

Association of Educational Attainment With Incidence of CKD in Young Adults



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Introduction: Chronic kidney disease (CKD) is greatly affected by social determinants of health. Whether low educational attainment is associated with incident CKD in young adults is unclear.

Methods: We evaluated the association of education with incident CKD in 3139 Coronary Artery Risk Development in Young Adults participants. We categorized education into low (high school and less), medium (college), and high (master's and professional studies) groups. Incident CKD was defined as new development of estimated glomerular filtration rate (eGFR) <60 ml/min per 1.73 m² or urine albumin to creatinine ratio (ACR) ≥30 mg/g. Change in eGFR over 20 years was a secondary outcome.

Results: At baseline, mean age was 35.0 ± 3.6 years, 47% were Black, and 55% were women. Participants with lower educational attainment were less likely to have high income and health insurance and to engage in a healthy lifestyle. Over 20 years, 407 participants developed CKD (13%). Compared with individuals with low educational attainment, those with medium and high educational attainment had an unadjusted hazard ratios for CKD of 0.79 (95% confidence interval [CI] 0.65–0.97) and 0.44 (95% CI, 0.30–0.63), respectively. This association was no longer significant after adjusting for income, health insurance, lifestyle, and health status. Low educational attainment was significantly associated with a change in eGFR in crude and adjusted analyses, although the association was attenuated in the multivariable models (low: –0.83 [95% CI, –0.91 to –0.75], medium: –0.80 (95% CI, –0.95 to –0.64), and high: –0.70 (95% CI, –0.89 to –0.52) ml/min per 1.73 m² per yr).

Conclusions: Health care access, lifestyle, and comorbid conditions likely help explain the association between low educational attainment and incident CKD in young adults.

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KEYWORDS: chronic kidney disease; education; educational attainment; socioeconomic status

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Chronic kidney disease (CKD) poses a major public health challenge, with a prevalence of 15% in the US population.¹ Diabetes, hypertension, and cardiovascular disease are established risk factors for

development and progression of CKD to end-stage renal disease.¹ Socioeconomic factors are also associated with kidney function decline^{2–12} and may contribute to racial disparities in kidney outcomes.^{10,11,13–16}

Educational attainment is 1 marker of socioeconomic status (SES) that influences other measures of SES, including financial resources, occupation, and social resources. Education is associated with health behaviors, access to medical care, occupation, and place of residence.^{15,17} Although education is inversely associated with most major chronic diseases,⁹ data on the relationship of educational attainment with kidney

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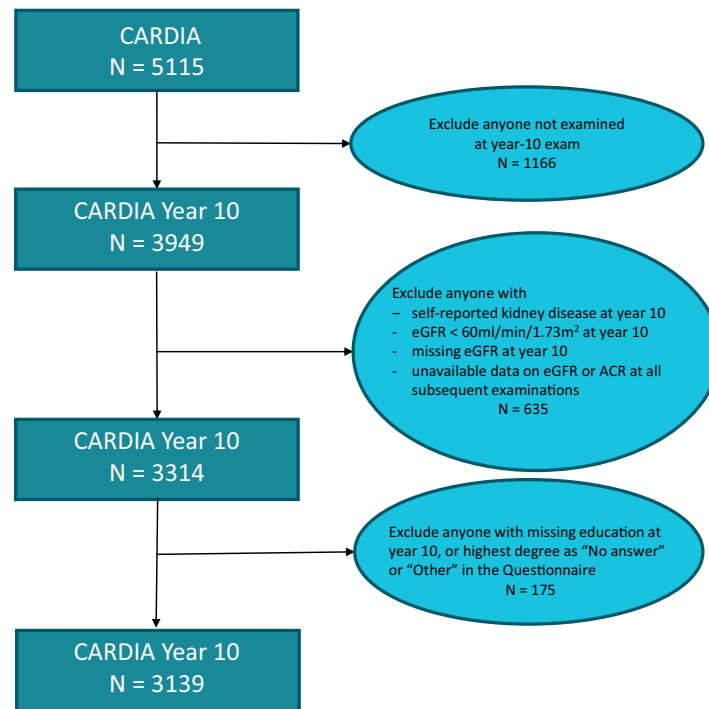


