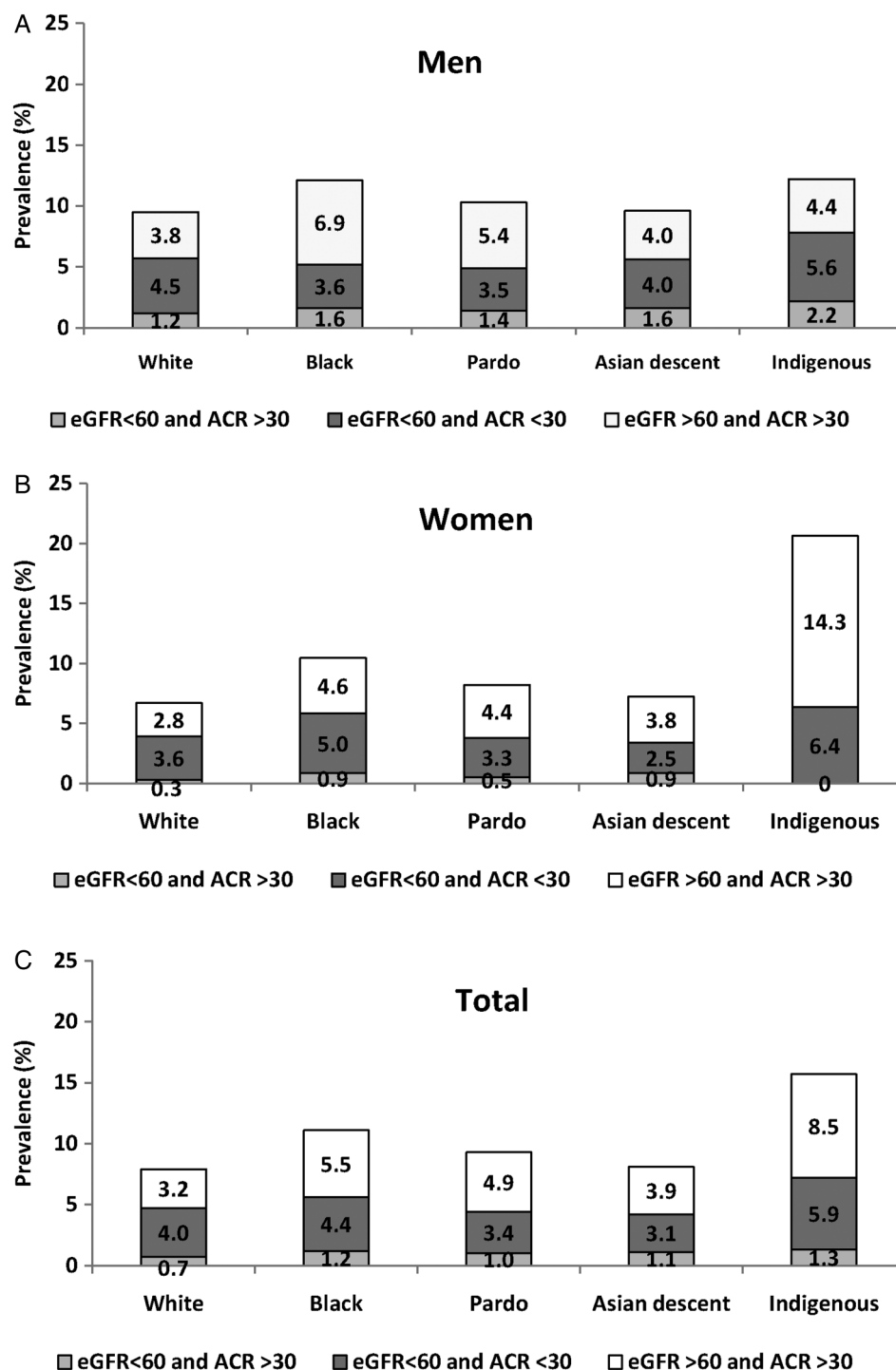
depending on the measure of association that is used, that is, rate difference or rate ratio. When relative risk is used, the increase in the magnitude of the association between lower eGFR and all-cause mortality as well as end-stage renal disease (ESRD) progression in older groups is less pronounced. In contrast, the increase in the risk differences of all-cause mortality and ESRD progression between individuals with lower and higher eGFR is more pronounced for the older than for the younger groups.

