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Healthy Lifestyle and Risk of Kidney Disease Progression, Atherosclerotic Events, and Death in CKD: Findings From the Chronic Renal Insufficiency Cohort (CRIC) Study

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Abstract

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Contributions: Research idea and study design: JPL, ACR, WY; data acquisition: ACR, CAA, WY, XZ, MJF, LMD, JCF, AF, NJ, EL, LCN, ACP, MR, JAW, JPL; data analysis/interpretation: ACR, CAA, WY, XZ, MJF, LMD, JCF, AF, NJ, EL, LCN, ACP, MR, JAW, MLD, JPL; statistical analysis: WY, XZ; supervision or mentorship: JPL. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. ACR and JPL take responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Background—In general populations, healthy lifestyle is associated with fewer adverse outcomes. We estimated the degree to which adherence to a healthy lifestyle decreases the risk of renal and cardiovascular events among adults with chronic kidney disease (CKD).

Study Design—Prospective cohort.

Setting & Participants—3006 adults enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study.

Predictors—Four lifestyle factors (regular physical activity, body mass index [BMI] 20–<25 kg/m², nonsmoking, and “healthy diet”), individually and in combination.

Outcomes—CKD progression (50% decrease in estimated glomerular filtration rate or end-stage renal disease), atherosclerotic events (myocardial infarction, stroke, or peripheral arterial disease), and all-cause mortality.

Measurements—Multivariable-adjusted Cox proportional hazards.

Results—During median follow-up of 4 years, we observed 726 CKD progression events, 353 atherosclerotic events, and 437 deaths. BMI ≥ 25 kg/m² and nonsmoking were associated with reduced risk of CKD progression (HRs of 0.75 [95% CI, 0.58–0.97] and 0.61 [95% CI, 0.45–0.82] for BMIs of 25–<30 and ≥ 30, respectively, vs. 20–<25 kg/m²; HR for nonsmoking of 0.68 [95% CI, 0.55–0.84] compared to current smoker reference group) and reduced risk of atherosclerotic events (HRs of 0.67 [95% CI, 0.46–0.96] for BMI 25–<30 vs. 20–<25 kg/m² and 0.55 [95% CI, 0.40–0.75] vs. current smoker). Factors associated with reduced all-cause mortality were regular physical activity (HR, 0.64 [95% CI, 0.52–0.79] vs. inactive), BMI ≥ 30 kg/m² (HR, 0.64 [95% CI, 0.43–0.96] vs. 20–<25 kg/m²) and nonsmoking (HR, 0.45 [95% CI, 0.34–0.60] vs. current smoker). BMI <20 kg/m² was associated with increased all-cause mortality risk (HR, 2.11 [95% CI, 1.13–3.93] vs. 20–25 kg/m²). Adherence to all four lifestyle factors was associated with 68% lower risk of all-cause mortality compared to adherence to no lifestyle factors (HR, 0.32; 95% CI, 0.11–0.89).

Limitations—Lifestyle factors were only measured once.

Conclusions—Regular physical activity, nonsmoking, and BMI ≥ 25 kg/m² were associated with lower risk of adverse outcomes in this cohort of individuals with CKD.

Keywords

Chronic kidney disease (CKD); healthy lifestyle; lifestyle modification; physical activity; body mass index (BMI); diet; smoking; modifiable risk factor; CKD progression; renal disease trajectory; mortality; cardiovascular events

Chronic kidney disease (CKD) is a growing health problem with an estimated prevalence of 11.5%.^{1–4} Individuals with CKD are at high risk for progressive kidney failure, cardiovascular events, and death.^{5–7} Therefore, there is a compelling need to effectively reduce risk in this population.

Although adherence to a healthy lifestyle is associated with lower risk of adverse outcomes in the general population,^{8–14} the influence of healthy lifestyle on outcomes among persons with CKD has not been well studied. Because current guideline recommendations for

lifestyle modifications in CKD are largely based on general population studies, it is not known whether these recommendations can be applied to patients with CKD.

We used data from the Chronic Renal Insufficiency Cohort (CRIC) Study, a prospective follow-up study of adults with mild-to-moderate CKD at baseline, to evaluate the association of four lifestyle factors (regular physical activity, body mass index [BMI] 20–<25 kg/m², nonsmoking and “healthy diet”) individually and in combination, with risk of CKD progression, atherosclerotic events, and all-cause mortality. We hypothesized that adherence to a healthy lifestyle would be associated with reduced risk of these outcomes among persons with CKD.

Methods

Study Population

The CRIC Study is an ongoing multicenter, prospective, observational study of risk factors for progression of CKD and cardiovascular disease (CVD). The design, methods and baseline characteristics of study participants have been previously published.^{15,16} Briefly, 3939 men and women aged 21–74 years with estimated glomerular filtration rate (eGFR) 20–70 ml/min/1.73m² were recruited from June 2003 through December 2008 at seven US clinical centers. Exclusion criteria included inability to consent, institutionalization, pregnancy, and certain severe chronic conditions.^{15–17} Current analyses were restricted to 3006 participants with complete data for the exposure of interest. The study protocol was approved by the Institutional Review Board of participating centers (University of Illinois at Chicago approval number 2003-0149) and is in accordance with the Declaration of Helsinki. All participants provided informed consent.

Procedures

Sociodemographic information, medical history, and information about medications was obtained by self-reported questionnaires. Physical activity was measured using the Multi-Ethnic Study of Atherosclerosis (MESA) Typical Week Physical Activity Survey,¹⁸ a self-reported survey of intentional physical activity summarized as metabolic equivalent task (MET) score; the intensity levels (moderate, 3–5 MET; vigorous, >6 MET) were based on the Compendium of Physical Activities.¹⁹ Diet was assessed using the Diet History Questionnaire which is a food frequency questionnaire developed by the National Cancer Institute that has been validated and shown to provide reasonable nutrient estimates,²⁰ including the dietary components used in the present study. The Diet History Questionnaire consists of 124 food items consumed over the preceding 12 months (portion size and frequency), based on national dietary data (US Department of Agriculture). BMI was calculated as weight in kilograms divided by height in meters squared. GFR was estimated annually using a CRIC-specific equation.²¹ A 24-hour urine sample collected at study entry was used to measure protein and sodium excretion.