Figure 1. Study sample flowchart. From 5115 Coronary Artery Risk Development in Young Adults (CARDIA) participants, we excluded individuals with baseline chronic kidney disease or missing information, with a resulting sample size of 3139. Among those with available albumin-to-creatinine ratio (ACR) measurements at year 10 ($n = 2814$), no one had albuminuria, or $\text{ACR} > 30 \text{ mg/g}$. eGFR, estimated glomerular filtration rate.

outcomes, particularly in young adults, are scarce. Existing studies are limited by cross-sectional analyses,^{3,9} focus on CKD progression rather than onset,^{18,19} and perform evaluations in middle-aged to older populations.²⁰ The primary objective of our study was to investigate the association of educational attainment with incident CKD over 20 years in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Our secondary objective was to examine the association of educational attainment with rate of estimated glomerular filtration rate (eGFR) decline. We hypothesized that low educational attainment would be associated with higher rates of developing CKD and eGFR decline over 20 years in participants of the CARDIA study. Furthermore, we examined the contribution of health-related behaviors, comorbid conditions, and socioeconomic factors on the relationship between educational attainment and CKD.¹⁵

METHODS

The CARDIA Study

The CARDIA Study was a prospective cohort study designed to evaluate early determinants of cardiovascular disease. In 1985 and 1986, CARDIA recruited 5115 White and Black men and women aged 18–30 years from 4 sites in the United States (Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California). Patients were examined at

baseline and years 2, 5, 7, 10, 15, 20, 25, and 30. Institutional review boards approved the study, and all participants provided written informed consent.

Study Design

We chose the year 10 study visit (1995–1996) as the baseline because by this time, most participants would have completed pursuits for higher education, and because this was the first point when eGFR and albumin to creatinine ratio (ACR) values were available. Of the 5115 CARDIA participants, 3949 attended the year 10 study visit; we analyzed data from 3139 of those individuals (Figure 1). We excluded participants with self-reported kidney disease or $\text{eGFR} < 60 \text{ ml/min per } 1.73 \text{ m}^2$ at year 10 (1995–1996), unavailable data on eGFR at year 10, or missing eGFR or ACR at all subsequent examinations. Among those with available ACR measurements at year 10, none had albuminuria or $\text{ACR} > 30 \text{ mg/g}$ ($n = 2814$) (Supplementary Figure S1b). We also excluded individuals with missing education data at year 10.

Exposure, Outcomes and Covariates

The main exposure of interest was self-reported educational attainment, obtained at year 10, which was categorized into 3 levels: (i) high school and less ($n = 1433$), (ii) college (included associate's and bachelor's degrees; $n = 1252$), and (iii) master's, doctoral, or professional ($n = 454$). We chose not to have a separate group for educational attainment of less than high

Table 1. Baseline characteristics of study participants according to educational attainment, Coronary Artery Risk Development in Young Adults year 10

