The association of exercise and sedentary behaviours with incident end-stage renal disease: the Southern Community Cohort Study

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ABSTRACT

Objective To examine whether lifestyle factors, including sedentary time and physical activity, could independently contribute to risk of end-stage renal disease (ESRD).

Study design Case-cohort study.

Setting South-eastern USA.

Participants The Southern Community Cohort Study recruited ~86 000 black and white participants from 2002 to 2009. We assembled a case cohort of 692 incident ESRD cases and a probability sample of 4113 participants.

Predictors Sedentary time was calculated as hours/day from daily sitting activities. Physical activity was calculated as metabolic equivalent (MET)-hours/day from engagement in light, moderate and vigorous activities.

Outcomes Incident ESRD.

Results At baseline, among the subcohort, mean (SD) age was 52 (8.6) years, and median (25th, 75th centile) estimated glomerular filtration rate (eGFR) was 102.8 (85.9–117.9) mL/min/1.73 m2. Medians (25th–75th centile) for sedentary time and physical activity were 8.0 (5.5–12.0) hours/day and 17.2 (8.7–31.9) MET-hours/day, respectively. Median follow-up was 9.4 years. We observed significant interactions between eGFR and both physical activity and sedentary behaviour (p<0.001). The partial effect plot of the association between physical activity and log relative hazard of ESRD suggests that ESRD risk decreases as physical activity increases when eGFR is 90 mL/min/1.73 m2. The inverse association is most pronounced at physical activity levels >27 MET-hours/day. High levels of sitting time were associated with increased ESRD risk only among those with reduced kidney function (eGFR ≤30 mL/min/1.73 m2); this association was attenuated after excluding the first 2 years of follow-up.

Conclusions In a population with a high prevalence of chronic kidney disease risk factors such as hypertension and diabetes, physical activity appears to be associated with reduced risk of ESRD among those with preserved kidney function. A positive association between sitting time and ESRD observed among those with advanced kidney disease is likely due to reverse causation.

Strengths and limitations of this study

► The Southern Community Cohort Study (SCCS) is a large, unique cohort of black and white participants with low socioeconomic status and a high burden of risk factors for end-stage renal disease.

► The case-cohort design selected participants for measurement of serum creatine, therefore, baseline kidney function could be evaluated.

► Physical activity and sedentary behaviours were self-reported rather than objectively measured; however, a validated questionnaire developed for the SCCS was used for ascertainment of these measures.

► Only baseline data on physical activity and sedentary behaviours were included and behaviours may have changed after enrolment.

INTRODUCTION

In 2015, the age-adjusted incidence of end-stage renal disease (ESRD) in USA was 357 per million.1 With the growing burden of ESRD, there has been increasing focus on modifiable risk factors, such as physical activity and sedentary behaviours. Through physical activity, control of primary risk factors for ESRD, such as diabetes, obesity and hypertension, may lead to diverse benefits on the metabolic environment of kidney dysfunction. Recent studies have shown that higher physical activity levels are associated with better physical functioning, lower risk of chronic kidney disease (CKD) and slower decline in estimated glomerular filtration rate (eGFR).2–8 Studies that examined sedentary behaviours are limited but suggest that higher sedentary time is associated with reduced kidney function and increased CKD risk.4 9 The association between physical activity, sedentary time and ESRD is not well...
established though, with few studies suggesting an association between physical activity and ESRD and none with the ability to disentangle exercise behaviours from socioeconomic status (SES).10,11

We investigated whether sedentary time and physical activity were independently associated with risk of incident ESRD. We hypothesised that higher physical activity and shorter sedentary time would be associated with decreased risk of ESRD. To examine this association, we used a case-cohort design within the Southern Community Cohort Study (SCCS), a unique population of individuals with lower SES, a high burden of kidney disease risk factors, and robust measures of physical activity and sedentary time.

