Life course pathways from parental education to age-related decrements in kidney function among Black and white American adults

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ABSTRACT

Objective: Using cross-sectional data on Black and white adults, this analysis examined whether age-related decrements in kidney function across adulthood were associated with parental education, and whether the association was differentially influenced by race. Further, this study assessed racial differences in life course pathways from parental education to age-related decrements in kidney function, through current SES and health-related risk factors.

Method: Data from the main survey and the Biomarker Project of the Midlife in the United States (MIDUS) Wave 2 and Refresher samples were combined, resulting in 1861 adults (54.5\% female; age 25–84, \( M_{\text{age}} = 53.37 \)) who self-identified as non-Hispanic Black (n = 326) and non-Hispanic white (n = 1535). Estimated glomerular filtration rate (eGFR) was based on serum creatinine, calculated using the CKD-EPI formula. Adults SES was based on education, income, and financial strains. Health-related risk factors included obesity, elevated blood pressure (BP), and insulin resistance. Hypotheses were tested by utilizing multiple linear regression and regression-based moderated mediation analysis.

Results: Lower parental education was associated with steeper age-related decrements in eGFR (\( B = 0.38, SE = 0.15, p = .013, 95\% CI = 0.08, 0.68 \)), due to higher eGFR among younger participants and lower eGFR among older participants. In addition, age-related decrements in kidney function were steeper among Black relative to white adults (\( B = 0.41, SE = 0.13, p < .01, 95\% CI = 0.16, 0.66 \)), driven by higher proportion of younger Black adults that met criterion for renal hyperfiltration. Furthermore, parental education and race were associated with age-related decrements in kidney function in an additive rather than interactive way. There were some racial differences in the life course pathways from parental education to age-related decrements in eGFR, glucose regulation, and hypertension. Among Black adults, lower parental education was associated with elevated eGFR among younger participants through insulin resistance. Among white adults, lower parental education was linked to higher eGFR among younger adults and lower eGFR among older adults, and the association was mediated by current SES, elevated BP, and insulin resistance.

Discussion: Early life SES can have a long-lasting influence on the preclinical renal senescence that is associated with the normal biology of aging for both Black and white adults.

1. Introduction

Early life is a critical period for kidney development with long-term implications for kidney health and functioning in adulthood (Kett and Denton, 2010). Nephrogenesis occurs primarily between 9 and 36 weeks of gestation (Rosenblum et al., 2017) and it takes up to two years for...
Kidneys to be functionally mature postnatally (Kett and Denton, 2010). Kidney programming during this period, especially through lower nephron endowment (the kidney’s functional unit), is recognized as the developmental antecedent of several chronic conditions in adulthood, including chronic kidney disease (CKD), a major public health concern in the United States and worldwide (Kett and Denton, 2010). Furthermore, abnormal programming of kidney regulation and structure in early life is associated with adverse birth outcomes, including preterm birth and low birth weight (Gurusinghe et al., 2017). Adverse birth outcomes are profoundly influenced by social factors, especially SES, making kidney function important to consider as a possible mediator on the path to adult health disparities. Parental education level, an indicator of familial SES during fetal development and childhood is linked to lower nutrient intake, higher exposure to environmental toxicants, more psychological stressors, and reduced access to high quality parental care, all factors known to increase the likelihood of adverse birth outcomes and compromises in child development (Aizer and Currie, 2014).

1.1. The multi-hit model of disparities in kidney function across adulthood

Fig. 1A illustrates the multi-hit etiological model of disparities in adult kidney functioning, which could increase the likelihood of progressing to CKD (Nahas, 2010): 1) early life programming of kidney structure and regulation, 2) age-related changes in kidney structure and functioning, and 3) occurrence of other health-related risk factors, including obesity, hypertension, and diabetes that may accelerate renal dysfunction and senescence. Specifically, exposure to a number of factors associated with being raised in lower SES families can be the first risk that increases the likelihood of exposure to a second hit later in adulthood. Lower nephron endowment at birth can contribute to a compensatory hyperfiltration in adulthood and a dysregulation of the renin-angiotensin-aldosterone system (RAAS), which has been recognized as one of the paths to hypertension in adulthood (Dotsch et al., 2012; Singh and Denton, 2015). Furthermore, low birth weight in a premature or small-for-gestational age infant that is followed by

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**Fig. 1.** (A) A life course model of risk from parental education to age-related declines in kidney function through contemporaneous adult SES and health factors. Variables in the solid boxes were included in the current analysis. (B) Unhealthy age-related profiles of kidney function across adulthood are characterized by elevated eGFR among younger adults followed by a steeper decline clearance rates that can progress to Stages 3–5 chronic kidney disease (CKD) among older adults.
catch-up growth increases the probability of obesity, metabolic syndrome, and type 2 diabetes (Desai et al., 2013). Thus, exposure to early and later risk factors can accentuate the normal kidney aging process, which increase the chance of developing CKD (Surachman et al., 2020a; Vart et al., 2015a).