Baseline characteristics	Total (n = 3139)	High school or less (n = 1433)	College (n = 1252)	Master's, doctoral, or professional (n = 454)	P
Participants (%)	100	45.6	39.9	14.5	
Age, yr	35.0 ± 3.6	34.6 ± 3.7	35.1 ± 3.6	36.0 ± 3.1	<0.001
Black (%)	47.4	64.0	40.1	15.2	<0.001
Female (%)	54.9	53.2	58.1	51.5	0.01
Income (>\$34,999/yr) (%)	58.8	41.4	68.1	87.9	<0.001
Health insurance (%)	92.2	88.3	94.6	97.6	<0.001
Smoker					<0.001
Never (%)	59.8	48.0	67.7	75.4	
Former (%)	16.6	14.8	17.7	19.3	
Current (%)	23.6	37.2	14.7	5.3	
Physical activity total intensity score (exercise units)	270.0 (130.0–479.0)	247.0 (102.0–478.0)	281.0 (144.0–478.0)	304.0 (167.0–481.0)	0.0002
Body mass index, kg/m ²	27.3 ± 6.2	28.2 ± 6.7	26.7 ± 5.9	25.9 ± 5.0	<0.001
Systolic blood pressure, mm Hg	109.6 ± 12.1	111.3 ± 12.4	108.7 ± 12.0	106.6 ± 10.5	<0.001
Total cholesterol, mg/dl	177.5 ± 33.9	178.5 ± 35.1	176.5 ± 31.8	177.0 ± 35.7	0.30
Diabetes (%)	1.5	2.1	1.3	0.0	0.005
Cardiovascular disease, %	4.4	6.1	3.2	2.4	<0.001
ACR, mg/g	3.9 (2.7–5.9)	4.0 (2.8–6.3)	3.7 (2.6–5.6)	3.7 (2.6–5.4)	<0.001
eGFR, ml/min per 1.73 m ²	110.2 ± 16.0	112.5 ± 16.5	109.3 ± 15.7	105.2 ± 13.9	<0.001
eGFR 60–90 ml/min per 1.73 m ² (%)	10.5	8.3	11.3	15.2	<0.001
Angiotensin-converting enzyme inhibitors (%) ^a	0.22	0.35	0.16	0	0.44

ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate. Results are reported as proportions, means ± SD, or medians (interquartile range).
^aNo one was prescribed an angiotensin II receptor blocker.

school because there were only 127 individuals who met this criterion.

The primary outcome of interest was the incidence of CKD, defined as eGFR <60 ml/min per 1.73 m² or ACR ≥30 mg/g. We also examined the mean annualized rates of eGFR change over 20 years of follow-up as a secondary outcome. We estimated eGFR using the Chronic Kidney Disease Epidemiology Collaboration equation.²¹

We also assessed other potential CKD risk factors including demographics (age, race, and sex), lifestyle factors (smoking, physical activity, body mass index, and total cholesterol), socioeconomic factors (income [>\$34,999 or <\$34,999] and health insurance), and systolic blood pressure, diabetes, and cardiovascular disease. The physical activity score was calculated by adding a weighted sum of number of months of specific exercises.²²

Statistical Analysis

We compared year 10 (exam 5) characteristics of the study population according to education levels. Statistical significance was determined using one-way analysis of variance for continuous variables with normal distribution, Wilcoxon-Mann-Whitney tests for continuous variables with skewed distribution, and chi-square tests for categorical variables.

We applied multivariable Cox models to study the associations of education levels with risks for incident CKD. Model 1 stratified by center and adjusted for demographic factors (age, sex, and race) and measures of kidney function at baseline (eGFR and ACR). Model 2 further adjusted for socioeconomic variables including income and health insurance. Model 3 further adjusted for traditional cardiovascular risk factors (physical activity score, smoking, body mass index), and model 4 further adjusted for cardiovascular disease, total cholesterol, diabetes, and systolic blood pressure. We report hazard ratios with 95% confidence intervals (CIs); participants who had high school or less serve as the reference category. There was no violation of the proportional hazards assumption using the Schoenfeld residual for the effect of education.

We used linear mixed models to examine differences in longitudinal change in eGFR between participants who had college or less education versus a master's degree or more. All models included a random intercept for each participant and a random slope for time as a continuous variable to account for within-participant correlation. Model 1 stratified by center and adjusted for demographic factors (age, sex, and race) and CKD-specific risk factors (eGFR and ACR). Model 2 further adjusted for socioeconomic variables including income and health insurance. Model 3 further adjusted for physical activity score, smoking, and body mass index. Model 4 further