We found that the prevalence of ACR≥30 mg/g is higher for black individuals and indigenous individuals as compared to white individuals. Similar to what we have observed, the NHANES III survey in the USA found greater odds of

albuminuria for black individuals compared with white individuals.[38] Albuminuria is an important marker for the onset and progression of CKD, and for CVD.[50] Since albuminuria is a direct manifestation of kidney injury, it may be viewed as a better indicator of outcomes related to CKD than GFR when it is estimated from serum creatinine.[51] However, the combination of albuminuria with estimated GFR may improve the ability to predict ESRD onset and most likely the risk of fatal and non-fatal cardiovascular outcomes.[52 53]

The reasons for the higher prevalence of CKD in black, 'pardo' and indigenous individuals than in white individuals could not be fully explained by the sociodemographic factors and health risk factors in this study. Similar differences in the

Table 3 Factors associated with the prevalence of CKD* in participants of the ELSA Brasil cohort in the univariate, age and gender adjusted and multivariate analysis, 2008–2010 (N=14 636)

Variables	Crude OR		Adjusted age and sex		Full adjustment	
	OR	95% CI	OR₁	95% CI	OR₂	95% CI
Gender						
Male	1		1		1	
Female	**0.76**	**0.68 to 0.85**	**0.77**	**0.69 to 0.87**	0.90	0.79 to 1.02
Age in years (mean/SD)	**1.09**	**1.08 to 1.10**	**1.09**	**1.08 to 1.10**	**1.07⁺⁺**	**1.06 to 1.08**
Race/skin colour						
White	1		1		1	
Black	**1.45**	**1.24 to 1.69**	**1.69**	**1.44 to 1.98**	**1.23⁺**	**1.03 to 1.47**
'Pardo'	**1.17**	**1.03 to 1.35**	**1.40**	**1.21 to 1.60**	**1.16⁺**	**1.00 to 1.35**
Asian descent	*1.01*	*0.69 to 1.50*	0.94	0.63 to 1.40	0.90	0.59 to 1.23
Indigenous	**2.16**	**1.38 to 3.36**	**2.09**	**1.32 to 3.31**	**1.72⁺⁺**	**1.07 to 2.76**
Education						
University	1		1		1	
High school	**1.23**	**1.08 to 1.40**	**1.51**	**1.32 to 1.73**	**1.15**	**1.00 to 1.34**
Elementary	**2.34**	**2.01 to 2.73**	**1.74**	**1.49 to 2.03**	**1.23⁺**	**1.03 to 1.47**
Income per capita (quintile)						
1—Highest	1		1		1	
2	**0.76**	**0.63 to 0.92**	1.04	0.86 to 1.26	0.95	0.77 to 1.16
3	0.83	0.69 to 1.00	**1.29**	**1.06 to 1.57**	1.03	0.83 to 1.28
4	**0.80**	**0.66 to 0.96**	**1.32**	**1.08 to 1.60**	0.90	0.70 to 1.14
5—Lowest	1.01	0.85 to 1.21	**1.61**	**1.33 to 1.95**	0.98	0.76 to 1.25
Social class						
High	1		1		1	
Middle	0.98	0.85 to 1.12	**1.48**	**1.28 to 1.72**	1.03	0.83 to 1.27
Low	**1.42**	**1.22 to 1.64**	**1.57**	**1.35 to 1.83**	0.89	0.67 to 1.17
Occupational nature						
Non-manual non-routine	1		1		1	
Non-manual routine	**1.20**	**1.05 to 1.17**	**1.39**	**1.21 to 1.60**	0.99	0.81 to 1.22
Manual	**1.50**	**1.29 to 1.73**	**1.50**	**1.29 to 1.75**	1.01	0.76 to 1.35
Smoking						
No	1		1		1	
Yes	1.08	0.92 to 1.28	1.19	1.00 to 1.41	**1.21⁺**	**1.01 to 1.44**
CVD						
No	1		1		1	
Yes	**3.03**	**2.51 to 3.66**	**1.71**	**1.40 to 2.09**	**1.33⁺**	**1.08 to 1.64**
Diabetes						
No	1		1		1	
Yes	**3.33**	**2.96 to 3.75**	**2.36**	**2.09 to 2.67**	**1.79⁺⁺**	**1.57 to 2.04**
Hypertension						
No	1		1		1	
Yes	**3.81**	**3.38 to 4.29**	**2.56**	**2.26 to 2.91**	**2.02⁺⁺**	**1.77 to 2.31**
Obesity						
No	1					
Yes	**1.66**	**1.46 to 1.88**	**1.67**	**1.47 to 1.90**	**1.17⁺⁺**	**1.02 to 1.35**
Total/HDL Chol	**1.20**	**1.14 to 1.26**	**1.23**	**1.16 to 1.30**	**1.14⁺⁺**	**1.08 to 1.21**