Questions remain, however, regarding the specific ways that SES contributes to the known disparities in kidney health and how exposure to risk factors in childhood summate with other social factors and poor health in adulthood. The life course framework indicates that socioeconomic inequalities in early life, even small ones, may accumulate and engender greater risk in adulthood (Dannefer, 2020). The accumulation of socioeconomic (dis)advantage reflects a chain of risk associated with SES across the life course (Ben-Shlomo and Kuh, 2002). Parental education level captures early childhood SES context, as it is associated with the ability to generate and provide material and psychosocial resources associated with children’s optimal development (Evans, 2004; Ross and Mirowsky, 2011). Furthermore, lower parental education has also been linked to lower educational attainment and income among children, initiating a path to transgenerational influences (Dannefer, 2020). This transmission and funneling of risk over time has become accentuated in the United States as the avenues for upper mobility have become more limited (Chetty et al., 2014). Thus, in addition to direct effects on the kidney that may already be initiated during the prenatal period, parental education level may influence the propensity for obesity and unhealthy diets, contributing to the chance of poor kidney functioning in adulthood. In addition, kidney health and disease in adulthood have been directly linked to other health conditions, including hypertension and diabetes (Surachman et al., 2020a; Vart et al., 2015b).

1.2. Are SES disparities in kidney function across adulthood conditional on race?

There is well-established evidence of Black-white racial disparities in the three factors of the multi-hit model. First, adverse birth outcomes, especially premature births, continue to be more common among Black women (Fang et al., 1999; Gage et al., 2013). Second, there is clear evidence of racial disparities in kidney functioning across adulthood (Costello-White et al., 2015; Peralta et al., 2011). While kidney function will continuously decline in all adults (Weinstein and Anderson, 2010), longitudinal studies show faster age-related decreases in kidney function among Black relative to white adults (Peralta et al., 2011, 2013). In addition to a higher chance of developing CKD (Peralta et al., 2011), declining kidney function is associated with increased cardiovascular disease (Shlipak et al., 2009) and overall mortality (Rifkin et al., 2008). Using cross-sectional data, Costello-White et al. (2015) found racial differences in estimated glomerular filtration rate (eGFR), a proxy of kidney function, when comparing Black Americans, white Americans, and Japanese adults, which were particularly pronounced when focusing on clearance patterns in the middle-aged adults. The younger Black adults were more likely to show signs of renal hyperfiltration (RHF), which has been associated with fatty liver disease, hypertension and diabetes (Kanbay et al., 2019). Individuals with RHF tend to show earlier age-related decline in renal clearance, and a faster progression to later stages of CKD (Low et al., 2018). Third, there is well-established evidence for many other Black-white racial disparities in health-related risk factors in adulthood that contribute to the development of CKD, including obesity (Wang and Beydoun, 2007), hypertension (Musemwa and Gadegbeki, 2017), and diabetes (Gaskin et al., 2014).

The racial disparities observed between Black and white individuals in the three factors in the multi-hit model mentioned above provide support for the weathering hypothesis (Geronimus et al., 2006). According to this hypothesis, Black individuals may tend to show an earlier health deterioration due to more frequent exposures to social and environmental stressors across their life course (Geronimus et al., 2006). An earlier health deterioration among Black women is one of the main contributors to Black-white racial disparities in adverse birth outcomes (Geronimus, 1996), in addition to more limited access to high quality prenatal care. Furthermore, the high prevalence of RHF among Black adults can be viewed as part of adaptive response to early renal deterioration (e.g., nephron loss) due to hypertension, which will also activate maladaptive renal and systemic hemodynamics response, that will ultimately contribute to progressive declines in kidney function and CKD (Helal et al., 2012).

Systemic racism is a fundamental cause of the racial disparities in health between Black and white adults (Phelan and Link, 2015). There are at least two different pathways in which systemic racism creates racial disparities in health: through racial differences in SES across the life course and through racial disparities in non-SES related factors (Phelan and Link, 2015; Surachman et al., 2021). The pervasive inequality in socioeconomic opportunities due to structural barriers driven by racism continues to cause SES inequalities between Black and white individuals, including differences in educational attainment (Phelan and Link, 2015; Williams et al., 2019). However, race is not a simple proxy of SES, indicating that racial disparities in health cannot be fully explained by SES and both factors can independently influence health (Kawachi et al., 2005). There are also non-SES related factors that contribute to racial disparities in health, including discrimination and stigmatization (Phelan and Link, 2015). A study by Cobb et al. (2020) showed that daily experiences of discrimination, which are more common among Black adults, were associated with a higher risk of CKD, independent of SES. Thus, when considering the association between parental education and race on age-related decrements in kidney function, it would follow the additive (both parental education and race are independently linked to the age-related decrements in kidney function), but not necessarily an interactive pattern (i.e., the impact of parental education on kidney function appears to be conditional on race).

Finally, we anticipated that there could be Black-white differences with respect to the life course pathways from parental education to kidney functioning in adulthood. Relative to white adults, Black adults have been constrained from achieving positions that provide higher income and thereby blocked from accumulating wealth across generations, even when able to attain similar levels of education (Williams and Sternthal, 2010). Furthermore, according to the diminishing return hypothesis, even when achieving higher levels of SES, Black adults often do not enjoy the health benefits experienced by white adults do (Williams et al., 2010). Multiple studies have provided support for the diminishing return hypothesis when examining the link between SES, race, and multiple health outcomes, including inflammatory physiology (Surachman et al., 2021, 2020b) and blood pressure (Assari, 2019). However, a systematic consideration of how parental education level contributes to the influence on early rearing conditions on later kidney health among Black and white adults has not been considered previously.

