Association of Fitness With Racial Differences in Chronic Kidney Disease

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Introduction: Non-white minorities are at higher risk for chronic kidney disease than non-Hispanic whites. Better cardiorespiratory fitness is associated with slower declines in estimated glomerular filtration rate and a lower incidence of chronic kidney disease. Little is known regarding associations of fitness with racial disparities in chronic kidney disease.

Methods: A prospective cohort of 3,842 young adults without chronic kidney disease completed a maximal treadmill test at baseline in 1985−1986. Chronic kidney disease status was defined as estimated glomerular filtration rate of <60 mL/min/1.73 m^2 during 10-, 15-, 20-, 25-, and 30-year follow-up assessments (through 2006). Analyses were completed in 2019. Multivariable Cox models were used to determine hazard ratios and 95% CI for incidence of chronic kidney disease. Multivariable models included race, gender, age, field center, education, baseline estimated glomerular filtration rate, and time-varying covariates of healthy diet index, smoking status, alcohol intake, BMI, systolic blood pressure, and fasting glucose. Percent attenuation quantified the association of fitness to racial disparities in chronic kidney disease.

Results: Chronic kidney disease incidence was higher among blacks (*n*=83/1,941, 1.61 per 1,000 person years) than whites (43/1,901, 0.82 per 1,000 person years). Every 1-minute shorter treadmill duration was associated with 1.14 (95% CI=1.04, 1.25) times higher risk of chronic kidney disease. Blacks were 1.72 (95% CI=1.13, 2.63) times more likely to develop chronic kidney disease compared with whites. The risk was reduced to 1.54 (95% CI=1.01, 2.39) with fitness added. This suggests that fitness is associated with 20.4% (95% CI=5.8, 43.0%) of the excess risk of chronic kidney disease attributable to race.

Conclusions: Low fitness is a modifiable factor that may contribute to the racial disparity in chronic kidney disease.
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INTRODUCTION

Chronic kidney disease (CKD) is an independent contributor to end-stage renal disease, cardiovascular disease morbidity, and mortality.[1−3] With a prevalence estimate of 13% in the U.S. population,[4] preventing and treating CKD in early stages to stop progression to end-stage renal disease is particularly important. Racial and ethnic minorities have a higher risk for CKD.[5,6] Although a proportion of the elevated risk of CKD may be attributable to genetic differences (i.e., apolipoprotein L1 [APOL1]),[7] a large proportion may be explained by the higher burden of hypertension and diabetes.[8,9] Adults who maintain higher levels of physical activity and fitness are less likely to develop hypertension and diabetes compared with less active and less fit individuals.[10−13] By extension, epidemiologic and exercise trial research demonstrates that higher fitness is associated with reduced risk of rapid decline in estimated glomerular filtration rate (eGFR), proteinuria, and CKD incidence.[14−17]

Fitness is an independent predictor for all-cause and disease-specific mortality across race/ethnic groups.[18,19] Prior investigations described lower levels of physical activity and poorer fitness among blacks compared with whites.[20−22] The present study determines the associations of low fitness with racial disparities in CKD incidence. The hypothesis is that lower fitness among blacks partially explains the higher rates of CKD in black versus white adults.

METHODS

Study Sample

The Coronary Artery Risk Development in Young Adults (CARDIA) cohort study recruited 5,115 black and white young adults in 1985−1986 from four areas of the U.S. (Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California). CARDIA recruited a balanced cohort across race, age, gender, and educational attainment.[23] Participants have undergone in-person examinations at baseline and years 2, 5, 7, 10, 15, 20, 25, and 30. Retention rates among surviving participants at exams were 91%, 86%, 81%, 79%, 74%, 72%, 72%, and 71%, respectively. Appendix Figure 1 (available online) provides a flow chart of sample selection. After applying exclusions for having CKD at baseline; missing fitness, CKD, or covariate data at baseline; and no follow-up visit documenting CKD status, there were 3,842 participants. All participants provided written informed consent. IRB approvals were received from each field center institution.