METHODS

Study population

The SCCS is a prospective cohort study that recruited ~86,000 primarily low-income black and white adults, aged 40–79 years, in south-eastern USA (2002–2009).12 Participants eligible for enrolment spoke English and had not been treated for cancer in the 12 months before enrolment. The majority (86%) were recruited at participating community health centres (CHCs), which provide primary healthcare for uninsured populations. A detailed description of SCCS methods has been published (http://www.southerncommunitystudy.org).13 All participants provided written informed consent. We used the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) cohort checklist when writing our report.14

Incident ESRD was identified by linking the SCCS cohort, using date of birth, social security number, and first and last names, with the nationwide US Renal Data System (USRDS) through 31 March 2015, the latest date for which data were available. ESRD cases in this registry are certified by a physician diagnosis and filed using a medical evidence report form (to the Medicare ESRD programme), or when chronic dialysis or kidney transplant occurs, irrespective of the glomerular filtration rate. The USRDS is a national registry and therefore, ascertainment of ESRD cases is virtually complete.1 Participants with an ESRD diagnosis prior to SCCS enrolment ( prevalent cases) were excluded from the analysis.

Approximately 46% of the cohort donated baseline blood samples during CHC recruitment, which have been frozen at −80°C. Participants were selected for measurement of creatine using a case-cohort design, including all those with stored blood who had an incident ESRD diagnosis (n=737), and a probability sample of the entire cohort who donated blood (n=4238).15,16 Baseline serum levels of creatine were measured using the Jaffe (rate) method on a Beckman Coulter DXC 600 clinical chemistry analyser. The creatine assays were calibrated, and daily quality checks performed at three levels before sample testing. This sample constitutes 13% of SCCS participants who donated blood, and is comparable with respect to baseline sociodemographic characteristics including racial distribution, low income and high prevalence of CKD risk factors.17 The weighted subcohort included 70.8% black participants and 29.2% white participants, and the SCCS population included 67.3% black participants and 28.6% white participants. In the subcohort and overall SCCS population, about 32% had an education level below the twelfth grade, the majority had an annual income of <$15,000, and the prevalence of hypertension and diabetes was similar at 56% and 22%, respectively.

Patient and public involvement

There was no patient or public involvement in study design and conduct, dissemination of results, and evaluation in this study.

Data collection

Standardised computer-assisted personal interviews were administered at enrolment to obtain data on demographic, medical and lifestyle variables.13 Sections included demographic characteristics (education, income, residence), tobacco use, personal and family medical history, medication use, emotional well-being, occupation, physical activity and diet. Body mass index (BMI) was calculated from self-reported height and weight. History of hypertension, diabetes and hypercholesterolaemia as well as stroke and cardiovascular disease were self-reported by asking whether a doctor had ever diagnosed the participant with the condition. Self-reported height and weight were compared with clinic recorded measurements for over 20% of participants. In a series of validation studies, biomarkers, repeat interviews or medical records were used to assess the reliability of variables such as smoking status and self-reported diseases including diabetes.13

Usual sedentary and active behaviours were assessed using a validated Physical Activity Questionnaire (PAQ) developed specifically for the SCCS.18 For sedentary behaviours, participants were asked questions about the amount of time per day typically spent sitting in a car or bus, at work, viewing television or movies, and other activities that involve sitting such as sitting at meals, talking on the phone, reading, playing games or sewing. For physical activity, participants were asked about time typically spent performing light, moderate and strenuous activities at home and at work, as well as time spent doing moderate and vigorous exercise/sports. Time spent doing work and home activities was assessed separately for week and weekend days, and exercise and sports participation was assessed for a typical week. Examples of light work were given to participants and included standing at work, shopping, cooking, and child or elderly care. Moderate work examples included shop work, cleaning house, gardening, moving lawn and home repair. Examples of strenuous work included loading or unloading trucks, construction, farming or other hard labour. Moderate sports included activities such as bowling, dancing and golfing, while vigorous sports included jogging, aerobics,
tennis, swimming and weightlifting. For all questions, participants provided open-ended duration responses (hours and minutes). The reliability and validity of the SCCS PAQ was evaluated in 118 randomly selected SCCS participants via use of accelerometers.\textsuperscript{18}

**Statistical analysis**

The study population was restricted to black and white participants enrolled at CHCs, to ensure that participants had similar SES and equal access to healthcare regardless of race and had the opportunity to donate a blood specimen. Participants with missing data for any exercise metric (n=79) or demographic characteristic (n=212), and those with baseline eGFR >150 mL/min/1.73 m\(^2\) (n=5), were excluded; thus, a total of 692 ESRD cases and 4113 subcohort members were included in the analyses (Figure 1).