1.3. The current study

In summary, the regulation and functioning of the adult kidney may be traced back to earlier life events and linked to the socioeconomic environment during childhood. Using cross-sectional data from young and older adults, this analysis tested three hypotheses related to the influence of parental education on the age-related decrements in eGFR, a marker of renal clearance, and the life course pathways from parental education to age-related decrements in adult kidney function:

**H1.** Lower parental education would be associated with less healthy profiles of kidney function, especially reflected by renal hyperfiltration in middle-aged adults (Fig. 1B).

**H2.** Both parental education and race would be associated with age-related decrements in kidney function. However, the association between parental education and age-related decrements in kidney function across adulthood may not be conditional on race.
H3. The association between parental education and age-related decrements in kidney function in adulthood would be mediated by the participant’s current SES and health-related risk factors, which include obesity, hypertension, and type 2 diabetes. However, the exact pathways could be different between Black and white adults due to well-established evidence of diminishing returns when considering the beneficial links between SES and health among Black adults.

This analysis adds to the new knowledge about the developmental origins and life course pathways contributing to the progression to kidney disease in adulthood.

2. Methods

2.1. Participants and procedures

Data from Midlife in the United States (MIDUS), a national study examining factors associated with age-related changes in health and well-being across the adult life span, were used to evaluate racial differences in the eGFR of middle-aged and older adults (Brim et al., 2019). MIDUS began in 1995–1996 (MIDUS 1) and included 7108 English-speaking adults (ages 25–74) from the continental United States, recruited through random digit dialing (RDD). Approximately a decade later (2004–2005), a longitudinal follow-up was conducted (MIDUS 2) and included 4963 longitudinal participants (70% longitudi- nal retention rate; 75% mortality-adjusted retention rate). Similar to the protocol in MIDUS 1, participants in MIDUS 2 were contacted first by phone for a baseline interview and then asked to complete self-administered questionnaires by mail (SAQs; response rate = 81%).

To increase the minority representation among MIDUS 2 partici- pants, a supplemental sample consisting mostly of Black adults was recruited from Milwaukee County, WI during 2005–2006. The Mil- waukee Oversample included 592 adults (ages 35–85; 70.7% response rate) who completed in-person baseline interviews, and the majority also completed the SAQs (SAQ response rate = 67.2%). In addition, new biomarker assessments were introduced in MIDUS 2, (Biomarker Proj- ect). Biological indicators of health were assessed including serum creatinine which provided an indicator of kidney function. The MIDUS 2 Biomarker Project (2004–2009) included 1255 participants from the national sample and Milwaukee Oversample who had completed both baseline interviews and the SAQs.

In 2011–2014, additional participants were recruited through RDD to participate in the MIDUS Refresher study (MIDUS R). The main goal was to broaden the age range, in particular to increase the number of younger participants now that the original MIDUS participants had gotten older. Recruitment was designed to reflect sociodemographic characteristics of MIDUS 1 samples (Kirsch and Ryff, 2016). MIDUS R included 3577 adults (response rate 59%; ages 25–74) who completed baseline phone interviews. Similar to MIDUS 2, participants in MIDUS R were then asked to complete SAQs by mail (response rate = 73%). With the same goal of achieving more racial diversity, an additional sample consisting mostly of Black adults was recruited from Milwaukee County, WI (MIDUS R Oversample 2012–2013). It included 508 adults (response rate = 47.7%; ages 25–64) who completed in-person interviews, and the majority also completed SAQs (58.9%). Finally, biomarkers were also assessed in MIDUS R during 2012–2016. The MIDUS R Biomarker Project included 863 participants selected from the national sample and Milwaukee Oversample of MIDUS R who completed the baseline inter- view and SAQs.

2.1.1. Biomarker assessment protocol

Participants in both MIDUS 2 and MIDUS R Biomarker Projects stayed overnight at one of the three clinical research units (CRUs) located either in Madison, WI, Washington DC, or Los Angeles, CA. The CRU site for each participant was based on the one that imposed the least travel burden. Fasted blood samples to determine serum creatinine levels were collected on the morning of the second day before partici- pants had breakfast. Blood samples were collected by trained phlebot- omists, spun in refrigerated centrifuges, and frozen sera stored in ultracold freezers until analyzed using standardized procedures (Wein- stein et al., 2018). All serum creatinine tests were conducted with a colorimetric assay in the same CLIA clinical laboratory (Unity Meriter Labs, Madison, WI).

2.1.2. Analytic sample

More detailed information on the participant selection process is presented in Supplemental Material 1. In brief, the analytic sample included participants who completed the Biomarker Projects of MIDUS 2 and MIDUS R. Out of a potential pool of 2118 participants (MIDUS 2 = 1255, MIDUS R = 863), 1930 were selected who self-identified as non-Hispanic Black (n = 369) and non-Hispanic white (n = 1561). Participants with missing information for either serum creatinine (n = 20) or parental education (n = 49) were excluded. The final sample included 1861 adults (non-Hispanic Black adults = 326, non-Hispanic white adults = 1535).

2.2. Measures

2.2.1. Parental education

Our operationalization of parental education followed a recom- mendation from Ferrarro et al. (2016). As part of the baseline interview, participants reported the highest level of formal education of their father or male household head and their mother or female household head. Educational attainment was scored on a 12-point scale (1 = no school/some grade school [1–6 years]; 6 = 1–2 years of college, no degree yet; 12 = Ph.D., Ed.D., MD etc.). If information on the father’s highest level of education level was not available, the mother’s or female household head’s highest level of education was substituted. In the cases when both father’s and mother’s education levels were available, only father’s education level was used. Parental education was then categor- ized as a binary variable: no high school/GED degree (coded as 0) and graduated from high school/GED or higher (coded as 1).