Table 2. Educational attainment and risk for incident CKD

Model	High school or less	College	Master's, doctoral, or professional	P
n	1433	1252	454	
Events, n (%)	217 (15.14)	157 (12.54)	33 (7.27)	
Events due to eGFR criterion, n (%)	30 (2.09)	24 (1.92)	6 (1.32)	
Events due to ACR criterion, n (%)	164 (11.44)	116 (9.27)	27 (5.95)	
Events due to eGFR plus ACR criterion, n (%)	23 (1.61)	17 (1.36)	0	
Unadjusted	Reference	0.79 (0.65–0.97)	0.44 (0.30–0.63)	<0.001
Model 1	Reference	0.93 (0.74–1.17)	0.54 (0.36–0.82)	0.01
Model 2	Reference	1.02 (0.81–1.29)	0.61 (0.40–0.93)	0.10
Model 3	Reference	1.11 (0.87–1.41)	0.69 (0.45–1.05)	0.37
Model 4	Reference	1.14 (0.90–1.45)	0.73 (0.47–1.12)	0.57

ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate.

Data are shown as hazard ratio (confidence interval). Median follow-up was 20 years in 3139 participants at risk. Model 1 was stratified by center, adjusted for age, sex, race, baseline estimated glomerular filtration rate, and baseline ACR. Model 2 was model 1 plus income and health insurance. Model 3 was model 2 plus physical activity score, smoking, and body mass index. Model 4 was model 3 plus cardiovascular disease, total cholesterol, diabetes, and systolic blood pressure.

adjusted for cardiovascular disease, total cholesterol, diabetes, and systolic blood pressure.

We performed a sensitivity analysis that used a more stringent definition for incident CKD, which required an eGFR of <60 ml/min per 1.73 m² or ACR of ≥30 mg/g at least twice during the follow-up. For this analysis, we had the following sample size for the exposure groups: (i) high school and less (n = 1269); (ii) college (n = 1116); and (iii) master's, doctoral, or professional (n = 407). Then, we applied multivariable Cox models to study the associations of education levels with risks for incident CKD (n = 166) with same model adjustment as in the primary analysis.

All analyses were performed using SAS statistical software (version 9.4, SAS Institute, Cary, NC, USA). All statistical tests were 2-sided; *P* < 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

The CARDIA participants included in the current study were slightly healthier, younger, and less likely to identify as Blacks compared with those who were excluded (Supplementary Table S1). Table 1 lists baseline characteristics of the study population stratified by educational attainment. Participants with lower educational attainment were younger, were more often Black, had lower income (<\$34,999), and were less likely to have health insurance than those with higher educational attainment. Participants with lower educational attainment were also more likely to be former or current smokers, engage in less physical activity, and have higher systolic blood pressure, body mass index, and total cholesterol levels and a higher prevalence of comorbid conditions including diabetes and cardiovascular disease. Individuals with lower educational attainment had higher baseline eGFR consistent with the findings of younger age in the low

educational attainment group, compared with the other 2 educational groups.

Education and Incident CKD

As shown in Table 2, a total of 407 participants (247 Blacks and 160 Whites) developed CKD over the 20-year follow-up. Supplementary Table S2 displays baseline characteristics according to the incident CKD status of participants. For 307 participants, the CKD definition was met on the basis of ACR criteria only, whereas the eGFR criteria applied only to 60 participants, and both criteria applied to 40 participants. Using high school and less (low educational attainment) as the reference, the unadjusted hazard ratio for CKD was 0.79 (95% CI, 0.65–0.97) for college (medium educational attainment) and 0.44 (95% CI, 0.30–0.63) for master's doctoral, and professional (high educational attainment). This association was attenuated after adjusting for demographics and baseline eGFR and ACR. The relationship was no longer significant once we adjusted for socioeconomic and lifestyle factors, and health status (Table 2). In the final models, only income and black race remained statistically significant predictors of incident CKD.