Healthy Lifestyle Factors Definition

Four different lifestyle factors ascertained at study entry were considered (physical activity, BMI, cigarette smoking and diet) based on their association with cardiovascular and overall

health.^{22;23} Physical activity was categorized as ideal (moderate 150 minutes/week, vigorous 75 minutes/week, or moderate plus vigorous 150 minutes/week), less than ideal (not inactive but not meeting criteria for ideal) and inactive (no reported leisure time physical activity).²² BMI was categorized as <20 kg/m², 20–<25 kg/m², 25–<30 kg/m² or 30 kg/m². Participants were classified as current, past or never smoker based on responses to the questions “Have you smoked at least 100 cigarettes during your entire life?” and “Do you smoke cigarettes now?” A “healthy diet” score was constructed by allocating one point for each of five dietary factors which were adapted from the American Heart Association’s recommendations for cardiovascular health promotion in the general population:²² above the median consumption of fruits/vegetables (2.8 cups/d), fish (1.3 ounces or 37 grams/wk) and whole grains (0.88 ounces or 25 grams/day); and below the median 24-hour urine sodium excretion (152 mEq/d) and consumption of sweets/sugar-sweetened beverages (19.3 ounces or 571 ml/week) with a possible score from 0 to 5. Finally, we created binary categories for each of the four lifestyle factors (i.e., ideal vs. not ideal) and computed an overall healthy lifestyle score (0 to 4) by allocating one point for each ideal category: ideal physical activity (vs. less than ideal or inactive),^{22;24} past or never smoker (vs. current smoker),^{22;24} “healthy diet” score of 4–5 (vs. 0–3),²² and BMI 20–<25 kg/m² (vs. <20, 25–<30 or 30 kg/m²);²⁴ we assumed a BMI 20–<25 kg/m² as a proxy of ideal adiposity and of a behavior denoting attention to ideal body weight maintenance.

Outcomes

We evaluated the following outcomes: 1) CKD progression, defined as 50% decrease in eGFR from baseline or occurrence of end-stage renal disease (ESRD; ie, receipt of long-term dialysis therapy or kidney transplantation); 2) atherosclerotic cardiovascular events (myocardial infarction, stroke, or peripheral arterial disease); and 3) death from any cause. Ascertainment of time to eGFR halving was imputed assuming a linear decline in kidney function between annual visits. Ascertainment of ESRD was supplemented by cross-linkage with the US Renal Data System. Cardiovascular events were adjudicated by review of hospital records.¹⁵ Deaths were ascertained from reports by next of kin, death certificates, hospital records, and linkage with the Social Security Death Master File. Participants were followed up until the occurrence of death, withdrawal from the study, or May 2011 when the database was locked for analysis. Median follow-up was 4 years.

Statistical Analysis

Descriptive statistics were summarized as mean $\pm$ standard deviation or median (interquartile range) for continuous variables, and frequency (proportion) for categorical variables. Chi-squared and analysis of variance tests were used to compare categorical and continuous variables, respectively. Cox proportional hazards models were used to examine the association between healthy lifestyle and outcomes. For analyses of CKD progression and cardiovascular events, death was treated as a censoring event. For each outcome, we fitted three nested Cox proportional hazards models that adjusted sequentially for potential explanatory variables. We explored effect modification by age (<65 and $\geq$ 65 years), gender, and self-reported history of CVD at baseline. Interaction terms were included in the regression models and analyses stratified by these variables were conducted. All analyses were performed using SAS 9.3 (SAS Institute Inc, Cary, NC).

Results

Baseline Characteristics, Overall and by Healthy Lifestyle Factors

For the 3006 participants included in these analyses, the mean age was 58 ± 11 (standard deviation) years, 48% were female, 47% non-Hispanic white, 45% had diabetes, the mean eGFR was 43 ± 14 ml/min/1.73 m² and median proteinuria was 0.17 g/24 hr. Compared with individuals included in the study (N=3006), those who were excluded due to missing data (n=933) had similar mean age (58 years) and were more likely to be male (63% vs. 52%; $p < 0.001$) and to belong to “other” racial/ethnic group (41% vs. 9%; $p < 0.001$). Baseline mean eGFR among excluded individuals was lower and urine protein excretion was higher compared with included participants (41 vs. 43 ml/min/1.73m² and 1.5 vs. 0.9 g/24, respectively; $p < 0.001$ for each comparison).

Tables 1 and 2 show baseline sociodemographic and clinical characteristics by healthy lifestyle factors. As compared to inactive individuals, participants with ideal physical activity were more likely to be younger, male and non-Hispanic white, had higher socioeconomic status, lower prevalence of diabetes and CVD, lower systolic blood pressure (BP), higher eGFR and lower proteinuria. As compared to individuals with BMI ≥ 30 kg/m², individuals with BMI 20– <25 kg/m² were younger, more likely to be female and non-Hispanic white, had a lower prevalence of diabetes and CVD, and lower systolic BP. As compared to current smokers, individuals who never smoked were more likely to be female, non-Hispanic white, had higher socioeconomic status, lower prevalence of CVD, lower BP, higher eGFR, and lower proteinuria. As compared to individuals with a diet score of 0, individuals with a score of 5 were older, female and non-Hispanic white, had higher socioeconomic status, and lower systolic BP.

Healthy Lifestyle Score Distribution

The distribution of the healthy lifestyle scores was as follows: 166 (6%) had a score of 0; 1031 (34%) had a score of 1; 1250 (42%) had a score of 2; 484 (16%) had a score of 3; and 75 (2%) had a score of 4 (Table 3). Compared with participants who adhered to none of the four lifestyle factors, those who adhered to all factors were more likely to be female and non-Hispanic white and had higher socioeconomic status and lower prevalence of hypertension, diabetes and CVD at baseline.

Outcomes

During a median follow-up of 4 years, participants experienced 726 CKD progression events, 355 atherosclerotic cardiovascular events, and 437 deaths (Tables 4 and 5, and Figure 1).

CKD Progression—In a model adjusting for clinical center, sociodemographic and clinical variables, ideal level of physical activity was associated with 28% risk reduction in CKD progression as compared to no reported leisure time physical activity (Model 2: HR, 0.72; 95% CI, 0.61–0.86). However, this difference was no longer significant with additional adjustment for eGFR and proteinuria (Model 3: HR, 0.98; 95% CI, 0.82–1.17). In contrast, in the fully adjusted model, as compared to BMI 20– <25 kg/m², BMI 25– <30

kg/m² was associated with 25% lower risk (Model 3: HR, 0.75; 95% CI, 0.58–0.97), and BMI ≥ 30 kg/m² with 39% lower risk (HR, 0.61; 95% CI, 0.45–0.82) for CKD progression. Compared to current smokers, both past and never smokers had reduced risk for CKD progression (Model 3: HRs of 0.79 [95% CI, 0.64–0.98] and 0.68 [95% CI, 0.55–0.84], respectively). No significant association between diet score and CKD progression was observed. There was no significant association between the overall healthy lifestyle score and CKD progression. There were no statistically significant differences in slope of urine protein-creatinine ratio between the healthy lifestyle factor categories, individually or in combination (data not shown).