Measures

The primary exposure was cardiorespiratory fitness measured at baseline with a maximal graded exercise treadmill test. The test used a modified Balke protocol consisting of 2-minute stages (maximum 18 minutes) of progressively increasing speed and grade. Stage 1 was 3.0 miles per hour at 2% grade (4.1 METs),

progressing to Stage 9 at 5.6 miles per hour at 25% grade (19.0 METs). A previous publication further details the conversion formula from treadmill duration to METs.[24] The test was terminated for the following reasons: volitional fatigue (84.1%); shortness of breath (7.4%); refusal to continue (1.4%); abnormal electrocardiogram, blood pressure, or chest pain (1.5%); medical reason (4.7%); or completion of protocol (0.3%).

The primary outcome was incident CKD, defined as an eGFR of <60 mL/minute/1.73 m^2 during any follow-up assessment at years 10, 15, 20, 25, and 30. The CKD−Epidemiology Collaboration equation estimated GFR[25] from fasting serum creatinine measurements available at years 0, 10, 15, 20, 25, and 30, measured by nephelometry according to National Institute of Standards and Technology standards.[26]

Years 10−30 examinations included a collection of urine albumin and creatinine using a single, untimed spot urine sample. The nephelometric procedure assessed albumin and the Jaffe method measured creatinine. Urine albumin creatinine ratio (UACR) was calculated following previous calculations used in CARDIA accounting for racial and gender differences in creatinine excretion.[27]

Age, race, gender, and education were queried during clinic visits. An interviewer-administered diet history questionnaire collected alcohol intake as average mL/day. Diet was quantified based on the Healthy Eating Index using data collected from CARDIA's comprehensive food frequency questionnaire.[28] Smoking history classified participants as current, former, or never smokers. Body weight and height measured with light clothing to the nearest 0.09 kg and 0.5 cm, respectively, was used to calculate BMI (kg/m^2). Fasting glucose was measured using standard laboratory techniques. Three blood pressure measurements were taken by trained staff and the mean of the last two measurements was calculated.

Statistical Analysis

All analyses were conducted in 2018−2019 using SAS statistical software, version 9.4. Chi-square tests and *t*-tests compared baseline categorical and continuous variables, respectively. Fitness, quantified as treadmill test duration, by race and gender was compared as a continuous variable and as a categorical variable. Within this sample, groups were created as low fitness (lowest gender-specific quintile), moderate fitness (Quintiles 2−3), and high fitness (upper Quintiles 4−5), as has been done previously to emphasize the group at highest risk (<20th percentile).[29,30]

Extended Cox regression models using PROC PHREG examined the association of baseline fitness with incident CKD. Extended Cox models allow for a more robust model by accounting for covariates at each timepoint rather than using static baseline variables.[31] The primary exposure, fitness, was assessed both as a continuous variable (per 1 minute lower treadmill duration) and a categorical variable comparing low versus high (reference), low versus moderate (reference), and moderate versus high (reference). Participants who did not develop CKD by their last available exam were censored. Incidence of CKD was confirmed at 5-year intervals. Therefore, knowledge of event occurrence is between two successive visits rather than the exact date. The discrete model option handled time to event ties. The discrete-time method better accounts for interval censored data at non-continuous treat times.[32]

Model 1 included baseline fitness only; Model 2 added demographics (race, gender, age, maximum education, and field center); Model 3 added time-varying lifestyle factors (diet, smoking, and alcohol); Model 4 added time-varying cardiometabolic risk factors (BMI, systolic blood pressure, and fasting glucose). Model 5 added baseline eGFR. The proportional hazards assumption was not violated in a model restricted to baseline values for all exposures. Multiple imputation using SAS PROC MIanalyze handled missing covariate data.[33] All variables were included in the imputation methods. A range of 0%−2.4% of covariate data were missing for variables during each follow-up exam except diet, with 11% missing at the year 20 exam. Ten replication data sets imputed the values for the 6.0% total missing data points. Sensitivity analyses comparing before and after incorporating multiple imputation into the extended Cox models showed stable estimates. Given no significant interactions by gender or race X fitness using multiplicative interaction terms, results were pooled for the entire sample.