2.2.2. Current socioeconomic status

Current SES was a composite score (0–10) based on five indicators (Surachman et al., 2020a): (1) participant’s educational attainment (graduated from high school/GED = 0, some college = 1, bachelor’s degree or higher = 2); (2) household size-adjusted household income-to-poverty ratio (<150% = 0; ≥150%, <300% = 1; >300% = 2); (3) perception of current financial status (low = 0; medium = 1; high = 2); (4) perception of the availability of sufficient money to meet needs (not enough = 0; enough = 1; more money = 2); and (5) perception of hardship with respect to paying bills (difficult = 0; not very difficult = 1; not at all difficult = 2).

2.2.3. Health-related risk factors

Health-related risk factors included several indicators associated with worse kidney function. These factors included: 1) obesity (BMI ≥ 30 kg/m² = 1, otherwise coded as 0); 2) hypertension (systolic and diastolic BP ≥ 140/90 or self-report of diagnosis of hypertension by physician = 1, otherwise coded as 0); and 3) insulin resistance (HbA1c ≥ 6.5% or fasting blood glucose ≥ 126 mg/dl or self-reported diagnosis of type 2 diabetes by a physician = 1, otherwise coded as 0).

2.2.4. Age

Participants reported their birth dates during the Biomarker Project. Thus, each participant’s age (years) was based on age at the time of blood sample collection.

2.2.5. Kidney function

Estimated glomerular filtration rate (eGFR) was calculated from serum creatinine using the CKD-EPI formula (Levey and Stevens, 2010).
The CKD-EPI formula takes age, gender, and race into consideration when calculating eGFR. Serum creatinine was assayed from overnight fasted blood collected during the Biomarker Project using Roche Cobas Analyzer (Unity Meriter Lab, Madison, WI). The assay range was 0.06–30.5 mg/dL, with an inter-assay coefficient of variation of 2.08% across the 2 phases of MIDUS.

2.2.6. Covariates

As indicated by Bolignano et al. (2014), sex is an important factor to consider when evaluating the aging kidney. We included sex (0 = female, 1 = male) as a covariate in the analysis. In addition, study wave (0 = MIDUS Refresher, 1 = MIDUS 2) was also included as a covariate in the analysis.

2.3. Statistical analysis

Multiple linear regression and regression-based moderated mediation analyses were utilized to examine the main hypotheses. eGFR was first regressed on age. The inverse association between age and eGFR indicative of the normal age-related decrement in eGFR was characterized by higher eGFR among younger participants and a lower eGFR in older participants. To examine the potential influence of parental education, parental education as a binary variable (HS/High School/higher) and the seven indirect associations through current SES and each of the health-related risk factors (see Supplementary Material 2 for details). The moderated mediation model simultaneously tested the interaction of parental education on age-related decrements in eGFR was controlled for gender and 2 MIDUS phases (MIDUS 2 = 1, MIDUS Refresher = 0). A significant interaction between age and parental education would indicate that age-related decrements in eGFR were influenced by parental education. Further, the possibility of a three-way interaction between age, parental education, and race was tested (Model 2). A significant three-way interaction would indicate that the influence of parental education on age-related decrements in eGFR was conditional on race. To examine possible mediation by current SES and health-related risk factors, we included current SES (score) and each of the health-related risk factors (as a binary variable) and their interactions with age into the model (Model 3).

Regression-based moderated mediation analysis was utilized to examine life course pathways from parental education to the age-related decrements in eGFR among Black and white participants. Detailed information regarding the Regression-based moderated mediation analysis is provided in Supplementary Material 2. In brief, eGFR was regressed on age (standardized), parental education (as a binary variable), current SES (standardized), and the 3 health-related risk factors (as binary variables). In addition, the modeling considered if age was moderating the prediction of eGFR by parental education, current SES, and each of the health-related risk factors (see Supplementary Material 2 for details). The moderated mediation model simultaneously tested the direct association of parental education with age-related decrements in eGFR and the seven indirect associations through current SES and each health-related risk factors (see Supplementary Material 2 for details). Age conditional direct and indirect effects were tested in three different age categories, younger (mean age –1 SD), middle (mean age), and older (mean age +1 SD). Significance of the indirect effects was tested using bootstrapping procedures. Unstandardized indirect effects were computed for each of 10,000 bootstrapped samples, and the 95% confidence intervals were computed by determining the indirect effects at the 2.5th and 97.5th percentiles. The moderated mediation analysis was conducted separately for Black and white participants using Mplus version 8.1.

3. Results

Table 1 provides descriptive summary on the sociodemographic and health characteristics of the participants. Black participants were younger, more likely to have parents without a high school degree, less likely to have attended college, and reported being in a lower SES category currently. A higher percent of the Black participants had a larger BMI indicative of obesity, and had high blood pressure, and/or met criteria for type 2 diabetes compared to their white counterparts. Finally, Black adults had significantly a higher mean eGFR level (M = 101.8 mL/min/1.73 m², SD = 23.4) when compared to white participants (M = 88.7, SD = 17.1). The difference in mean eGFR was driven by the higher values in younger adults, which were indicative of renal hyperfiltration (Fig. 2A). In addition, younger participants raised by families with lower parental education had a significantly higher mean eGFR compared to younger participants who reported childhood backgrounds in families with higher parental education (Fig. 2B). Zero-order correlations between variable of interests (across all participants and within each racial group) are presented in Supplementary Material 3.