Sedentary time was calculated as hours/day based on the sum of all individual sedentary behaviours. Total physical activity was calculated as the sum of light, moderate and strenuous household/occupational work as well as moderate and vigorous sports; values were transformed from hours/day into summary measures of energy expenditure, defined as metabolic equivalent (MET)-hours/day. MET values for specific activities and intensities were based on the compendium of physical activities.\textsuperscript{19} MET-hours reflect the weighted average of the intensity (MET) and duration (hours) of activity behaviours. Two MET-hours/day is roughly equivalent to participating in 1 hour of a light activity, 0.5 hours of a moderate activity such as walking, or 0.25 hours of a vigorous activity such as jogging.\textsuperscript{18} For example, 1 MET-hour is roughly equivalent to the energy expenditure associated with walking very briskly (4 METs) for 15 min (0.25 hours).

Using sampling weight techniques, we described baseline characteristics of subcohort participants using means and SD or medians and 25th and 75th centiles. For descriptive purposes, sedentary time (hours/day) and physical activity (MET-hours/day) were also categorised into quartiles based on the subcohort distribution. Incidence rates (IRs) were calculated from bootstrap probability resamples; the reported IRs were the means of the bootstrap replicates with CIs at the 2.5th and 97.5th centiles of the bootstrap distribution.

We calculated HRs and 95% CIs for the association of sedentary time and physical activity with ESRD from Cox regression models that accounted for the case-cohort design and the weighted sample.\textsuperscript{15} Participants were considered at risk from the date of SCCS enrolment until the first occurrence of incident ESRD, death or 31 March 2015. Total sedentary time and physical activity were

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**Figure 1**  Study selection of the SCCS case-cohort. eGFR, estimated glomerular filtration rate; SCCS, Southern Community Cohort Study.
modelled as restricted cubic splines with four knots and mutually adjusted in a single model. Additional covariates included age at enrolment (years), sex, race, education (< or ≥ high school), income (< or ≥ $15,000), BMI (kg/m²), smoking (never or former/current), baseline eGFR (mL/min/1.73m²) and history of diagnosis of diabetes, hypertension and hypercholesterolaemia (yes/no). Baseline serum levels of creatine were used for estimation of eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Continuous predictors (age, eGFR, and BMI) were added to the model as restricted cubic splines with four knots. To examine interactions between sedentary time or physical activity and baseline kidney function on ESRD risk, multiplicative interaction terms between the non-linear, continuous predictors of sedentary time/physical activity and non-linear, continuous eGFR were added to the model.

We constructed partial effect plots of eGFR and physical activity or sedentary time on the log relative hazard scale, which display the predicted outcome as a function of a single covariate while holding all other covariates constant for different levels of baseline kidney function. We also plotted the HRs of ESRD as a function of continuous MET-hours/day or sitting hours/day, again holding all other covariates constant for different levels of baseline kidney function. The CIs in the HR plots were generated using bootstrap resampling methods.

To examine if the relationship with ESRD differed for different types of sitting, we also modelled the individual sedentary behaviours, sitting in the car/bus, sitting at work, watching TV/movies and other sitting. The multivariable Cox model included sitting hours for each category modelled as restricted cubic splines and mutually adjusted. Non-nested likelihood ratio tests were used to compare this model to the Cox model including total sitting hours.

Finally, in sensitivity analyses to examine the potential for reverse causation among those with advanced kidney disease, we calculated HRs and 95% CIs and constructed partial effect plots as above, excluding the first 2 years of follow-up. All analyses were conducted using R. For main effects and interaction terms, p ≤ 0.05 was considered statistically significant.