Testing the hypothesis that baseline fitness was associated with racial disparities in CKD incorporated two different strategies, percentage attenuation and population attributable fraction (PAF). Percentage attenuation quantified the reduction in the effect estimate associated with race in a multivariable model including all established confounders (Model 1) when adding fitness (Model 2). The percentage excess risk explained used the following formula: $100 \times (\beta_{Model\,1} - \beta_{Model\,2})/(\beta_{Model\,1})$, where β=log(hazard ratio [HR])[34] and 95% CIs using bootstrap methods with 1,000 re-samplings.

PAF quantifies the proportion of cases of incident CKD that could be prevented if all participants moved from low fitness to moderate or high fitness. The formula for PAF is as follows: $P_d\,(HR_{adj} - 1)/HR_{adj} \times 100\%$, where P_d is the proportion of low fitness individuals among cases, and HR_{adj} is the RR of incident CKD in the fully adjusted model.[35,36] Race-specific extended Cox regression analysis determined the HR for the association between fitness and incident CKD.

The definition of CKD as eGFR <60 mL/min/1.73 m^2 was selected as the primary outcome because it allowed for the longest follow-up and largest sample size possible in the CARDIA study. To test the robustness of the association, secondary analysis added albuminuria to the CKD definition using extended Cox regression models, with incident CKD defined as low eGFR <60 mL/minute/1.73 m^2 or UACR >30 mg/g at years 15, 20, 25, and 30 follow-up. This analysis included 2,714 participants with measured UACR and did not have albuminuria at year 10, the first visit with UACR available.

Moderate to vigorous physical activity (MVPA) was added (with and without fitness included) to the Cox regression models. MVPA was assessed with a questionnaire asking about frequency of participation in sports and exercise during the past 12 months.[37] No associations were found between self-reported MVPA and incident CKD and are therefore not included in the final results. Models were also tested quantifying cardiometabolic covariates using categorical definitions for obesity,[38] diabetes,[39] and Stage 1 and Stage 2 hypertension,[40] and did not impact the results. Variants in the gene encoding APOL1 were also considered. Renal risk variants in APOL1 are associated with a more rapid decline in eGFR in blacks.[7] A sensitivity analysis included a Cox regression model adding APOL1 as a dichotomous variable (two copies of the gene variant versus zero or one copy) in the fully adjusted model.[41]

RESULTS

Table 1 provides baseline characteristics for the total sample and across fitness categories. Participants' mean age was 24.8 (SD=3.6) years, 50.5% (*n*=1,941) were black, and 53.5% (*n*=2,055) were women. Participants in the low fitness group had lower educational attainment and higher measures of BMI, blood pressure, and fasting glucose. Mean eGFR for the total sample was 97 (SD=17) mL/min/1.73 m^2 at baseline and the median UACR was 3.9 mg/g (IQR, 2.7−5.9 mg/g) at year 10.

The prevalence of being in the low fitness group was 31.7% for black women vs 7.4% for white women (*p*<0.001) and 24.5% for black men vs 12.0% for white men (*p*<0.001; Figure 1). Appendix Figure 1 (available online) displays the unadjusted and adjusted treadmill durations, of which blacks had significantly shorter durations than whites (*p* < 0.001).

Average time from baseline to end of surveillance was 27.9 years. During 102,685 person years of follow-up, 4.5% of blacks and 2.3% of whites developed CKD (blacks: *n*=83, 1.61 [95% CI=0.82, 3.13] cases per 1,000 person years; whites: *n*=43, 0.81 [95% CI=0.61, 1.10] cases per 1,000 person years). During follow-up, those who developed CKD had declines in eGFR by an average of 51.4 (SD=27.3) mL/min/1.73 m^2 between year 10 and year 30 (99.1 [SD=22.2] at year 10 to 48.4 [SD=18.1] mL/min/1.73 m^2 at year 30). The mean eGFR decreased by an average of 17.6 (SD=14.4) mL/min/1.73 m^2 for those without CKD (111.0 [SD=15.7] at year 10 to 93.0 [SD=14.5] mL/min/1.73 m^2 at year 30).