3.1. Parental education and age-related decrements in eGFR

Multiple linear regression analysis was used to examine whether parental education was associated with age-related differences eGFR. Age was negatively associated with eGFR, indicating a declining age pattern in creatinine clearance across adulthood (B = –0.84, SE = 0.03, p < .001, CI = –0.90, –0.78). The mean eGFR decreased by 0.84 mL/min/1.73 m² per year. Controlling for gender and the two MIDUS phases, there was a significant interaction between participant age and parental education when evaluating the eGFR of all participants (Table 2; Model 1; B = 0.24, SE = 0.07, p < .001, CI = 0.12,0.37). The inverse age-eGFR association between age and eGFR among participants with lower parental education was significantly steeper when compared to participants raised by families with a higher parental educational attainment (Fig. 2C). Among younger adults, lower parental education was associated with a slightly higher eGFR relative to those who reported higher parental education. Conversely, among older adults.

<table>
<thead>
<tr>
<th>Age, M (SD)</th>
<th>Black adults</th>
<th>White adults</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50, n (%)</td>
<td>167 (51.2)</td>
<td>577 (37.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>50-64, n (%)</td>
<td>131 (40.2)</td>
<td>605 (39.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥65, n (%)</td>
<td>28 (8.6)</td>
<td>353 (23.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>223 (68.4)</td>
<td>791 (51.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Parents without high school degree, n (%)</td>
<td>153 (46.9)</td>
<td>467 (30.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Current SES, score, M (SD)</td>
<td>3.65</td>
<td>6.25</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Participants without college education, n (%)</td>
<td>123 (37.7)</td>
<td>297 (19.3)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Note: a Significant difference between Black and white participants. Significance of mean age, mean current SES, and mean eGFR based on t-tests. Other comparisons were based on Chi-square tests. b eGFR < 60 mL/min/1.73 m² is one of the clinical criterions for compromised renal clearance and an indicator of Stage 3 CKD when low. c eGFR > 120 mL/min/1.73 m² is commonly used as an indicator of renal hyperfiltration. eGFR = estimated glomerular filtration rate; MIDUS = Midlife in the United States.
adults, lower parental education tended to be associated with a lower eGFR.

3.2. Parental education, race, and age-related decrements in eGFR

The interaction between age and parental education remained significant after adding race and the interaction between race and age into
Table 2
Summary from linear regression analysis predicting eGFR among Black (n = 326) and white (n = 1535) adults.

<table>
<thead>
<tr>
<th>Model 1: Parental education and age-related decrement in eGFR</th>
<th>Model 2: Parental education, race, and age-related decrement in eGFR</th>
<th>Model 3: Full Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>93.92 (1.23)**</td>
<td>98.70 (1.60)**</td>
</tr>
<tr>
<td>95% CI</td>
<td>91.53, 96.32</td>
<td>95.57, 101.84</td>
</tr>
<tr>
<td>Age (centered)</td>
<td>-1.02 (0.05)</td>
<td>-1.29 (0.11)**</td>
</tr>
<tr>
<td>95% CI</td>
<td>-1.23, -0.92</td>
<td>-1.51, -1.07</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.28 (0.74)</td>
<td>0.43 (0.72)</td>
</tr>
<tr>
<td>95% CI</td>
<td>-1.73, 1.17</td>
<td>-0.99, 1.85</td>
</tr>
<tr>
<td>Study wave</td>
<td>-0.61 (0.76)</td>
<td>-1.09 (0.75)</td>
</tr>
<tr>
<td>95% CI</td>
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<td>-2.55, 0.37</td>
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<tr>
<td>Parental educ. (no HS = 0, HS/higher = 1)</td>
<td>-2.42 (0.82)</td>
<td>0.99 (1.87)</td>
</tr>
<tr>
<td>95% CI</td>
<td>-4.03, -0.82</td>
<td>-2.68, 4.67</td>
</tr>
<tr>
<td>Age + Parental education</td>
<td>0.24 (0.07)</td>
<td>0.38 (0.15)*</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.12, 0.37</td>
<td>0.08, 0.68</td>
</tr>
<tr>
<td>Race (Black = 0, white = 1)</td>
<td>-6.88 (1.48)**</td>
<td>-9.78, -3.98</td>
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<tr>
<td>95% CI</td>
<td>-9.17, -4.60</td>
<td>1.73 (1.90)</td>
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<tr>
<td>Age + Race</td>
<td>0.41 (0.13)*</td>
<td>0.16, 0.66</td>
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<tr>
<td>95% CI</td>
<td>0.22, 0.59</td>
<td>-0.02, 0.59</td>
</tr>
<tr>
<td>Three-way interaction</td>
<td>Race + Parental education</td>
<td>-2.30 (2.09)</td>
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<tr>
<td></td>
<td>95% CI</td>
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</tr>
<tr>
<td></td>
<td>-0.22 (0.17)</td>
<td>-0.55, 0.12</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>-0.12, 0.52</td>
</tr>
<tr>
<td></td>
<td>0.03 (0.01)*</td>
<td>-0.26 (0.15)</td>
</tr>
<tr>
<td>Obesity (0, no, 1 = yes)</td>
<td>0.43 (0.77)</td>
<td>1.08, 1.95</td>
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<tr>
<td>95% CI</td>
<td>-0.02 (0.06)</td>
<td>-0.14, 0.11</td>
</tr>
<tr>
<td>Age * Obesity</td>
<td>-1.83 (0.80)</td>
<td>-3.40, -0.26</td>
</tr>
<tr>
<td>95% CI</td>
<td>-4.13 (0.36)</td>
<td>-0.25, 0.01</td>
</tr>
<tr>
<td>Elevated BP (0 = No, 1 = yes)</td>
<td>2.85 (1.03)*</td>
<td>0.84, 4.87</td>
</tr>
<tr>
<td>95% CI</td>
<td>-0.30 (0.08)</td>
<td>-0.47, -0.14</td>
</tr>
<tr>
<td>Insulin resistance (0 = No, 1 = yes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age * Insulin resistance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R²</td>
<td>170.02</td>
<td>110.33</td>
</tr>
<tr>
<td>Adjusted R²</td>
<td>0.31</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Note:
- * p < .05
- ** p < .01
- *** p < .001.