**RESULTS**

At baseline, mean (SD) age of subcohort participants was 52 (8.6) years (table 1). Most participants were women (60%), black (71%), reached high school (68%) and had income < $15,000 (62%). Approximately 75% were overweight or obese (BMI ≥ 25 kg/m²) and 55%, 23% and 35% reported a diagnosis of hypertension, diabetes and hypercholesterolaemia, respectively. Median (25th–75th centile) baseline eGFR was 102.8 (85.9–117.9) mL/min/1.73m² in the subcohort and 62.9 (36.0–98.1) among ESRD cases. Median (25th–75th centile) for total sedentary time and physical activity in the subcohort were 8.0 (5.5–12.0) hours/day and 17.2 (8.7–31.9) MET-hours/day, respectively. The most common sedentary activity was watching TV or movies; for physical activity, most energy expenditure came from moderate activities and sports.

Demographic characteristics by quartiles of physical activity and sedentary time are presented in table 2. Median (25th–75th centile) total physical activity in the highest activity quartile for the subcohort was 41.3 (35.2–55.5) MET-hours/day, compared with 4.2 (2.0–6.2) in the lowest quartile (table 2A). Compared with individuals in the lower quartiles, subcohort members in the highest quartile of physical activity were younger, had higher education and income, and had lower prevalence of obesity, hypertension, hypercholesterolaemia and diabetes. Median baseline eGFR was highest among those in the highest quartile of physical activity.

Median (25th–75th centile) total sitting hours in the subcohort was 15.5 (13.8–18.0) hours/day in the highest sedentary time quartile and 4.0 (3.0–5.0) hours/day for participants in the lowest quartile (table 2B). Total physical activity was higher among participants in the third and fourth quartiles of sedentary time compared with the lower two quartiles. Subcohort participants in the fourth quartile of sedentary time were more likely than those in lower quartiles to be black and obese, and to have at least high school education or annual income > $15,000. Prevalence of hypertension, hypercholesterolaemia and diabetes did not vary consistently across quartiles of sitting time, nor did median baseline eGFR.

Participants were followed for a median (range) of 9.4 (0.1–12.8) years. Age-adjusted IRs for ESRD were 2.61/1000, 2.38/1000, 2.24/1000 and 1.68/1000 person-years in the first to fourth quartiles of physical activity, respectively; corresponding IRs in quartiles of sitting time were 2.13/1000, 2.06/1000, 2.07/1000 and 2.64/1000 person-years (table 2). In unadjusted Cox models, the HRs for an IQR increase in physical activity or sedentary time were 0.65 (95% CI 0.58 to 0.73) and 1.09 (95% CI 1.00 to 1.20), respectively. In the multivariable model including both physical activity and sedentary time, and the interactions between physical activity*eGFR and sedentary behaviour*eGFR, both interactions were statistically significant (chunk test p < 0.001). Therefore, we present partial effect plots based on the multivariable model to further tease out the shape of the association between eGFR, physical activity and sitting.

The partial effect plots show the association between physical activity (figure 2A) or sedentary time (figure 2B) and log relative hazard of ESRD, by levels of baseline eGFR. When eGFR is 30, the shape of the association suggests that risk of ESRD increases as activity increases. In contrast, when eGFR is 90, log relative hazard of ESRD decreases as activity increases, and the inverse association is most pronounced at levels of physical activity above 27 MET-hours/day. The predicted log relative hazard of ESRD is uniformly higher when eGFR is 30 compared with when eGFR is 60, and log relative hazard is lowest when eGFR is 90.

In the second plot, when eGFR is 30, the shape of the association shows increasing ESRD risk as sedentary time

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Pike M, et al. BMJ Open 2019;9:e030661. doi:10.1136/bmjopen-2019-030661
Table 1  Baseline characteristics of the probability sample (subcohort) of SCCS participants and ESRD cases