*CKD: ACR>30 mg/g and/or eGFR<60 mL/min/1.73 m² estimated by the CKD-EPI equation without correction for race/skin colour.
+: p,0.05; ++ p<0.01.
Bold indicates results that are statistically significant at p<0.05.
OR₁: OR adjusted for age and sex; OR₂: adjusted for all the variables that remained statistically significant (gender, age, race/skin colour, education, smoking, cardiovascular disease, diabetes, hypertension, obesity, total cholesterol/HDL ratio). Income, social class and occupational nature were not kept in the multivariable model.
ACR, albumin-creatinine ratio; CKD, chronic kidney disease; CVD, cardiovascular disease; CKD-EPI, CKD epidemiology collaboration; ELSA, The Brazilian Longitudinal Study of Adult Health; HDL, high-density lipoprotein; Total/HDL Chol, total/HDL cholesterol ratio.

prevalence and incidence of CKD by race have been reported by studies carried out elsewhere.[38 39 54] In ELSA-Brasil, the overall prevalence of hypertension and of uncontrolled and resistant hypertension was greatest among black and 'pardo' individuals.[55 56] Similarly, the prevalence of obesity and diabetes was greatest among black and indigenous ELSA participants.[57] For this reason, we believe that the differences in CKD prevalence by race in ELSA-Brasil are mostly explained by health inequalities that were not captured by the adjustments made in the multivariable analysis.

Results of a Brazilian validation study did not recommend applying the correction for race in the estimation of GFR using CKD-EPI.[25] However, the small number of black individuals prevented the authors from performing a stratified

analysis by race/skin colour. The validation study in South Brazil found that CKD-EPI with race correction underestimated GFR by 12 mL/min/1.73 m^2 (SD=16) in individuals with reduced GFR (<60 mL/min/1.73 m^2) and overestimated GFR by 9 mL/min/1.73 m^2 (SD=22) in those with higher GFR. Results of this study also showed that, compared to MDRD, CKD-EPI performed worse only for black individuals when the race correction factor was applied. The authors then reanalysed the data for the set of 48 individuals of African origin without correction for race, and reported that the bias in GFR estimated by CKD-EPI was reduced in those with low GFR.[26] Moreover, the use of the CKD-EPI race correction for black South Africans led to an overestimation of measured GFR by 12 mL/min/1.73 m^2, indicating a different relationship between serum creatinine and GFR for Black South Africans than for North American and European Blacks.[58] Brazilian black individuals come from a different region of the African continent than black individuals settled in the USA.[59 60] Thus, applying the race correction factor of the CKDEPi equation to black seems unsuited to Brazilian black individuals. However, we need to investigate in a larger sample of black Brazilians whether some degree of adjustment for race is necessary to improve GFR estimates, such as those made by Asian countries.[61–63] The ELSA follow-up strategy might also help to answer this question as we will be able to trace creatinine changes with time as well as to monitor CKD-related morbidity and mortality.[64]