Similarly, meeting criteria for type 2 diabetes was associated with a larger difference in eGFR between younger and older adults (Table 2, Model 3; B = -0.30, SE = 0.08, p < .001, 95% CI = -0.47, -0.14).

3.3. Life course pathways from lower parental education to unhealthy profiles in kidney function among Black and white adults

A regression-based moderated mediation analysis was conducted to examine the pathways from parental education level during childhood to the renal clearance patterns seen in middle-aged and older adult life. The analysis was conducted separately for each racial group.

3.3.1. Life course pathways among Black adults

Results from the moderated mediation analysis for the Black group are presented in Fig. 3A. Lower parental education was associated with the likelihood of hypertension among the black participants (B = -0.23, SE = 0.05, p < .001) as well as glucoregulatory indices of insulin resistance (B = -0.17, SE = 0.05, p < .01). In turn, insulin resistance was associated with a larger difference in eGFR between the younger and older adults (B = -7.11, SE = 2.74, p = .010). The indirect effect analysis indicated the mediation through insulin resistance was driven primarily by the significant effect and higher eGFR among younger adults (B = -2.03, SE = 1.03, p = .04), and was not evident among older participants (B = 0.44, SE = 0.58, p > .05). Thus, the pathway from parental education and familial conditions during childhood did not appear to be mediated by the current SES of the participants as parental education level was not associated with current SES among the Black participants (B = 0.13, SE = 0.11, p > .24).

3.3.2. Life course pathways among white adults

The moderated mediation analysis for the white participants is presented in Fig. 4A. Lower parental education during childhood was associated with a higher eGFR among white participants (B = 0.38, SE = 0.15, p < .01, 95% CI = 0.08, 0.68). Further, the interaction between age and race on eGFR was statistically significant (Table 2, Model 2; B = 0.41, SE = 0.13, p < .01, 95% CI = 0.16, 0.66). The age-related decrement in eGFR among Black participants was significantly steeper compared to white participants (Fig. 2D). The eGFR of the younger Black adults was elevated relative to similarly aged white adults. However, the eGFR of the older Black participants did not differ from the older white participants. This pattern indicated that the steeper slope of the age-related differences among Black relative to white adults was driven primarily by the higher eGFR values of the younger Black adults. Closer examination indicated there were 117 participants who met the RHF criteria of an eGFR > 120 mL/min/1.73 m². The majority (n = 101, 86.3%) were younger than 50 years. The proportion of Black participants who met RHF criteria (n = 85; 72.6%) was significantly higher than that of white participants (n = 32; 27.4%). Finally, among both Black and white participants who met the criteria of RHF, the majority in both races were younger than 50 years (81.2% among Black adults, 100% among white adults).

The three-way interaction for age, race, and parental education did not attain statistical significance (Table 2, Model 2; B = -0.22, SE = -0.17, p = .20, 95% CI = -0.55, 0.12). This suggested that the differences in age-related differences in eGFR related to parental education were not conditional on race (Fig. 2E). As hypothesized, the association between parental education, race, and parental education followed the additive pattern, rather than the interactive pattern. After adding current SES, the 3 health-related risk factors (obesity, hypertension, and insulin resistance), and their interactions with age, the interaction between age and parental education was reduced to non-significance (Table 2, Model 3; B = 0.29, SE = 0.16, p = .07, 95% CI = -0.02, 0.59). This suggests that the link between parental education and age-related differences in eGFR may be mediated by current SES and overall health. Lower SES in adulthood was also indicative of a steeper age-related difference in eGFR between younger and older adults (Table 2, Model 3; B = 0.03, SE = 0.01, p = .03, 95% CI = 0.01, 0.05).
associated with lower current SES ($B = 0.30$, $SE = 0.06$, $p < .001$). Further, low parental education was also associated with a likelihood of being overweight in adulthood ($B = -0.08$, $SE = 0.03$, $p = .004$), being hypertensive ($B = -0.16$, $SE = 0.03$, $p < .001$), and meeting criteria for type 2 diabetes ($B = -0.06$, $SE = 0.02$, $p = .005$). Current SES was also associated with obesity ($B = -0.07$, $SE = 0.01$, $p < .001$), hypertension ($B = -0.03$, $SE = 0.01$, $p = .036$), and insulin resistance ($B = -0.04$, $SE = 0.01$, $p < .001$). The unhealthy patterns of high BP ($B = -1.77$, $SE = 0.84$, $p = .035$) and insulin resistance ($B = -2.77$, $SE = 1.36$, $p = .041$) linked with the age-related changes in eGFR. Thus, among white adults, the pathways to kidney health appeared to reflect both the connection between childhood and adult SES as well as the general association between low SES and overall poor health. The indirect effect analysis indicated that both the social and obesity-related physiological pathways were statistically significant in younger and older adults. Among white participants, the higher eGFR among younger adults and lower eGFR among older adults resulted in the appearance of stronger influence of age, with a steeper decline.