| Subcohort participants (n=4113) | ESRD cases (n=692) |
|---------------------------------|--------------------|
| Age at enrolment, years         | 52.2±8.6           | 53.8±8.0          |
| Women                           | 59.8               | 51.5              |
| Race                            |                    |                   |
| White                           | 29.3               | 12.4              |
| Black                           | 70.7               | 87.6              |
| Education                       |                    |                   |
| <High school                    | 32.3               | 40.3              |
| ≥High school                    | 67.7               | 59.7              |
| Household income                |                    |                   |
| <$15,000/year                   | 61.6               | 65.8              |
| ≥$15,000/year                   | 38.4               | 34.2              |
| Cigarette smoking               |                    |                   |
| Current/former smoker           | 67.3               | 58.3              |
| Never smoker                    | 32.7               | 41.7              |
| BMI, kg/m²                      | 30.3±7.3           | 32.8±8.8          |
| Overweight or obese (BMI ≥25 kg/m²) | 74.8             | 82.5              |
| Hypertension                    | 55.5               | 86.0              |
| Hypercholesterolaemia           | 34.5               | 49.3              |
| Diabetes                        | 22.6               | 68.5              |
| eGFR, ml/min/1.73 m²            | 102.8 (85.9–117.9) | 62.9 (36.0–98.1) |

Sedentary and physical activity measures

| Sitting, hours/day | 8.0 (5.5–12.0) | 8.2 (6.0–12.0) |
|--------------------|----------------|----------------|
| Car or bus, hours/day | 1.5±1.8 | 1.5±2.0 |
| At work, hours/day | 1.2±2.3 | 0.9±2.3 |
| TV or movies, hours/day | 3.8±2.9 | 4.3±3.1 |
| Home computer, hours/day | 0.5±1.1 | 0.3±0.9 |
| Other, hours/day* | 2.3±1.9 | 2.4±2.0 |
| Physical activity, hours/day | 5.4 (2.9–9.4) | 4.3 (2.3–7.4) |
| Household/occupational activity, MET-hours/day | | |
| Light | 7.3±6.2 | 5.9±5.4 |
| Moderate | 9.7±8.7 | 8.6±7.9 |
| Strenuous | 5.0±11.7 | 3.1±9.4 |
| Sports, MET-hours/day | | |
| Moderate | 10.0±8.8 | 8.9±8.1 |
| Vigorous | 5.6±12.0 | 3.5±9.6 |
| Total physical activity, MET-hours/day† | 17.2 (8.7–31.9) | 13.9 (6.9–24.6) |

Values are listed as mean±SD or % or median (25th–75th centile).
*Includes sitting at meals, talking on the phone, reading, playing cards or sewing.
†Includes light, moderate and strenuous household/occupational activity as well as moderate and vigorous sports.
BMI, body mass index; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; MET, metabolic equivalent; SCCS, Southern Community Cohort Study.

increases. In contrast, when eGFR is 60 or 90, the shape of the association is slightly decreasing or flat with increasing sedentary time. As for physical activity, the predicted log relative hazard of ESRD is uniformly higher when eGFR is 30 compared with when eGFR is 60 or 90.

The continuous HR plots present the associations between physical activity (figure 3A) or sedentary time (figure 3B) and risk of incident ESRD. The HR plots are separated into three levels of eGFR (30, 60, 90mL/min/1.73m²). Each panel has its own reference level, which is seen at the pinch.
Table 2  Baseline characteristics of the subcohort of SCCS participants by quartiles of: (A) physical activity (B) sedentary time