Table 2 shows the extended Cox regression models for incident CKD. Each 1-minute lower treadmill duration was associated with a 1.14 times higher incidence of CKD (HR=1.14, 95% CI=1.04, 1.25) in the fully adjusted model. Participants in the low fitness group were 2.44 (95% CI=1.42, 4.20) times more likely compared with the high fitness group and 1.83 (95% CI=1.19, 2.85) times more likely compared with the moderate fitness group to have incident CKD after adjusting for all covariates. Appendix Table 1 (available online) provides a summary of Cox models in the subset (*n*=2,714) with measured UACR available. When adding albuminuria to the incident CKD definition, the associations remained similar.

In supplementary analysis (*n*=3,433), including APOL1 as a covariate, blacks who carried two gene variants, had 2.14 (95% CI=1.23, 3.74) times higher risk of incident CKD versus individuals with zero or one gene variant. Fitness test duration remained significantly associated with incident CKD when APOL1 was added to the final model (HR=1.14, 95% CI=1.04, 1.25).

Table 1. Baseline Characteristics for Total Sample and by Fitness Groups

Characteristics	Total	Low fitness[a]	Moderate fitness[b]	High fitness[c]
n	3,842	736	1,564	1,542
Age, years, M±SD	24.8±3.6	25.4±3.6	24.6±3.7	24.9±3.5
Black race, *n* (%)	1,941 (50.5)	553 (75.1)	893 (57.1)	495 (32.1)
Gender, woman, *n* (%)	2,055 (53.5)	414 (56.3)	814 (52.1)	827 (53.6)
Education attainment, years, M±SD	15.5±3.0	14.6±4.0	15.2±2.6	16.2±2.6
Smoking, *n* (%)				
Never	2,252 (58.6)	380 (51.6)	888 (56.8)	984 (63.8)
Former	497 (12.9)	80 (10.9)	184 (11.8)	233 (15.1)
Current	1,093 (28.5)	276 (37.5)	492 (31.5)	325 (21.1)
Alcohol intake, mL/d, M±SD	11.7±21.1	11.6±24.0	12.0±22.1	11.4±18.5
Healthy Diet Index score, M±SD	44.7±2.7	40.6±11.1	42.3±11.7	48.5±13.2
BMI, M±SD	24.4±4.8	29.1±6.7	24.3±3.9	22.3±2.6
SBP (mmHg), M±SD	110±11	113±11	110±10	109±11
DBP (mmHg), M±SD	69±9	70±10	68±9	68±9
Fasting glucose (mg/dL), M±SD	82.3±13.0	83.4±13.4	82.7±16.1	81.4±8.4
Maximal treadmill duration, minutes, M±SD				
Women	8.3±2.3	5.2±1.0	7.6±0.6	10.5±1.4
Men	11.8±2.3	8.3±1.4	11.2±0.7	13.9±1.1
Maximal treadmill METs, M±SD				
Women	11.0±2.1	8.2±1.0	10.4±0.7	13.1±1.3
Men	14.2±2.1	11.0±1.3	13.7±0.8	16.2±0.9
eGFR, CKD-EPI equation (mL/minute/1.73 m^2), M±SD	97.0±16.8	99.4±17.5	98.2±17.3	94.6±15.7
UACR (mg/g) at year 10 (*n*=2,714), median (IQR), *n*	3.9 (2.7, 5.9)	4.3 (2.9, 7.0), 577	3.8 (2.7, 5.8), 1,026	3.7 (2.6, 5.5), 1,111
APOL1 (*n*=3,433), high-risk,[d] *n* (%)	217 (6.3)	66 (10.0)	106 (7.6)	45 (3.3)

Note: Values for categorical variables are given as *n* (%); values for continuous variables are given as M±SD or median (IQR).
[a]Low fitness: bottom lowest gender-specific quintile (bottom 20%).
[b]Moderate fitness: quintiles 2−3 (middle 20%−60%).
[c]High fitness: quintiles 4−5 (top >60%).
[d]High-risk category for APOL1 are individuals with two copies of the gene variant.
APOL1, apolipoprotein L1; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; UACR, urine albumin creatinine ratio.

Black race was significantly associated with incident CKD (HR=1.72, 95% CI=1.13, 2.63). Adding fitness duration to the model attenuated the HR to 1.54 (95% CI=1.01, 2.39), resulting in fitness associated with 20.4% (95% CI=5.8%, 43.0%) of the excess risk of incident CKD attributable to race. In race-specific extended Cox regression analysis, 22.5% and 10.8% of incident CKD was attributable to low fitness in blacks and whites, respectively (Table 3).