4. Discussion

Using cross-sectional information on eGFR values of middle-age and older Black and white Americans, this analysis has shown that parental educational attainment, a proxy of early life SES, is associated with age-related decrements in renal clearance. While it was already known that early life conditions, especially prenatal events such as gestational age at delivery, are part of a critical period for kidney development (Kett and Denton, 2010), it appears that economic and social disadvantage may also contribute to kidney health in adulthood. Further, this analysis examined the life course pathways from parental education to age-related decrements in eGFR, which proved to be differentially manifest in Black and white Americans. Several notable racial differences in the life course pathways from parental education to the age-associated pattern of renal senescence were evident after considering current SES and relevant health-related risk factors, including obesity, hypertension and type 2 diabetes.

4.1. Age-related decrements in kidney function

Numerous clinical nephrology studies have characterized the process of renal senescence that occurs in most adults, including the age-related decrease in the size of the kidney, especially in the cortical region, the changes in the structure of the glomeruli which may become sclerotic, and the decrease in filtration rates, altering the concentrations of proteins and other soluble analytes in both urine and circulation (Hommos et al., 2017). Among the MIDUS participants, age-related decrement in eGFR averaged 0.84 mL/min/1.73 m$^2$ per year, consistent with the previous estimations of an annual decline fall of 0.40 and 1.07 mL/min/1.73 m$^2$ (Baba et al., 2015; Wetzels et al., 2007). However, there are also important differences in these age-associated renal profiles across racial groups, and the potential for social disparities in general health to affect the emergence and pace of kidney aging. Many
of the younger Black participants had high eGFR values, which may be indicative of a renal hyperfiltration that can result in wear-and-tear on the glomeruli and increase the likelihood of a later progression to CKD. The high eGFR in the younger Black participants resulted in a larger difference when compared to the older Black participants, and the appearance of a steeper slope of decline. A similar pattern was evident in some of the younger white participants but more evident in the context of obesity, hypertension, and type 2 diabetes. The co-occurrence of poor renal health and elevated blood pressure, as well as the adverse effects of diabetes on the kidneys is well known to nephrologists.

Across both Black and white adults, the current analysis also replicated many previous reports of an age-related decline in renal clearance, which can be tracked by measuring the levels of creatinine in serum and urine, as well as by quantifying other proteins and analytes, including albumin and cystatin (Costello-White et al., 2015; Peralta et al., 2011, 2013). Similar to the findings by Costello-White et al. (2015), we found there appeared to be a larger difference in the eGFR of younger and older Black adults suggested when compared to the age-related differences in the white participants. This racial difference was driven primarily by the higher eGFR in the younger Black adults, which can tax and damage sensitive aspects of the glomeruli. However, not all studies have confirmed that RHF can be used as a single indicator of risk. Using longitudinal data, RHF among Black adults was not found to be significantly associated with a higher likelihood of CKD (Chaiken et al., 1998). However, we did find that a higher percentage of the younger Black adults had a high eGFR that would meet the criteria for RHF when compared to the white adults. In younger adults, RHF was also more likely to be associated with obesity, high BP, and high HA1c levels indicative of type 2 diabetes (Low et al., 2018; Magee et al., 2009; Melsom et al., 2011; Oh et al., 2020; Palatini, 2012). Our modeling suggests that RHF is one of the indicators of risk in mid-adulthood, and consistent with the multifactorial etiology of renal senescence.
4.2. Parental education and age-related decrements in kidney function

The novelty of our findings is the demonstration that social factors, including familial context during childhood, can act through these pathways to impact kidney physiology in adulthood. Specifically, lower educational attainment of parents was associated with a larger age-related difference in eGFR, due to the higher eGFR values among younger participants and the lower clearance of the older participants. The conclusion that social and economic disadvantage can have a long-term impact on adult health is not new, but it has been more common to focus on other physiological systems, especially related to cardiovascular disease. In addition, the research has emphasized the importance of adult SES to a greater degree (Varti et al., 2016b). Our findings indicate that parental education level can serve as a proxy for social advantage and disadvantage during childhood, and it appeared to affect the eGFR in both Black and white adults. Furthermore, this analysis corroborates previous studies showing that SES and race linked to health can act in an additive rather than an interactive one (Kawachi et al., 2005). We showed that there were distinct pathways from parental education to age-related decrements in kidney function among Black and white adults.

Our analysis also conveys the value of considering a life course perspective. Societal constraints on upper mobility can result in there being a connection between childhood SES and the economic and social success of adulthood. In our analyses, we also observed a correlation between the participants’ reporting of the education level of their parents and their own current SES, albeit more evident among the white participants. Our statistical modeling was able to discern independent and additive contributions of both childhood SES and current standing to the measures of kidney health in the MIDUS participants. It should also be mentioned that at the time when the older MIDUS participants were children, there would been even more prominent social constraints on the opportunities available to most Black participants due to discrimination and institutional racial barriers that would limit access to educational and occupational advancement. Thus, it may not be surprising that the dual influence of childhood SES and adult SES was evinced differently among the Black and white participants.