Atherosclerotic Events—As compared with physical inactivity, ideal physical activity was not associated with a reduced risk for atherosclerotic events (Model 3: HR, 0.84; 95% CI, 0.66–1.07). There was a significant interaction between physical activity and age ($p < 0.001$). Fully adjusted HRs for ideal physical activity (vs. inactivity) were 0.62 (95% CI, 0.46–0.85) for individuals younger than 65 years and 1.35 (95% CI, 0.89–2.06) for participants aged 65 years or older. However, BMI $25 < 30$ kg/m² was associated with a significantly lower risk for atherosclerotic events (Model 3: HR, 0.67 [95% CI, 0.46–0.96] vs. BMI $20 < 25$ kg/m²). Compared to current smokers, both past and never smokers had reduced risk for atherosclerotic events in fully adjusted models (Model 3: HRs of 0.73 [95% CI, 0.54–0.99] and 0.55 [95% CI, 0.40–0.75], respectively). A higher diet score was not associated with decreased risk for atherosclerotic events. No significant association was observed between the overall healthy lifestyle score and risk of atherosclerotic events.

All-Cause Mortality—Compared with physical inactivity, both less than ideal and ideal physical activity were associated with reduced risk of all-cause mortality after adjustment for clinical site, demographic and clinical factors (Model 2: HRs of 0.74 [95% CI, 0.57–0.96] and 0.60 [95% CI, 0.49–0.74], respectively). However, in a fully adjusted model including eGFR and proteinuria at baseline, only ideal level of physical activity was associated with lower risk of all-cause mortality (Model 3: HR, 0.64; 95% CI, 0.52–0.79). Compared to a BMI $20 < 25$ kg/m², BMI < 20 kg/m² was associated with increased risk for all-cause mortality in a fully adjusted model (Model 3: HR, 2.11; 95% CI, 1.13–3.93), and BMI ≥ 30 kg/m² was associated with 36% lower all-cause mortality risk (HR, 0.64; 95% CI, 0.43–0.96). Compared to current smokers, both past and never smoking status were associated with reduced risk for all-cause mortality in a fully adjusted model (Model 3: HRs of 0.63 [95% CI, 0.48–0.81] and 0.45 [95% CI, 0.34–0.60], respectively). No significant association was observed between diet score and mortality. Significant reduction in all-cause mortality risk was observed with adherence to 1, 2, 3 or 4 healthy lifestyle factors vs. 0 factors. As compared to a lifestyle score of 0, a score of 4 was associated with a 68% reduction in all-cause mortality (Model 3: HR, 0.32; 95% CI, 0.11–0.90).

Discussion

In this cohort of persons with mild-to-moderate CKD, adherence to components of a healthy lifestyle (regular physical activity, BMI $20 < 25$ kg/m², nonsmoking, and “healthy diet”) was associated with reduced risk for adverse outcomes, including progression of CKD, atherosclerotic events and all-cause mortality. This is one of few studies to evaluate the

association between a combination of healthy lifestyle factors or behaviors and clinical outcomes in the setting of CKD. We found that current physical activity and nonsmoking recommendations for the general population were applicable to this cohort. Furthermore, we found a paradoxical association between BMI and outcomes and no significant association between “healthy diet” and outcomes. Additionally, adherence to all four lifestyle factors was associated with a 68% decrease in risk of all-cause mortality compared to adherence to none of the healthy lifestyle factors but not significantly associated with CKD progression or atherosclerotic events.

A number of studies in general populations have suggested that adherence to various healthy lifestyle factors is associated with better clinical outcomes.^{8–14} The Nurses’ Health Study demonstrated that a healthy lifestyle is associated with lower risk of death.¹² In addition, a recent meta-analysis showed that the relative risk for all-cause mortality decreases proportionate to the number of healthy lifestyle factors.¹⁴ However, the impact of healthy lifestyle has not been thoroughly evaluated in patients with CKD.^{7;25;26} Consequently, CKD guidelines which recommend lifestyle modifications are based on findings in general populations^{23;24} and therefore may not be generalizable to the CKD population.

Numerous previous studies have examined the influence of individual lifestyle factors on CKD outcomes. In analyses from the Cardiovascular Health Study²⁶ and the National Health and Nutrition Examination Survey (NHANES) 1988–1994,²⁷ lower levels of physical activity were associated with increased mortality among people with CKD. Our finding of an association between ideal levels of physical activity and lower all-cause mortality is consistent with these earlier reports. Although it has been hypothesized that regular exercise may slow the progression of CKD,²⁸ we did not find a significant association between ideal physical activity and CKD progression after adjusting for eGFR and proteinuria. Of note, we found a significant interaction between physical activity and age in the association with risk of atherosclerotic events, suggesting that recommended levels of physical activity are associated with lower risk of events for individuals younger than 65 years but not for those aged 65 years or older. While physical activity has been shown to improve cardiovascular health among older persons,²⁹ it is possible that in individuals with CKD the extent of vascular disease may be too advanced to be modified by physical activity.

Similar to our findings regarding physical activity, we found that nonsmoking reduced the risk for CKD progression, atherosclerotic events, and mortality. As opposed to general population studies,^{8–10} not many studies have evaluated the relationship between smoking and CKD. In a 25-year follow-up study of MRFIT (Multiple Risk Factor Intervention Trial), Ishani *et al.*³⁰ reported that cigarette smoking was associated with 84% increased risk for ESRD in middle-age men compared with nonsmoking. Furthermore, our results are consistent with those of other studies in which lower risk of cardiovascular events and death among nonsmokers with CKD was reported.^{26;31;32} Our findings strengthen the accumulating evidence regarding the importance of nonsmoking in the CKD population.