DISCUSSION

In this population-based sample of young adults followed for up to 30 years, low fitness may be associated with the higher rates of incident CKD in blacks versus whites. The relationship of low fitness with the development of risk factors for CKD, such as hypertension and diabetes, is well established. This study adds to the literature by demonstrating that even after accounting for these intermediate factors, low fitness itself is associated with CKD. The findings also expand upon prior research, finding that the proportion of CKD associated with low fitness was twofold greater in blacks versus whites.

The results are consistent with two epidemiologic studies on fitness and incident CKD. Among 5,812 male Veterans, every 1 MET higher maximal treadmill test resulted a lower risk of CKD (HR=0.72, 95% CI=0.75, 0.82).[14] The Cooper Center Longitudinal Study of 17,979 men and women fitness per 1 MET increment was associated with an HR of 0.94 (95% CI=0.89, 0.99) for incident CKD.[17] In these studies, as with the current, the low fitness group had a significantly higher risk for CKD compared with both the moderate and high fitness groups. This provides evidence for the robustness of the negative impact of low fitness on CKD. Even modest improvements in fitness or avoidance of very low fitness may have a meaningful impact on incident CKD.[42−46] MVPA and fitness can help prevent the occurrence or
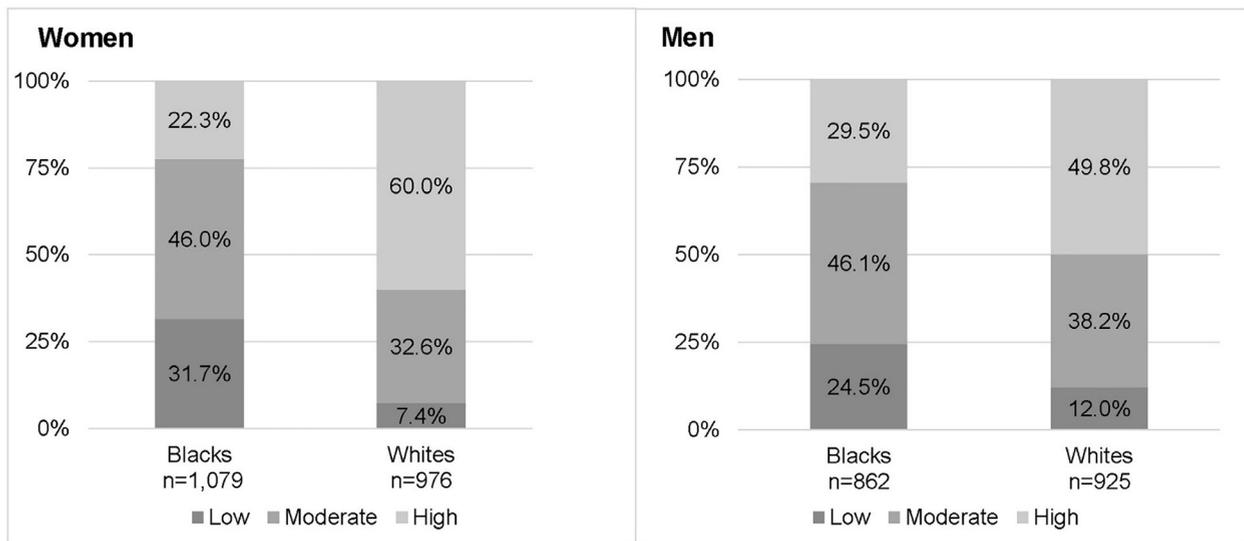
Figure 1. Distribution of low, moderate, and high fitness by race in women and men.
Note: Low fitness: bottom lowest gender-specific quintile (bottom 20%); moderate fitness: quintiles 2—3 (middle 20%—60%); high fitness: quintiles 4—5 (upper >60%). *p*<0.01 for difference in fitness group proportions by race for both women and men.

progression of CKD through counteracting metabolic and cardiovascular risk factors and maintaining muscle mass and function.[10–13] The Kidney Disease Improving Global Outcomes clinical practice guidelines recommends regular MVPA in patients with CKD to improve exercise capacity, reduce cardiovascular risk, and improve health-related quality of life.[47]

Blacks were nearly two times more likely to develop CKD compared with whites, consistent with previous studies from CARDIA and other cohorts.[5,6,48] Fitness explained 20% of the excess risk in blacks versus whites.