If our finding of greatest prevalence of CKD among black and 'pardo' individuals cannot be generalised to the Brazilian population, as is most likely, the similar distributions by race/skin colour of patients under RRT and the 2010 population census[17 18] indicate that black, 'pardo' and indigenous individuals may have less access to RRT than other skin colour groups. It is also possible that the finding of de Moura et al[18] that the proportion of black and indigenous individuals among Brazilian RRT patients is similar to that expected by population census is caused by lower survival of black and indigenous RRT patients when compared to white ones.[18] The Reasons for Geographic and Racial Differences in Stroke (REGARDS) study followed up over 2700 individuals with CKD stages 3 and 4 and found that black patients had higher mortality than white ones even after adjusting for important sociodemographic and clinical factors after 4-years follow-up.[65]

In the fully adjusted analysis, only education, among the four SE indicators considered, remained associated with higher chances of CKD in a graded fashion. After controlling for clinical and laboratorial risk factors for CKD, the magnitude of the ORs reduced and was of borderline significance for participants with "high school" as compared to those with university degree. These factors probably reflect a downward bias caused by overadjustment for potential mediators in the causal pathway between socioeconomic conditions and CKD. For instance, adverse socioeconomic status is an independent risk factor for CVDs, and CVD increases the risk of CKD. Thus, part of the association between socioeconomic status and CKD is lost when we include CVD as an adjusting factor in the association between socioeconomic indicators and CKD.[66] The same reasoning would apply to other adjusting factors, such as hypertension and diabetes.

The strength of this study is the quality of its data collection and the size and diversity of the sample studied. The various means of ascertainment permit a full accounting of the prevalence of CKD, which has not been accomplished previously in a large survey of Brazilian adults. Even though the interpretation

of association found in cross-sectional studies is often threatened by reverse causation, this is not the case for the association between race/skin colour and CKD.

Weaknesses were also identified in this study. As ELSA-Brasil was conducted in six of Brazil's state capitals, these results offer limited scope for generalisation to Brazil's overall adult population. Our sample, consisting of employees from university and research institute employees with stable employment and most with high educational achievement, is not representative of the Brazilian population. However, comparisons between the prevalence of important risk factors for CKD, such as hypertension and diabetes, indicate that they are close to the prevalence estimated from the probabilistic sample of a Brazilian telephone interview survey (VIGITEL)[41] in the same age ranges. The small number of missing data (3.1%) makes it unlikely that missing data had a relevant influence on our overall results.

Another concern is that persistence of reduced GFR and/or of high ACR is required to confirm CKD, and this might have led to non-differential misclassification of some individuals, biasing the associations towards the null. In this study, serum creatinine was measured in a single blood sample and ACR was tested in a single sample of 12 h urine collection. Our measure is thus more likely to express the true biological mean of the daily excretion of these two substances than one single morning sample.[67] Fluctuations in creatinine have been shown to have a strong influence on CKD prevalence.[68] Longitudinal data will help to confirm the findings of this study.

In conclusion, in this large cohort of Brazilians, we found that almost 1 in every 10 participants had CKD, and that CKD was especially prevalent among those with less education, as well as black or 'pardo' and indigenous individuals. The results suggest social inequalities in the prevalence of CKD and point to the need to prevent this important health problem, as Brazilians are ageing fast and the rapid increase in obesity prevalence in the country threatens the prevention and control of diabetes and hypertension, the most common CKD risk factors.

What is already known on this subject

▶ Chronic kidney disease (CKD) is a major worldwide public health problem, but data on CKD in developing countries are scarce.
▶ The numbers of patients on maintenance dialysis or kidney transplants in Latin America have increased in recent years.
▶ However, data on early stages of CKD are not available for Latin American countries.

What this study adds

▶ On the basis of the 2012 KDIGO[6] criteria for low glomerular filtration rate and high urine albumin excretion, about 1 in every 10 adults from three regions of Brazil enrolled in the Brazilian Longitudinal Study of Adult Health (ELSA)-Brasil cohort has CKD.
▶ The prevalence of CKD is higher among low educated, black, 'pardo' and indigenous individuals.
▶ The most common clinical and laboratorial risk factors for CKD did not explain social inequality in CKD prevalence.

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