Education and Annualized Decline in eGFR

Supplementary Figure S1A depicts serial eGFR measurements in all participants. As can be seen from Figure 2, although individuals with low educational attainment had a higher baseline eGFR, the rate of decline inversely correlated with educational attainment. Table 3 displays the mean annualized change in eGFR stratified by educational attainment. In model 1, eGFR change was –0.84 (range, –0.92 to –0.77), –0.82 (range, –0.97 to –0.67), and –0.70 (range, –0.88 to –0.52) in the low, medium, and high education groups, respectively (*P* for trend = 0.005 across the 3 education groups). Lower educational attainment was associated with a steeper decline in eGFR, although the magnitude

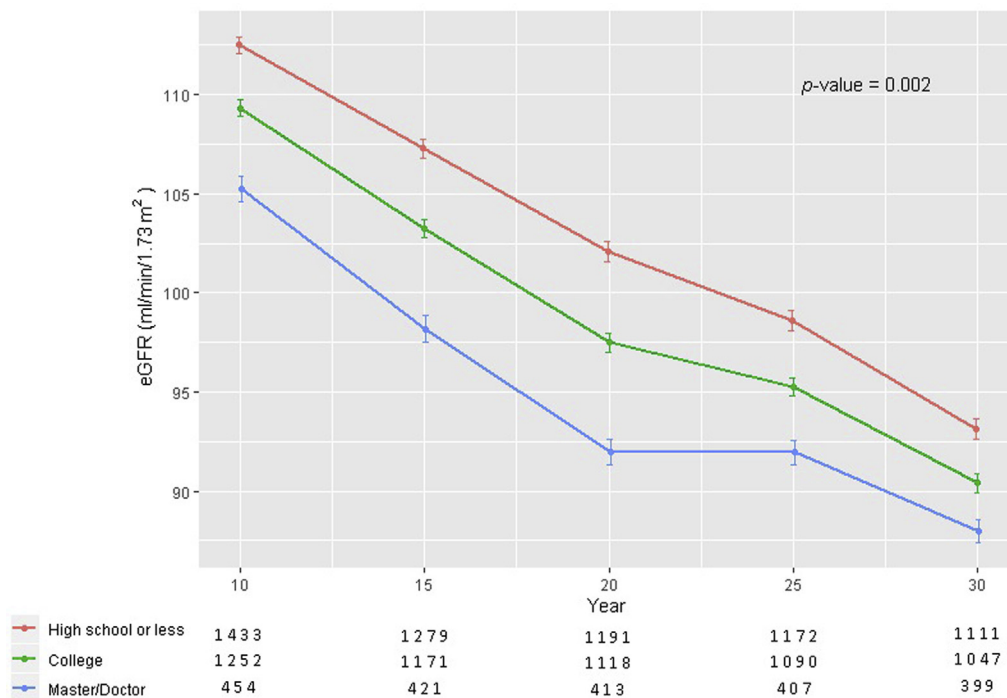


Figure 2. Serial estimated glomerular filtration rate (eGFR) values over 20 years categorized into low, medium, and high educational attainment groups. Mean annualized eGFR values for each educational group were plotted over 20 years (numerical values are given in Table 3). The slope of eGFR decline was steeper for individuals with lower educational attainment although the magnitude of difference was small.

of the difference was small. The relationship remained statistically significant with multivariable adjustment.

Sensitivity Analyses

Sensitivity analyses using a more stringent definition of incident CKD showed similar results (Table 4). Using high school and less (low educational attainment) as the reference, the unadjusted hazard ratio for CKD was 0.70 (95% CI, 0.51–0.97) for college (medium educational attainment) and 0.33 (95% CI, 0.18–0.62) for master’s, doctoral, or professional (high educational attainment). This association was attenuated after adjusting for demographics and baseline eGFR and ACR. The relationship was no longer significant once we adjusted for income, health insurance, lifestyle, and health status. In the final models, Black race remained a statistically significant predictor of incident CKD, but not income.

DISCUSSION

In a biracial cohort of 3139 healthy young adults, we examined the association between educational attainment and incident CKD. At baseline, prevalence rates of major risk factors for CKD were low, because only 1.5% had diabetes and the average systolic blood pressure was 109.6 mm Hg. Individuals with low educational attainment were more likely to have a lower SES, an unhealthy lifestyle, and a worse health status. This group of individuals also experienced a higher incidence of CKD over the course of 20 years; most met the incident CKD definition by virtue of developing albuminuria. When adjusted for socioeconomic factors, health-related behaviors, and health status, the results were no longer statistically significant. These variables are likely on the causal pathway between low educational attainment and incident CKD.