Interestingly, the prevalence of obesity (BMI ≥ 30 kg/m²) in our study participants at baseline was 50%, which is greater than that observed in the general US population.³³

Furthermore, we observed a paradoxical association between BMI and outcomes. Whereas an elevated BMI is associated with increased risk of adverse cardiovascular outcomes in the general population, in this cohort of participants with CKD, as compared to BMI 20–<25 kg/m², a BMI 25–<30 kg/m² (i.e., overweight) was associated with lower risk of CKD progression and atherosclerotic events, and a BMI ≥30 kg/m² was associated with lower risk of CKD progression and all-cause mortality. Although obesity has been previously associated with an increased risk for incident ESRD,^{34;35} only a few studies have evaluated BMI as a risk factor for progression of CKD. In general, these studies have been small and reported heterogeneous findings.^{36–38} Additionally, we are not aware of prior studies investigating the association between BMI and atherosclerotic events in CKD. Our findings regarding reduced risk for CKD progression among participants with CKD who had a BMI in the overweight/obese range were robust even after extensive adjustment for demographic and clinical factors including proteinuria. Moreover, we found that a BMI <20 kg/m² was associated with increased risk all-cause mortality, even after adjusting for serum albumin. A similar paradoxical association between BMI and adverse outcomes has been reported in underweight patients undergoing maintenance hemodialysis who experience an increased risk of death.^{39;40} This issue has not been as comprehensively evaluated in individuals with non-dialysis-dependent CKD. In a study of participants in the Modification of Diet in Renal Disease (MDRD) Study, BMI did not appear to be an independent predictor of all-cause mortality.⁴¹ Our finding of lower mortality risk with BMI ≥30 kg/m² is consistent with analyses of NHANES data and studies involving male veterans that found a significant inverse association between BMI and all-cause mortality in CKD.^{31;42} Reasons for this paradoxical association are not clear, but multiple hypotheses have been proposed and tested, including: 1) poor diagnostic performance of BMI in assessing body fat content (i.e. low negative predictive value of BMI for obesity) in individuals with CKD⁴³; 2) protein-energy malnutrition and inflammation in underweight patients, which could be caused by comorbid illnesses, oxidative stress, low nutrient intake due to poor appetite, etc.,⁴⁴ and 3) a truly beneficial effect of obesity on mortality in patients with CKD through mechanisms such as a more stable hemodynamic status, and mitigation of deleterious effects of stress responses and heightened sympathetic and renin-angiotensin activity.⁴² The current findings underscore the need for further research to evaluate the relationship between BMI and outcomes in patients with CKD and to determine what represents an ideal BMI for this population.

It is recognized that in the general population a diet high in vegetables, fruits, whole grains, and fish is associated with lower risk of cardiovascular morbidity and mortality.^{8–10;13;29} This benefit might be mediated by favorable effects on BP, glucose, and lipids. In contrast, we did not find an association between “healthy diet” and adverse outcomes. Our findings are consistent with other studies involving individuals with CKD that did not find any association of a “healthy diet” with ESRD incidence⁴⁵ or all-cause mortality.³¹ However, it is possible that the metrics used to define a “healthy diet” in the current study (a diet abundant in fruits, vegetables, whole grains, and fish, and low in sodium and sweets) may not have captured dietary components that are important for people with CKD. Further studies are needed to evaluate in greater detail the dietary components that are associated with improved health in individuals with CKD.

We found that adherence to all four lifestyle factors was associated with a 68% decrease in risk of all-cause mortality compared to adherence to no lifestyle factors. However, the risk did not decrease proportionately to the number of healthy lifestyle factors for the outcomes of CKD progression and atherosclerotic events. It is likely that the *a priori* designation of BMI 20–<25 kg/m² as constituting an ideal BMI confounded the association of adherence to multiple lifestyle factors with outcomes.

Strengths of our study include the large diverse sample of CKD patients with a wide range of decreased kidney function at baseline and the prospective design. However, the study has several limitations. As is the case with any observational study, residual confounding cannot be excluded. However, the study findings are generally consistent with those of prospective studies in other populations. Moreover, given the observational nature of our study, a cause-and-effect association between healthy lifestyle and the clinical outcomes evaluated cannot be established. In this study, physical activity, smoking habits, and diet were self-reported and therefore subject to measurement error, including the potential overestimation of physical activity given the high prevalence of ideal physical activity in our participants versus other studies of individuals with CKD.^{26;27} Nonetheless, we found a robust association between self-reported physical activity and reduced risk for adverse outcomes. Because of the pattern of data collection, we evaluated health behaviors only at baseline and therefore could not take into account changes in these behaviors over time. Furthermore, ascertainment of clinical outcomes, including eGFR estimation, could also be subject to error. However, our findings are robust and, to our knowledge, this represents the first CKD study to report associations between healthy lifestyle and a range of clinical outcomes.

In this CKD cohort, we found that regular physical activity, smoking abstinence, and BMI 25 kg/m² were associated with a range of improved outcomes. In general, our findings reinforce recommendations of clinical care guidelines which recommend lifestyle modifications, and suggest that current physical activity and nonsmoking recommendations for the general population are also applicable to persons with CKD. These findings are of particular significance given the heightened risk for adverse outcomes in patients with CKD. Therefore, further research is needed to investigate the optimal dietary recommendations and BMI levels to prevent disease progression and adverse outcomes among individuals with CKD.

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Figure 1. Multivariable adjusted (model 3) hazard ratios and 95% confidence intervals of CKD progression, atherosclerotic cardiovascular events and all-cause mortality by categories of each healthy lifestyle factor.

Table 1

Baseline Characteristics by Physical Activity and BMI

	Physical Activity#			BMI			
	Inactive (n=849)	<Ideal (n=565)	Ideal (n=1592)	<20 kg/m ² (n=70)	20–<25 kg/m ² (n=430)	25–<30 kg/m ² (n=844)	30 kg/m ² (n=1662)
Age (y)	60.06±10.11	58.34±10.92	57.16±11.33*	53.75±13.17	55.78±12.77	59.20±10.93	58.53±10.25*
Female sex	443 (52.2%)	296 (52.4%)	695 (43.7%)*	54 (77%)	232 (54%)	300 (35.5%)	848 (51%)*
Race/Ethnicity							
Non-Hispanic White	368 (43.3%)	262 (46.4%)	788 (49.5%)*	35 (50%)	238 (55.3%)	441 (52.3%)	704 (42.4%)*
Non-Hispanic Black	426 (50.2%)	237 (41.9%)	658 (41.3%)	29 (41%)	141 (32.8%)	297 (35.2%)	854 (51.4%)
Other	55 (6.5%)	66 (11.7%)	146 (9.2%)	6 (9%)	51 (11.9%)	106 (12.6%)	104 (6.3%)
Annual Household Income (US\$)							
\$20,000	320 (37.7%)	160 (28.3%)	332 (20.9%)*	21 (30%)	102 (23.7%)	196 (23.2%)	493 (29.7%)*
\$20,001 – 50,000	212 (25%)	155 (27.4%)	376 (23.6%)	11 (16%)	97 (22.6%)	205 (24.3%)	430 (25.9%)
\$50,001 – 100,000	138 (16.3%)	94 (16.6%)	395 (24.8%)	14 (20%)	99 (23%)	193 (22.9%)	321 (19.3%)
>\$100,000	50 (5.9%)	54 (9.6%)	237 (14.9%)	5 (7%)	55 (12.8%)	125 (14.8%)	156 (9.4%)
“Don’t wish to answer”	129 (15.2%)	102 (18.1%)	252 (15.8%)	19 (27%)	77 (17.9%)	125 (14.8%)	262 (15.8%)
Educational Attainment							
<High school	165 (19.4%)	104 (18.4%)	196 (12.3%)*	19 (27%)	54 (12.6%)	104 (12.3%)	288 (17.3%)*
High school graduate	210 (24.7%)	99 (17.5%)	259 (16.3%)	9 (13%)	82 (19.1%)	142 (16.8%)	335 (20.2%)
Some college	276 (32.5%)	176 (31.2%)	467 (29.4%)	15 (21%)	111 (25.8%)	241 (28.6%)	552 (33.2%)
College graduate	198 (23.3%)	186 (32.9%)	669 (42%)	27 (39%)	183 (42.6%)	356 (42.2%)	487 (29.3%)
Moderate physical activity (min/wk)	0	80 [55–120]	375 [233–640]*	125 [20–360]	180 [15–420]	180 [20–450]	120 [0–360]*
BMI (kg/m ²)	34.10 (9.21)	31.98 (7.63)	31.06 (7.13)*	18.51 (1.31)	23.01 (1.33)	27.62 (1.42)	37.29 (6.84)*
Current smoker	148 (17.4%)	87 (15.4%)	165 (10.4%)*	24 (34%)	86 (20.0%)	111 (13.2%)	179 (10.8%)*
“Healthy diet” Score**	2.28 (1.14)	2.55 (1.17)	2.61 (1.23)*	2.57 (1.20)	2.60 (1.26)	2.58 (1.17)	2.45 (1.21)*
Diabetes	432 (50.9%)	276 (48.8%)	659 (41.4%)*	15 (21%)	119 (27.7%)	308 (36.5%)	925 (55.7%)*
Dyslipidemia	710 (83.6%)	463 (81.9%)	1255 (78.8%)*	27 (39%)	292 (67.9%)	685 (81.2%)	1424 (85.7%)*