|                      | Q1: Subcohort (n=934) | Q2: Subcohort (n=994) | Q3: Subcohort (n=1045) | Q4: Subcohort (n=1140) |
|----------------------|------------------------|------------------------|------------------------|------------------------|
| ESRD incidence rate per 1000 person-year | 2.61 (1.54–3.87) | 2.38 (1.36–3.50) | 2.24 (1.25–3.30) | 1.68 (0.93–2.55) |
| Physical activity (MET-hours/day)* | 4.2 (2.0–6.2) | 10.6 (8.8–12.6) | 20.2 (17.2–23.5) | 41.3 (33.2–55.5) |
| Sitting (hours/day) | 7.5 (6.0–11.0) | 8.0 (6.0–12.0) | 9.0 (6.0–12.0) | 8.5 (5.8–12.0) |
| Age, years          | 54.6 (9.3) | 53.1 (8.9) | 52.4 (8.8) | 49.7 (7.1) |
| Women               | 49.9 | 67.0 | 70.7 | 51.5 |
| Black race          | 67.5 | 69.2 | 71.3 | 73.2 |
| Less than high school | 37.7 | 35.0 | 32.1 | 27.0 |
| Less than $15,000/year | 73.1 | 66.9 | 59.4 | 52.2 |
| Current/former smoker | 70.4 | 64.4 | 65.7 | 69.0 |
| BMI, kg/m²           | 30.9 (7.9) | 30.7 (7.4) | 30.9 (7.2) | 29.1 (6.8) |
| Overweight or obese (BMI ≥ 25 kg/m²) | 75.1 | 77.2 | 77.3 | 70.5 |
| Hypertension         | 63.5 | 56.7 | 58.7 | 47.1 |
| High cholesterol     | 38.7 | 38.1 | 38.7 | 25.7 |
| Diabetes             | 27.6 | 24.4 | 23.8 | 17.0 |
| eGFR, mL/min/1.73 m² | 99.2 (80.6–114.8) | 102.9 (84.8–116.8) | 102.1 (86.6–117.6) | 106.9 (89.9–120.3) |

(A) in the CIs where HR=1.0. The relative shape of the associations at each level of eGFR corresponds to what is shown in the partial effect plots; in particular, an inverse association between physical activity and risk of ESRD is apparent only among those with preserved kidney function, while an increased risk of ESRD with increasing sedentary time is observed among those with low eGFR.

In analyses examining the individual types of sitting, the non-nested likelihood ratio test indicated that the model with sitting hours by type did not significantly differ from the model with total sitting hours (p=0.98). In sensitivity analyses excluding the first 2 years of follow-up, the interactions between sedentary time*eGFR and physical activity*eGFR remained statistically significant (p<0.001 for
both); however, the positive association between sitting time and ESRD among those with advanced kidney disease was no longer apparent.

**DISCUSSION**

Among black and white participants at high risk for ESRD, we observed a significant interaction between physical activity and baseline kidney function, suggesting that among individuals with preserved kidney function, higher physical activity is associated with a lower risk of developing ESRD. Similarly, we observed heterogeneity of the association of sitting time on ESRD risk, as demonstrated by the higher risk of ESRD associated with longer sitting time among those with eGFR ≤ 30 mL/min/1.73 m², which appears to be explained by reverse causation.

While physical activity is widely accepted as an important modifiable risk factor for cardiovascular disease, the association is not well established in kidney disease. A number of observational and interventional studies have examined the risks and benefits of physical activity among patients undergoing maintenance dialysis. However, previous studies of incident kidney disease are limited and have reported inconsistent results. In a cross-sectional study of 10,463 patients with diabetes and hypertension, lack of exercise was a significant risk factor for CKD. In another cohort study of 6,972 patients with diabetes, participants who had more regular physical activity had a reduced risk of early diabetic CKD. Among 4,011 participants from the Cardiovascular Health Study, those with the highest amount of physical activity had a lower risk of rapid kidney function.

![Figure 2](image1.png)

**Figure 2** Partial effect plots of (A) Physical activity (MET-hours/day) (B) Total sitting time (hours/day) and log relative hazard of ESRD by baseline levels of eGFR. The plot is based on the multivariable Cox model that includes terms for physical activity, sedentary time, BMI, smoking status, age, sex, race, education, income, diabetes, hypertension, high cholesterol, eGFR, and the interactions between physical activity and eGFR and sedentary time and eGFR. BMI, body mass index; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; MET, metabolic equivalent.