Table 3. Mean annualized change in estimated GFR according to educational attainment groups

Models (total N = 3139)	High school or less	College	Master’s, doctoral, or professional	P
Unadjusted	-0.95 (-0.99 to -0.90)	-0.92 (-1.02 to -0.81)	-0.81 (-0.94 to -0.68)	0.002
Model 1	-0.84 (-0.92 to -0.77)	-0.82 (-0.97 to -0.67)	-0.70 (-0.88 to -0.52)	0.005
Model 2	-0.85 (-0.93 to -0.77)	-0.82 (-0.98 to -0.67)	-0.70 (-0.88 to -0.52)	0.005
Model 3	-0.83 (-0.91 to -0.75)	-0.81 (-0.96 to -0.65)	-0.69 (-0.87 to -0.51)	0.007
Model 4	-0.83 (-0.91 to -0.75)	-0.80 (-0.95 to -0.64)	-0.70 (-0.89 to -0.52)	0.017

Model 1 was adjusted for center, age, sex, race, baseline estimated glomerular filtration rate, and baseline albumin to creatinine ratio. Model 2 was model 1 plus income and health insurance. Model 3 was model 2 plus physical activity score, smoking, and body mass index. Model 4 was model 3 plus cardiovascular disease, total cholesterol, diabetes, and systolic blood pressure.

Table 4. Sensitivity analysis of educational attainment and risk for incident CKD, using a stringent definition of CKD^a

Models	High School or less	College	Master/ Doctorate/Professional	P
Total N = 2792	1269	1116	407	
Events, n (%)	94 (7.41)	61 (5.47)	11 (2.70)	
Events due to eGFR criterion, n (%)	40 (3.15)	32 (2.87)	5 (1.23)	
Events due to ACR criterion, n (%)	50 (3.94)	26 (2.33)	6 (1.47)	
Events due to eGFR plus ACR criterion, n (%)	4 (0.32)	3 (0.27)	0	
Unadjusted	Reference	0.70 (0.51–0.97)	0.33 (0.18–0.62)	<0.001
Model 1	Reference	0.91 (0.66–1.27)	0.46 (0.24–0.88)	0.04
Model 2	Reference	0.98 (0.69–1.38)	0.51 (0.26–0.98)	0.12
Model 3	Reference	1.08 (0.76–1.53)	0.57 (0.29–1.11)	0.31
Model 4	Reference	1.11 (0.78–1.58)	0.63 (0.32–1.25)	0.51

ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate.

Data are shown as hazard ratio (confidence interval). Median follow-up was 20 years in 2792 participants at risk.

^aCKD was defined as eGFR <60 ml/min per 1.73 m² or ACR ≥30 mg/g at least twice during the follow-up. Model 1 was adjusted for center, age, sex, race, baseline eGFR, and baseline ACR. Model 2 was model 1 plus income and health insurance. Model 3 was model 2 plus physical activity score, smoking, and body mass index. Model 4 was model 3 plus cardiovascular disease, total cholesterol, diabetes, and systolic blood pressure.

Choi *et al.*⁹ found that educational status was inversely associated with the onset of various chronic diseases including cardiovascular disease, diabetes, and hypertension. This study also suggested that the association was explained at least partly by behavioral risk factors including illiteracy, poor nutrition, inadequate physical activity, and smoking. Our study focused specifically on CKD. The 2 other longitudinal cohort studies that examined the association between educational attainment and CKD incidence^{20,23} lost statistical significance after adjusting for lifestyle behaviors, health care access, and comorbid conditions, similar to our study. Both these cohorts were older and had high rates of hypertension and diabetes at baseline. In contrast, we examined the association of educational attainment with risk for incident CKD in a population of young adults who had a low prevalence of comorbidities that are known to increase the risk for CKD. In addition, we adjusted our data for income. Interestingly, we found that most incident CKD cases were due to the new development of albuminuria and that the eGFR decline over 20 years was modest. We interpret these findings to reflect the young age of the study population and the slowly progressive course of CKD. Nevertheless, albuminuria and modest declines in GFR within the normal range are both established predictors of declining kidney function.^{24,25}