	Physical Activity [#]			BMI			
	Inactive (n=849)	<Ideal (n=565)	Ideal (n=1592)	<20 kg/m ² (n=70)	20–<25 kg/m ² (n=430)	25–<30 kg/m ² (n=844)	30 kg/m ² (n=1662)
Hypertension	763 (89.9%)	481 (85.1%)	1314 (82.5%)*	49 (70%)	326 (75.8%)	698 (82.7%)	1485 (89.4%)*
Any CVD	344 (40.5%)	180 (31.9%)	468 (29.4%)*	13 (19%)	117 (27.2%)	269 (31.9%)	593 (35.7%)*
CHF	100 (11.8%)	50 (8.8%)	129 (8.1%)*	4 (6%)	24 (5.6%)	74 (8.8%)	177 (10.6%)*
Stroke	96 (11.3%)	54 (9.6%)	135 (8.5%)	4 (6%)	40 (9.3%)	73 (8.6%)	168 (10.1%)
PVD	72 (8.5%)	44 (7.8%)	84 (5.3%)*	8 (11%)	21 (4.9%)	55 (6.5%)	116 (7%)
Systolic BP (mmHg)	129.38 (21.69)	128.05 (21.44)	125.75 (21.03)*	124.50 (24.27)	125.39 (23.61)	126.53 (20.91)	128.13 (20.78)*
Diastolic BP (mmHg)	70.14 (12.21)	71.34 (12.61)	71.71 (12.81)*	70.75 (11.55)	70.91 (12.77)	71.82 (12.58)	70.97 (12.64)
Hemoglobin A1C (%)	6.70 (1.54)	6.73 (1.56)	6.46 (1.43)*	6.00 (1.26)	6.13 (1.33)	6.37 (1.36)	6.83 (1.56)*
Total Cholesterol (mg/dL)	182.20 (42.81)	182.79 (44.58)	182.86 (43.26)	183.60 (40.17)	184.82 (44.89)	184.62 (44.79)	181.07 (42.33)
LDL Cholesterol (mg/dL)	101.54 (35.62)	103.30 (35.49)	102.84 (34.63)	100.42 (30.43)	101.77 (35.16)	104.79 (36.37)	101.72 (34.53)
eGFR (ml/min/1.73 m ²)	40.95 (13.09)	41.68 (12.81)	45.38 (13.70)*	42.74 (15.00)	43.44 (14.54)	43.23 (13.32)	43.55 (13.30)
Urine Protein (g/24 h)	0.22 [0.07–0.95]	0.19 [0.07–0.93]	0.14 [0.07–0.71]*	0.13 [0.07–0.41]	0.16 [0.07–0.72]	0.14 [0.07–0.67]	0.19 [0.08–0.93]*
ACEi or ARB use	582 (68.8%)	387 (69%)	1077 (68%)	31 (44%)	251 (58.9%)	535 (63.7%)	1229 (74.3%)*

Note: Values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation or median [interquartile range]. Conversion factor for cholesterol in mg/dL to mmol/L, ×0.02586.

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; LDL= Low density lipoprotein. ACEi, angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker; PVD, peripheral vascular disease; CHF, congestive heart failure

[#] Physical activity categorized as ideal (moderate 150 min/wk, vigorous 75 min/wk, or moderate + vigorous 150 min/wk), less than ideal (not inactive but not meeting criteria for ideal) and inactive (no reported leisure time physical activity).²²