It should also be acknowledged that there may have been an additional influence of prenatal factors, including delivery-related outcomes, that were not assessed in the MIDUS project. A number of studies have shown that prematurity and low birth weight can have a pervasive influence on the early life programming of the kidney, with effects on the nephron endowment (Brophy et al., 2018; Kett and Denton, 2010; Singh and Denton, 2015; Tiniakos et al., 2004; Wintour et al., 2003). Unfortunately, the occurrence of premature birth is still significantly more common among Black women, and provides another example of the early etiology of health disparities. The inter-generational continuity of these relationships is also evident in the fact that both gestational diabetes and gestational hypertension continue to be among the primary causes of premature birth. Our analyses confirmed the important associations between kidney health, hypertension and diabetes. It is important to better understand the factors that mediate the health effects of social and economic disadvantage.

One unanticipated finding was the absence of a significant association between parental education and current SES among Black participants, while it was strongly evident among white adults. This difference suggests that for Black participants, having parents with higher education does not guarantee a path to higher levels of adult SES. The finding is consistent with a previous analysis by Davis (1994) on the lack of intergenerational transmission of educational attainment among Black American men. Some possible contributors include the common incarceration of American Black men (Hagan and Foster, 2012) and the changes in family structures over time (Song, 2016). A more recent study, however, found that intergenerational educational mobility among younger cohort of Black adults was increasing (Bloome and Western, 2011). Despite the evidence for increasing educational mobility, however, income mobility among Black adults was declining (Bloome and Western, 2011). There is a well-documented evidence that educational attainment is not always perfectly correlated with income, wealth, and other indicators of SES among Black adults. For example, Black adults tend to earn a lower income and are more likely to be unemployed when compared to their white adult counterparts who have the same level of education (Williams and Sternthal, 2010). It is also possible that some aspects of our findings are unique to the Black participants in our study given that our Black sample was recruited mostly from Milwaukee County, WI. In addition, in contrast to white participants, current SES was not associated with any of the measured health-related risk factors. Other studies have found what seem to be similar discrepancy, when considering race (Surachman et al., 2021, 2020b), providing further support for the diminishing return hypothesis (Williams et al., 2010). Achieving a higher level of SES does not necessarily ensure better health among Black adults in the same way that it is manifest among white adults. In contrast, parental education during childhood was directly associated with health-related risk factors among Black adults, especially with elevated BP and insulin resistance. In turn, insulin resistance was associated with the age-related patterns in kidney function. Taken together, these findings provide a novel perspective on of the importance of early life SES in the context of kidney functioning and the mediation of good and poor health in adulthood.

The current study has multiple strengths. First, this study included participants from a wide age range enabling us to generate robust estimates of age-related differences in kidney function. Second, the extensive biological and clinical information from MIDUS Biomarker Projects allowed us to include multiple health-related risk factors in the analysis. Thus, our findings on the association among parental education, race, and age-related differences in kidney function across adulthood were generated from a substantive dataset. Finally, the MIDUS study also included detailed information on current SES, incorporating both objective (e.g., income and education) and subjective measures (e.g., subjective social status and financial strain). However, it should also be acknowledged that this analysis does have some limitations. First, the unavailability of longitudinal biological information in the MIDUS study precluded a prospective analysis. However, the cross-sectional examination of age-related differences still provided a unique opportunity to examine the link between social factors across the life course and kidney function. With the availability of the longitudinal biological information in the MIDUS study in the future, it will be possible to prospectively address these questions. It should also be acknowledged that parental education was based on retrospective reports and this could introduce some bias, even though a previous analysis indicated a high level of accuracy in terms of retrospective reports of parental education from a small subset of sibling participants in MIDUS (Ward, 2011). Finally, the indicator of kidney function was based on serum creatinine, which is sensitive to both diet and muscle mass. In addition, we utilized the CKD-EPI formula to calculate eGFR, which is currently under scrutiny because it incorporates a race adjustment into the formula (Diao et al., 2021). However, we conducted sensitivity analysis by excluding the race adjustment from the formula and still had similar findings. Lastly, the majority of the Black participants was recruited from Milwaukee County, which could limit the generalizability of the findings to other regions. Despite this limitation, our additional analyses indicated that Black adults in Wisconsin are comparable to the larger US Black population in terms the key sociodemographic variables (see Supplementary Material 4). Future studies should prioritize replicating the current findings by utilizing representative Black adult from different regions of the US, including the Southern states, which often have poorer health overall.

4.3. Conclusion

These analyses demonstrated that familial SES can have a long-
lasting influence on the preclinical renal senescence that is associated with the normal biology of aging. Lower parental education and race were independently associated with unhealthy kidney functioning in adulthood, a risk factor for the development of CKD. Furthermore, there were distinct life course pathways from parental education to kidney functioning in adulthood among Black and white adults. Among younger Black adults, lower parental education was associated with elevated kidney function, an indication of renal hyperfiltration, through insulin resistance. Among white adults, lower parental education, through current SES, elevated BP, and insulin resistance, was associated with elevated kidney function among younger adults and lower kidney function among older adults. A better understanding of the effect of parental educational attainment on adult filtration rates may help us to achieve more insights into the etiology of health disparities and the inter-generational perpetuation of risk.

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Declaration of Competing Interest
None.

Appendix A. Supporting information
Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2021.105291.

References