![Figure 3](image2.png)

**Figure 3** Plots of continuous HRs of (A) Physical activity (MET-hours/day) (B) Total sitting time (hours/day) and ESRD by baseline levels of eGFR. The plot is based on the multivariable Cox model that includes terms for physical activity, sedentary time, BMI, smoking status, age, sex, race, education, income, diabetes, hypertension, high cholesterol, eGFR, and the interactions between physical activity and eGFR and sedentary time and eGFR. The CIs in the HR plot were generated using bootstrap resampling methods. BMI, body mass index; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; MET, metabolic equivalent.
To our knowledge, this is one of few studies to investigate the association between physical activity and ESRD and one of the first to examine sedentary behaviours. Strengths of our study include the prospective design and the unique cohort of participants with low SES and a high burden of risk factors for ESRD. An important strength is the ascertainment of a broad range of physical activity and sedentary behaviours from a validated questionnaire developed specifically for the SCCS. Other strengths include the complete ascertainment of ESRD cases and the inclusion of baseline eGFR. A limitation of the study is that physical activity and sedentary behaviours were ascertained only at baseline and may have changed after enrolment. Moreover, the physical activity, sedentary behaviours and covariates were self-reported by participants rather than objectively measured. Although the probability sample is comparable to the whole cohort, the findings might not be generalisable to all SCCS participants. Finally, baseline data on proteinuria were not available.

In conclusion, this study found that in a population at high risk for ESRD, higher levels of physical activity were associated with reduced risk of ESRD in those with preserved kidney function, and sedentary time was not associated with increased ESRD risk except in participants with low baseline eGFR. Physical activity and sedentary behaviours are modifiable risk factors that may be targets for possible interventions, especially in those with preserved kidney function.

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Funding The Southern Community Cohort Study is supported by the National Cancer Institute (grants R01 CA092447 and U01 CA202979). Data collection performed by the Survey and Biospecimen Shared Resource which is supported by the Vanderbilt-Ingram Cancer Center (P30 CA68459). This study was supported in part by the US Department of Veterans Affairs under Award Number 1001CX00414, Clinical Translational Science Award UL1TR000445 from the National Center for Advancing Translational Sciences, Vanderbilt O’Brien Kidney Center Grant P30 DK114809-01 (EDS), P30 DK077934, T32 DK07569 and K24 DK62849 (TAI) from the National Institute of Diabetes and Digestive and Kidney Diseases, and Clinical Translational Science Award TL1TR002244.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Institutional Review Boards of Vanderbilt University Medical Center and Meharry Medical College.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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REFERENCES

1. United States Renal Data System. End-Stage renal disease (ESRD) in the United States. 2017 USRDS annual data report: epidemiology of kidney disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Kidney Diseases, 2017: 247–609. https://www.usrds.org/2017/view/default.aspx

2. Alkerwi Ala’a, Sauvageot N, El Bahi I, et al. Prevalence and related risk factors of chronic kidney disease among adults in Luxembourg: evidence from the observation of cardiovascular risk factors (ORISCAV-LUX) study. BMC Nephrol 2017;18:358.

3. Dunkerl D, Kohl M, Heinze G, et al. Modifiable lifestyle and social factors affect chronic kidney disease in high-risk individuals with type 2 diabetes mellitus. Kidney Int 2015;87:784–91.

4. Martens PJH, van der Berg JD, Stenhouwer CDA, et al. Amount and pattern of physical activity and sedentary behavior are associated with kidney function and kidney damage: the Maastricht study. PLoS One 2018;13:e0195306.

5. Michishita R, Matsuda T, Kawakami S, et al. The association between changes in lifestyle behaviors and the incidence of chronic kidney disease (CKD) in middle-aged and older men. Journal of Epidemiology 2017;27:389–97.

6. Qin X, Wang Y, Li Y, et al. Risk factors for renal function decline in adults with normal kidney function: a 7-year cohort study. J Epidemiol Community Health 2015;69:782–8.

7. Robinson-Cohen C, Katz R, Mozaffarian D, et al. Physical activity and rapid decline in kidney function among older adults. Arch Intern Med 2009;169:2116–23.

8. Su S-L, Lin C, Kao S, et al. Risk factors and their interaction on chronic kidney disease: a multi-centre case control study in Taiwan. BMC Nephrol 2015;16:83.

9. Glavinovic T, Ferguson T, Komenda P, et al. CKD and Sedentary Time: Results From the Canadian Health Measures Survey. Am J Kidney Dis 2018;72:529–37.

10. Jafar TH, Jin A, Koh W-P, et al. Physical activity and risk of end-stage kidney disease in the Singapore Chinese Health study. Nephrology 2015;20:61–7.