* P value <0.05

** range is 0–5

Table 2

Baseline Characteristics by Smoking Status and Diet Score

	Smoking Status			Diet Score					
	Current (n=400)	Past (n=1259)	Never (n=1347)	0 (n=129)	1 (n=501)	2 (n=873)	3 (n=848)	4 (n=524)	5 (n=131)
Age (y)	55.94±10.12	61.04±9.38	56.23±12.00 *	54.17±12.24	57.39±11.24	58.14±11.20	58.38±10.85	59.24±10.18	60.45±10.10 *
Female sex	194 (48.5%)	515 (40.9%)	725 (53.8%) *	50 (38.8%)	240 (47.9%)	397 (45.5%)	420 (49.5%)	251 (47.9%)	76 (58%) *
Race/Ethnicity									
Non-Hispanic White	128 (32%)	648 (51.5%)	642 (47.7%) *	56 (43.4%)	212 (42.3%)	381 (43.6%)	435 (51.3%)	260 (49.6%)	74 (56.5%) *
Non-Hispanic Black	257 (64.3%)	506 (40.2%)	558 (41.4%)	66 (51.2%)	252 (50.3%)	410 (47%)	335 (39.5%)	215 (41%)	43 (32.8%)
Other	15 (3.8%)	105 (8.3%)	147 (10.9%)	7 (5.4%)	37 (7.4%)	82 (9.4%)	78 (9.2%)	49 (9.4%)	14 (10.7%)
Annual Household Income (US\$)									
\$ 20,000	175 (43.8%)	317 (25.2%)	320 (23.8%) *	35 (27.1%)	157 (31.3%)	246 (28.2%)	222 (26.2%)	128 (24.4%)	24 (18.3%)
\$20,001 – 50,000	81 (20.3%)	361 (28.7%)	301 (22.3%)	40 (31%)	130 (25.9%)	221 (25.3%)	206 (24.3%)	113 (21.6%)	33 (25.2%)
\$50,001 – 100,000	56 (14%)	249 (19.8%)	322 (23.9%)	26 (20.2%)	96 (19.2%)	180 (20.6%)	175 (20.6%)	117 (22.3%)	33 (25.2%)
\$>100,000	21 (5.3%)	142 (11.3%)	178 (13.2%)	12 (9.3%)	48 (9.6%)	92 (10.5%)	97 (11.4%)	72 (13.7%)	20 (15.3%)
“Don’t wish to answer”	67 (16.8%)	190 (15.1%)	226 (16.8%)	16 (12.4%)	70 (14%)	134 (15.3%)	148 (17.5%)	94 (17.9%)	21 (16%)
Educational Attainment									
< High school	109 (27.3%)	211 (16.8%)	145 (10.8%) *	19 (14.7%)	98 (19.6%)	131 (15%)	118 (13.9%)	85 (16.2%)	14 (10.7%) *
High school graduate	93 (23.3%)	242 (19.2%)	233 (17.3%)	24 (18.6%)	112 (22.4%)	197 (22.6%)	144 (17%)	82 (15.6%)	9 (6.9%)
Some college	144 (36%)	390 (31%)	385 (28.6%)	46 (35.7%)	159 (31.7%)	274 (31.4%)	290 (34.2%)	119 (22.7%)	31 (23.7%)
College graduate	54 (13.5%)	416 (33%)	583 (43.3%)	40 (31%)	132 (26.3%)	271 (31%)	295 (34.8%)	238 (45.4%)	77 (58.8%)
Moderate physical activity (min/wk)	60 [0–315]	140 [0–375]	180 [10–420] *	140 [0–360]	120 [0–360]	120 [0–360]	140 [0–390]	240 [60–483]	200 [90–420] *
BMI (kg/m ²)	29.96 (7.56)	32.25 (7.51)	32.58 (8.39) *	33.45 (8.43)	32.45 (8.18)	32.24 (8.42)	32.38 (7.58)	31.06 (7.53)	30.73 (7.23) *
Current smoker	400 (100%)	0	0 *	21 (16.3%)	78 (15.6%)	135 (15.5%)	99 (11.7%)	59 (11.3%)	8 (6.1%) *
“Healthy diet” Score **	2.30 (1.16)	2.53 (1.17)	2.55 (1.24) *	0	1.00 (0.00)	2.00 (0)	3.00 (0)	4.00 (0)	5.00 (0) *
Diabetes	171 (42.8%)	626 (49.7%)	570 (42.3%) *	49 (38%)	219 (43.7%)	401 (45.9%)	398 (46.9%)	242 (46.2%)	58 (44.3%)
Dyslipidemia	314 (78.5%)	1071 (85.1%)	1043 (77.4%) *	103 (79.8%)	406 (81%)	709 (81.2%)	695 (82%)	417 (79.6%)	98 (74.8%)

	Smoking Status			Diet Score				
	Current (n=400)	Past (n=1259)	Never (n=1347)	0 (n=129)	1 (n=501)	2 (n=873)	3 (n=848)	4 (n=524)
Hypertension	349 (87.3%)	1103 (87.6%)	1106 (82.1%)*	116 (89.9%)	442 (88.2%)	748 (85.7%)	725 (85.5%)	428 (81.7%)
Any CVD	150 (37.5%)	505 (40.1%)	337 (25%)*	35 (27.1%)	171 (34.1%)	297 (34%)	298 (35.1%)	153 (29.2%)
CHF	39 (9.8%)	153 (12.2%)	87 (6.5%)*	14 (10.9%)	46 (9.2%)	91 (10.4%)	81 (9.6%)	40 (7.6%)
Stroke	55 (13.8%)	127 (10.1%)	103 (7.6%)*	10 (7.8%)	46 (9.2%)	77 (8.8%)	90 (10.6%)	48 (9.2%)
PVD	40 (10%)	108 (8.6%)	52 (3.9%)*	4 (3.1%)	41 (8.2%)	59 (6.8%)	64 (7.5%)	23 (4.4%)
Systolic BP (mmHg)	130.33 (23.39)	128.20 (21.53)	125.35 (20.37)*	127.43 (21.24)	127.45 (20.44)	127.73 (22.45)	126.96 (20.61)	127.63 (22.05)
Diastolic BP (mmHg)	73.66 (13.42)	70.16 (12.52)	71.44 (12.36)*	73.11 (12.80)	71.25 (12.88)	71.51 (12.59)	70.85 (12.75)	71.30 (12.25)
Hemoglobin A1C (%)	6.62 (1.55)	6.64 (1.47)	6.51 (1.49)	6.64 (1.67)	6.64 (1.61)	6.53 (1.39)	6.59 (1.51)	6.57 (1.45)
Total Cholesterol (mg/dL)	183.54 (46.55)	181.25 (44.42)	183.72 (41.36)	184.70 (45.96)	184.27 (42.50)	181.81 (44.38)	181.55 (44.33)	183.54 (40.96)
LDL Cholesterol (mg/dL)	102.50 (36.51)	100.40 (35.54)	104.60 (34.08)*	104.65 (37.40)	103.85 (34.28)	101.03 (35.25)	101.91 (36.03)	103.69 (33.42)
eGFR (ml/min/1.73m ²)	41.97 (13.88)	42.43 (12.96)	44.80 (13.81)*	43.39 (13.34)	41.51 (12.63)	43.36 (13.90)	44.10 (13.30)	44.14 (14.08)
Urine Protein (g/24 h)	0.31 [0.09–1.29]	0.17 [0.07–0.76]	0.14 [0.07–0.70]*	0.4 [0.08–1.55]	0.26 [0.08–0.94]	0.16 [0.07–0.82]	0.17 [0.08–0.81]	0.12 [0.07–0.68]
ACEi or ARB use	242 (61.1%)	886 (70.7%)	918 (68.4%)*	92 (71.3%)	349 (70.2%)	592 (68.2%)	583 (68.8%)	349 (67.1%)
								81 (62.3%)

Note: Values for categorical variables are given as number (percentage); values for continuous variables are given as mean $\pm$ standard deviation or median [interquartile range]. Conversion factor for cholesterol in mg/dL to mmol/L, $\times 0.02586$.