Additionally, the proportion of CKD attributable to low fitness was estimated as twofold greater in blacks versus whites (PAF: 22.5% versus 10.8%). A National Health and Nutrition Examination Survey study looked at collective lifestyle factors, finding that smoking, BMI, alcohol, and MVPA explained 23.7% of the excess prevalence of CKD among blacks.[49] Another study among the National Health and Nutrition Examination Survey cohort found that 20% of the excess prevalence of CKD among low-SES adults was explained by a combination of smoking, alcohol intake, sedentary time, diet,

Table 2. Associations of Baseline Fitness With Incident CKD in Full Sample and Fitness Groups

Association of fitness	Model 1,[a] HR (95% CI)	Model 2,[b] HR (95% CI)	Model 3,[c] HR (95% CI)	Model 4,[d] HR (95% CI)	Model 5,[e] HR (95% CI)
Duration with CKD					
Fitness per 1 minute lower duration	**1.13 (1.06, 1.21)**	**1.17 (1.07, 1.27)**	**1.16 (1.06, 1.26)**	**1.14 (1.04, 1.25)**	**1.14 (1.04, 1.25)**
Groups with CKD					
Low[f] vs high fitness (ref)	**3.76 (2.38, 5.94)**	**2.70 (1.65, 4.40)**	**2.57 (1.56, 4.24)**	**2.42 (1.40, 4.10)**	**2.44 (1.42, 4.20)**
Low vs moderate[g] fitness (ref)	**2.35 (1.56, 3.53)**	**1.98 (1.31, 3.00)**	**1.93 (1.27, 2.93)**	**1.83 (1.18, 2.83)**	**1.83 (1.19, 2.85)**
Moderate vs high[h] fitness (ref)	**1.60 (1.02, 2.52)**	1.37 (0.86, 2.18)	1.33 (0.83, 2.13)	1.32 (0.82, 2.10)	1.34 (0.83, 2.13)

Note: Boldface indicates statistical significance (*p*<0.05).
[a]Model 1: Unadjusted.
[b]Model 2: Model 1 + gender, race, age, maximal education throughout study, and field center.
[c]Model 3: Model 2 + time varying healthy eating index score, smoking status, alcohol intake.
[d]Model 4: Model 3 + time varying BMI, systolic blood pressure, and fasting glucose.
[e]Model 5: Model 4+ baseline eGFR.
[f]Low fitness: bottom lowest gender-specific quintile (bottom 20%).
[g]Moderate fitness: quintiles 2—3 (middle 20%—60%).
[h]High fitness: quintiles 4—5 (top >60%).
CKD, chronic kidney disease (eGFR <60 mL/min/1.73 m^2); HR, hazard ratio.

Table 3. Attributable Fraction of Fitness to CKD by Race and Total Sample

| Variable | Prevalence of low fitness in full population | | Prevalence of low fitness in people eventually developing CKD (P_d) | | Adjusted HR for low vs moderate/high fit, HR[b] (95% CI) | PAF[c] (%) |
	Low fit[a]/total, *n*	%	Low fit events/ total events, *n*	%		
Blacks	553/1,941	28.5	38/82	46.3	1.94 (1.20, 3.16)	22.5
Whites	183/1,901	9.6	9/43	20.9	2.07 (0.89, 4.83)	10.8
Overall	736/3,842	19.2	47/125	37.6	2.00 (1.31, 3.04)	18.9

[a]Low fit: bottom lowest gender-specific quintile (bottom 20%).
[b]HR adjusted for baseline gender, age, field center, maximal education throughout study, time varying healthy diet index, smoking status, alcohol intake, BMI, systolic BP, and fasting glucose, and baseline eGFR.
[c]PAF=(P_d [HR_{adj}−1])/HR_{adj} × 100%, Where P_d is the proportion of inactive people among cases, and HR_{adj} is the HR of CKD, comparing low to moderate/high fitness, adjusted for confounding factors.
CKD, chronic kidney disease (eGFR <60 mL/min/1.73m^2); eGFR, estimated glomerular filtration rate; HR, hazard ratio; PAF, population attributable fraction.

and MVPA.[50] This study also analyzed MVPA separately and found that MVPA contributed to a greater degree (8%) among the blacks-only analysis versus the entire pooled sample (4% of the effect).