The causal pathway linking educational status and CKD incidence is complex. Previous studies found that low educational attainment was associated with unhealthy modifiable behaviors including smoking, poor diet, and suboptimal physical activity.^{26,27} In addition, Thio *et al.*²³ performed formal mediation analyses showing that modifiable health-related behaviors partially mediate the association between educational attainment and CKD incidence in a European population. This may be because education provides psychosocial resources and empowers individuals with knowledge and decision-making capabilities which enable them to

make better lifestyle choices.^{28,29} Moreover, higher education leads to higher income, allowing people to obtain health insurance, afford copayments, and reside in neighborhoods with better access to health care.

Blacks have been shown to carry a high burden of CKD owing to a combination of genetic susceptibility from *APOL1* polymorphism and increased sociodemographic risk factors.^{30–33} In our analyses, 16.6% of Blacks versus 9.67% of Whites developed CKD over 20 years, and Black race remained a statistically significant predictor of incident CKD after adjusting for lifestyle, comorbid conditions, and access to health care. Intensive public health and research efforts are needed to overcome racial disparities in CKD, but our study suggests that targeting individuals with low educational attainment from a young age and encouraging healthy behaviors as much as possible within the constraints of available resources will help these individuals maintain their health and likely significantly decrease the risk for developing CKD. Studies suggest that education has a larger role in disease onset whereas income has a greater impact on disease progression.^{17,34}

Focusing specifically on CKD, previous work showed that individuals with lower educational attainment have a higher risk for disease progression to end-stage renal disease.^{18,19} In addition, Jardine *et al.*³⁵ found that education was an independent risk factor for CKD incidence in those diagnosed with diabetes mellitus. These studies suggest that education may enable individuals to make healthier lifestyle choices, which decreases their risk for developing CKD. Education may also help patients manage their health after being diagnosed with chronic conditions such as diabetes or CKD, and prevent further health decline. Encouraging data suggest that successful implementation of diabetes self-management intervention in a low-SES Latino population is possible.³⁶ Another study showed that in a research setting SES did not affect the efficacy of lifestyle

intervention on reducing diabetes incidence.³⁷ These findings motivate targeting individuals with low educational attainment with effective interventions in clinical practice to help decrease the risk for developing CKD.

Strengths of this study include an examination of the association between educational attainment and CKD incidence in a large number of healthy young American adults who were observed for 20 years. In addition to eGFR, we were able to incorporate urinary albumin into the definition of incident CKD. We had information on income, which enabled assessments of educational status independent of income. Whereas previous cross-sectional and longitudinal studies examining educational attainment and CKD incidence focused on a high school level of education, we examined the effect of college and professional degrees on CKD incidence.

Our study also had limitations. Because the CARDIA participants who were included were slightly healthier and younger and less likely to identify as Blacks compared with the excluded individuals, we cannot exclude the possibility of selection bias. We grouped together participants who had completed high school with those who had less than high school education owing to small sample size of the latter ($n = 127$). Although the combined creatinine and cystatin C eGFR calculation has been shown to be more accurate,³⁸ we used only the creatinine-based eGFR because information on cystatin C was available only for CARDIA years 10–20.

This study examined low education as a social determinant of health and revealed a subset of healthy young individuals who were at higher risk for developing CKD. Our results suggest that targeting modifiable factors that are correlated with low education, including access to health care, may have a favorable long-term impact on kidney health.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Supplementary File (Word)

Table S1. Characteristics of included and excluded CARDIA participants at the CARDIA study baseline visit, CARDIA year 0.

Table S2. Characteristics of study participants according to incident CKD status, CARDIA year 10.

Figure S1. Plots of (A) eGFR (mean/SD) and (B) UACR (median (IQR)) at each time point, with N displayed under time axis.

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