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; LDL= Low density lipoprotein. ACEi= angiotensin converting enzyme inhibitor. ARB= angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; PVD, peripheral vascular disease; CHF, congestive heart failure

* P value <0.05

** range is 0–5

Table 3

Baseline Characteristics by Healthy Lifestyle Score

Variable	Healthy Lifestyle Score				
	0 (n=166)	1 (n=1031)	2 (n=1250)	3 (n=484)	4 (n=75)
Age (y)	56.98 (10.01)	58.99 (10.62)	58.18 (10.83)	57.16 (12.00)	57.49 (12.53) *
Female sex	86 (51.8%)	518 (50.2%)	556 (44.5%)	232 (47.9%)	42 (56%) *
Race/Ethnicity					
Non-Hispanic White	54 (32.5%)	453 (43.9%)	587 (47%)	273 (56.4%)	51 (68%) *
Non-Hispanic Black	107 (64.5%)	488 (47.3%)	558 (44.6%)	155 (32%)	13 (17%)
Other	5 (3%)	90 (8.7%)	105 (8.4%)	56 (11.6%)	11 (15%)
Annual Household Income (US\$)					
\$20,000	77 (46.4%)	342 (33.2%)	304 (24.3%)	83 (17.1%)	6 (8%) *
\$20,001 – \$50,000	35 (21.1%)	280 (27.2%)	301 (24.1%)	109 (22.5%)	18 (24%)
\$50,001 – \$100,000	20 (12%)	171 (16.6%)	288 (23%)	124 (25.6%)	24 (32%)
>\$100,000	6 (3.6%)	83 (8.1%)	148 (11.8%)	91 (18.8%)	13 (17%)
Educational Attainment					
<High school	48 (28.9%)	180 (17.5%)	188 (15.1%)	47 (9.7%)	2 (3%) *
High school graduate	37 (22.3%)	230 (22.3%)	231 (18.5%)	65 (13.4%)	5 (7%)
Some college	65 (39.2%)	354 (34.3%)	364 (29.1%)	123 (25.4%)	13 (17%)
College graduate	16 (9.6%)	267 (25.9%)	466 (37.3%)	249 (51.4%)	55 (73%)
Moderate Physical Activity (min/wk)	0 [0–45]	0 [0–90]	270 [135–540]	360 [210–660]	360 [240–570] *
BMI (kg/m ²)	31.79 (8.05)	34.38 (8.33)	32.23 (7.49)	28.39 (6.41)	23.01 (1.23) *
Current smoker	166 (100%)	157 (15.2%)	70 (5.6%)	7 (1.4%)	0 (0%) *
“Healthy Diet” Score ***	1.97 (0.88)	2.08 (0.94)	2.43 (1.16)	3.56 (1.14)	4.27 (0.45) *
Diabetes	74 (44.6%)	541 (52.5%)	547 (43.8%)	181 (37.4%)	24 (32%) *
Dyslipidemia	129 (77.7%)	881 (85.5%)	1007 (80.6%)	363 (75%)	48 (64%) *
Hypertension	143 (86.1%)	922 (89.4%)	1077 (86.2%)	364 (75.2%)	52 (69%) *

Variable	Healthy Lifestyle Score				
	0 (n=166)	1 (n=1031)	2 (n=1250)	3 (n=484)	4 (n=75)
Any CVD	69 (41.6%)	381 (37%)	404 (32.3%)	123 (25.4%)	15 (20%)*
CHF	16 (9.6%)	120 (11.6%)	113 (9%)	26 (5.4%)	4 (5%)
Stroke	25 (15.1%)	101 (9.8%)	114 (9.1%)	42 (8.7%)	3 (4%)
PVD	18 (10.8%)	92 (8.9%)	65 (5.2%)	25 (5.2%)	0 (0%)
Systolic BP (mmHg)	130.45 (22.40)	128.84 (20.76)	126.80 (22.05)	124.29 (19.46)	123.35 (24.07)
Diastolic BP (mmHg)	71.71 (12.62)	71.15 (12.40)	71.42 (13.09)	70.80 (12.14)	69.60 (10.49)
Hemoglobin A1C (%)	6.69 (1.66)	6.76 (1.52)	6.53 (1.48)	6.39 (1.41)	6.05 (1.13)
Total cholesterol (mg/dL)	184.52 (45.52)	182.08 (44.54)	181.55 (42.22)	186.43 (43.68)	180.68 (38.59)
LDL Cholesterol (mg/dL)	103.30 (38.01)	102.01 (35.18)	102.01 (35.28)	105.65 (33.55)	97.75 (32.32)
eGFR (ml/min/1.73m ²)	41.56 (14.31)	41.33 (12.73)	44.39 (13.43)	45.86 (14.18)	44.68 (15.31)
Urine Protein (g/24 h)	0.32 [0.09–1.26]	0.23 [0.08–0.97]	0.15 [0.07–0.71]	0.12 [0.07–0.60]	0.12 [0.06–0.41]
ACEi or ARB use	106 (64.6%)	709 (69%)	881 (70.7%)	309 (64.4%)	41 (55%)

* p<0.05.

** range is 0–5

Note: Values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation or median [interquartile range]. Conversion factor for cholesterol in mg/dL to mmol/L, ×0.02586.

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; LDL= Low density lipoprotein. ACEi= angiotensin converting enzyme inhibitor. ARB= angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; PVD, peripheral vascular disease; CHF, congestive heart failure

Table 4
Event Rates and Hazard Ratios for Chronic Kidney Disease Progression in Each Risk Group