These studies included the behavior of MVPA, whereas cardiorespiratory fitness is a physiological measure, partially explained by MVPA, as well as genetics, environmental, and physiologic factors.[51] MVPA can have measurement error resulting in smaller effect estimates compared with its physiologic trait of fitness. This has been shown in prior studies of which fitness has a stronger magnitude of association with cardiovascular morbidity and mortality compared with self-reported MVPA.[52−54] This may also explain the absence of significant associations of MVPA with incident CKD in the sensitivity analyses.

Additional contributors to the racial disparity in CKD include clinical factors, such as higher prevalence and severity of diabetes and hypertension, and social determinants like education, healthcare access, and neighborhood conditions.[48,55] The present study found an independent association of fitness with CKD incidence after adjustment for other factors. The relationship of fitness with race may also have indirect associations through these contributors. Social determinants of health, including lack of safe places to exercise, limited time, and psychosocial stressors, can interfere with the ability to maintain fitness-enhancing activity.[55] Recent research has demonstrated that blacks may have a lower magnitude of improvement in fitness responses from formal exercise interventions.[56,57] Therefore, it may be more difficult to improve fitness levels in blacks versus whites, which could play a role in the contributions of fitness to race disparities in CKD.

Fitness can indirectly impact CKD by way of established associations with obesity, hypertension, and diabetes.[44,58−60] The extended Cox models accounted for time-updated risk factor development. The effect remained statistically significant, suggesting that fitness may act on multiple pathways, independent of obesity, diabetes, and hypertension, to influence CKD. Other mechanisms through which fitness has benefits on CKD may be anti-inflammatory effects, maintenance of muscle mass and function, and endothelial health.[45,58,61,62] As a pleiotropic factor, modifying fitness in young adults could be effective for reducing the later burden of CKD.

Strengths of this study include the 30 years of follow-up, rigorously measured outcomes, utilizing an objective physiological measure of fitness; a wealth of covariate data; and a diverse sample in race, gender, and SES. Furthermore, time-varying covariates allowed for more robust adjustment for factors that substantially affect the risk of CKD.[47] Additionally, supplemental analyses included the APOL1 gene variant. Fitness remained significantly associated with incident CKD when taking into account this indicator of genetic predisposition for CKD.

Limitations

The PAF should be interpreted with care, as it assumes a causal relationship between the risk factor and outcome. The observational design limits the ability to make conclusions regarding the causal pathway of fitness' association with race differences in CKD. The PAF provides the maximum impact fitness could have on incident CKD, assuming an improvement from low to moderate or high fitness occurs among all individuals. However, lifestyle interventions impact individuals differentially and health behaviors are difficult to maintain. There were few cases of CKD during follow-up, which is expected, given the baseline assessment began with healthy, young adults. There is potential of selection bias resulting from participant dropout from sickness. There may be residual confounding for factors not measured that may have

associations with CKD and, therefore, are not adjusted for in analyses. This study could not confirm the stability of eGFR over 3 months as recommended[47] because this measure occurred once every 5 years. However, eGFR is more stable at younger ages, and therefore a more reliable measure of kidney function during young and middle adulthood versus a sample of older adults. Furthermore, the sensitivity analyses including albuminuria in the CKD definition found similar associations.

CONCLUSIONS

The findings suggest that low fitness during young adulthood is a significant risk factor for the development of CKD. Given that blacks have poorer fitness compared with whites in this study and others,[22,63,64] physical activity interventions are an important strategy[18] to improve fitness and lower the likelihood of developing CKD. If such strategies are successful in blacks, it may be possible to reduce a portion of the racial disparity in CKD.

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SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2019.02.016.

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