11. Ricardo AC, Anderson CA, Yang W, et al. Healthy lifestyle and risk of kidney disease progression, atherosclerotic events, and death in CKD: findings from the chronic renal insufficiency cohort (CRIC) Study. Am J Kidney Dis 2015;65:412–24.

12. PRENTICE RL. A case-cohort design for epidemiologic cohort studies and disease prevention trials. Biometrika 1986;73:1–11.

13. Signorolo LB, Hargreaves MK, Blot WJ. The southern community cohort study: investigating health disparities. J Health Care Poor Underserved 2010;21(1 Suppl):26–37.

14. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. International Journal of Surgery 2014;12:1495–9.

15. Therneau TM, Li H. Computing the COX model for case-cohort data. Lifetime Data Anal 1999;5:99–112.

16. Sharp SJ, Pouliaiou M, Thompson SG, et al. A review of published analyses of case-cohort studies and recommendations for future reporting. PLoS One 2014;9:e101176.

17. Bock FS, Robinson-Cohen T., Morse C., et al. Baseline kidney function and racial disparities in end-stage renal disease risk in the southern community cohort study. BMC Nephrology 2019;20.

18. Buchowski MS, Matthews CE, Cohen SS, et al. Evaluation of a questionnaire to assess sedentary and active behaviors in the southern community cohort study. Journal of physical activity health 2012;9:765–75.

19. Ainsworth BE, Haskell WL, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.

20. Ikizler TA. Exercise as an anabolic intervention in patients with end-stage renal disease. Journal of Renal Nutrition 2011;21:52–6.

21. Johansen KL, Kaysen GA, Dalrymple LS, et al. Association of physical activity with survival among ambulatory patients on dialysis: the comprehensive dialysis study. Clin J Am Soc Nephrol 2013;8:248–53.

22. Seliger SL. Physical activity in ESRD: time to get moving. Clin J Am Soc Nephrol 2012;7:1927–9.

23. Segura-Orti E, Johansen KL. Exercise in end-stage renal disease. Semin Dial 2010;23:422–30.

24. Young BA, Katz R, Bouxsein ME, et al. Risk factors for rapid kidney function decline among African Americans: the Jackson heart study (JHS). Am J Kidney Dis 2016;68:229–39.

25. Tu HT. Progression of chronic renal failure. Arch Intern Med 2003;163:1417–29.

26. Jacobson H. Chronic renal failure: pathophysiology. The Lancet 1991;338:419–23.

27. Amann K, Wanner C, Ritz E. Cross-Talk between the kidney and the cardiovascular system: Figure 1. Journal of the American Society of Nephrology 2006;17:2112–9.

28. Akchurin OM, Kaskel F. Oxidative stress and inflammation in chronic kidney disease. Blood Purif 2015;39:84–92.

29. Ramos LF, Shintani A, Ikizler TA. Evidence for anti-inflammatory benefits of exercise in pre-dialysis chronic kidney disease. J Am Soc Nephrol 2010;21:164–73.

30. Thorp AA, Healy GN, Owen N, et al. Amount and sitting time and television viewing time with cardiometabolic risk disease. Arch Intern Med 2015;175:828–35.

31. Gould DW, Graham-Brown MPM, Watson EL, et al. Physiological benefits of exercise in pre-dialysis chronic kidney disease. Nephrology 2014;19:519–27.

32. Viana JL, Kosmadakis GC, Watson EL, et al. Evidence for anti-inflammatory effects of exercise in CKD. J Am Soc Nephrol 2014;25:2121–30.

33. Akchurin OM, Kaskel F. Update on inflammation in chronic kidney disease. Blood Purif 2015;39:84–92.

34. Himmelfarb J, McMonagle E, McMenamin E. Plasma protein thiol oxidation and carbonyl formation in chronic renal failure. Kidney Int 2015;87:1256–64.

35. Thorp AA, Healy GN, Owen N, et al. Deleterious associations of sitting time and television viewing time with cardiometabolic risk biomarkers: Australian diabetes, obesity and lifestyle (AusDiab) study 2004-2005. Diabetes Care 2010;33:327–34.