	No. of Events	Event Rate (/1,000 person-y)	Model 1 ^a	Model 2 ^b	Model 3 ^c
Physical Activity ^{***}					
Inactive	235	69.1	1.00 (reference)	1.00 (reference)	1.00 (reference)
<Ideal	152	60.5	0.91 (0.74–1.12)	0.88 (0.72–1.09)	1.01 (0.82–1.24)
Ideal	339	46.6	0.74 (0.63–0.88)	0.72 (0.61–0.86)	0.98 (0.82–1.17)
BMI					
<20 kg/m ²	16	58.0	0.89 (0.53–1.51)	1.13 (0.63–1.93)	1.02 (0.57–1.83)
20–<25 kg/m ²	112	61.4	1.00 (reference)	1.00 (reference)	1.00 (reference)
25–<30 kg/m ²	192	50.4	0.78 (0.62–0.99)	0.66 (0.52–0.83)	0.75 (0.58–0.97)
30 kg/m ²	406	55.8	0.84 (0.68–1.04)	0.57 (0.46–0.71)	0.61 (0.45–0.82)
Smoking					
Current	133	88.7	1.00 (reference)	1.00 (reference)	1.00 (reference)
Past	306	56.0	0.72 (0.58–0.88)	0.82 (0.66–1.02)	0.79 (0.64–0.98)
Never	287	46.1	0.60 (0.49–0.74)	0.69 (0.55–0.85)	0.68 (0.55–0.84)
“Healthy Diet” Score					
0	38	69.8	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	123	57.7	0.81 (0.56–1.17)	0.83 (0.57–1.20)	0.95 (0.65–1.38)
2	212	56.1	0.85 (0.60–1.20)	0.86 (0.61–1.22)	1.08 (0.76–1.53)
3	208	55.1	0.85 (0.60–1.20)	0.90 (0.64–1.28)	1.20 (0.84–1.71)
4	122	52.7	0.86 (0.59–1.24)	0.91 (0.63–1.32)	1.18 (0.81–1.72)
5	23	36.1	0.64 (0.38–1.09)	0.85 (0.50–1.43)	0.95 (0.56–1.62)
Healthy Lifestyle Score					
0	55	86.9	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	279	64.9	0.74 (0.56–0.99)	0.75 (0.56–1.01)	0.75 (0.56–1.02)
2	280	49.4	0.63 (0.47–0.85)	0.67 (0.50–0.90)	0.75 (0.56–1.01)
3	98	43.5	0.59 (0.42–0.82)	0.70 (0.50–0.98)	0.88 (0.63–1.25)
4	14	41.4	0.63 (0.35–1.14)	0.96 (0.53–1.76)	1.04 (0.56–1.91)

Note: chronic kidney disease progression defined as end-stage renal disease or 50% estimated glomerular filtration rate reduction. Unless otherwise indicated, values are given as hazard ratio (95% confidence interval).

Abbreviations: BMI, body mass index; CCID, clinical center identification;

* Model 1: Stratified by CCID.

** Physical activity categorized as ideal (moderate 150 min/wk, vigorous 75 min/wk, or moderate + vigorous 150 min/wk), less than ideal (not inactive but not meeting criteria for ideal) and inactive (no reported leisure time physical activity).²²

[†] Model 2: Stratified by CCID and adjusted for demographic (age, sex, race/ethnicity, education) and clinical variables (diabetes, dyslipidemia, hypertension, any cardiovascular disease, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

[‡] Model 3: Stratified by CCID and adjusted for variables in model 2 + splines of estimated glomerular filtration rate and log 24 urine protein. Models with BMI as main predictor were also adjusted for serum albumin and waist circumference.

Table 5

Hazard Ratios of Atherosclerotic Events and All-Cause Mortality in Each Risk Group

	Atherosclerotic Cardiovascular Events					All-Cause Mortality				
	No. of Events	Event Rate (/ 1,000 person-y)	Model 1 *	Model 2 †	Model 3 ‡	No. of Events	Event Rate (/ 1,000 person-y)	Model 1 *	Model 2 †	Model 3 ‡
Physical Activity**										
Inactive	123	29.9	1.00 (reference)	1.00 (reference)	1.00 (reference)	185	40.4	1.00 (reference)	1.00 (reference)	1.00 (reference)
<Ideal	73	25.1	0.89 (0.67–1.20)	1.00 (0.74–1.34)	1.01 (0.75–1.36)	81	25.2	0.65 (0.50–0.85)	0.74 (0.57–0.96)	0.77 (0.59–1.00)
Ideal	159	19.0	0.67 (0.53–0.85)	0.81 (0.64–1.03)	0.84 (0.66–1.07)	171	18.8	0.50 (0.41–0.62)	0.60 (0.49–0.74)	0.64 (0.52–0.79)
BMI										
<20 kg/m²	7	21.1	0.84 (0.38–1.85)	1.25 (0.56–2.78)	1.32 (0.59–2.98)	14	37.9	1.43 (0.80–2.57)	1.93 (1.07–3.49)	2.11 (1.13–3.93)
20–<25 kg/m²	52	24.0	1.00 (reference)	1.00 (reference)	1.00 (reference)	60	24.9	1.00 (reference)	1.00 (reference)	1.00 (reference)
25–<30 kg/m²	92	21.0	0.84 (0.6–1.18)	0.64 (0.45–0.9)	0.67 (0.46–0.96)	124	26.1	1.03 (0.75–1.40)	0.84 (0.62–1.15)	0.81 (0.58–1.13)
30 kg/m²	204	24.0	0.93 (0.69–1.27)	0.6 (0.44–0.82)	0.70 (0.45–1.07)	239	25.6	0.97 (0.73–1.28)	0.71 (0.53–0.96)	0.64 (0.43–0.96)
Smoking										
Current	64	34.7	1.00 (reference)	1.00 (reference)	1.00 (reference)	94	44.6	1.00 (reference)	1.00 (reference)	1.00 (reference)
Past	177	28.1	0.86 (0.64–1.15)	0.74 (0.55–1.00)	0.73 (0.54–0.99)	217	31.1	0.76 (0.60–0.97)	0.61 (0.47–0.79)	0.63 (0.48–0.81)
Never	114	15.8	0.47 (0.35–0.64)	0.55 (0.40–0.76)	0.55 (0.40–0.75)	126	16.2	0.39 (0.30–0.51)	0.43 (0.33–0.57)	0.45 (0.34–0.60)
“Healthy Diet” Score										
0	13	19.6	1.00 (reference)	1.00 (reference)	1.00 (reference)	16	21.4	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	60	23.8	1.24 (0.68–2.26)	1.06 (0.58–1.93)	1.05 (0.57–1.91)	79	28.3	1.31 (0.77–2.25)	1.10 (0.64–1.88)	1.03 (0.60–1.77)
2	115	25.9	1.39 (0.78–2.47)	1.14 (0.64–2.03)	1.17 (0.65–2.08)	140	28.7	1.43 (0.85–2.40)	1.18 (0.70–1.98)	1.15 (0.69–1.94)
	95	21.6	1.18 (0.66–2.10)	0.97 (0.54–1.73)	0.98 (0.55–1.77)	122	25.6	1.30 (0.77–2.19)	1.08 (0.64–1.82)	1.09 (0.65–1.84)
4	58	21.9	1.22 (0.67–2.24)	1.14 (0.62–2.09)	1.17 (0.64–2.16)	66	22.6	1.16 (0.67–2.00)	1.02 (0.59–1.77)	1.00 (0.58–1.73)
5	14	19.9	1.15 (0.54–2.47)	1.10 (0.51–2.37)	1.01 (0.47–2.18)	14	18.2	1.02 (0.50–2.11)	0.87 (0.42–1.83)	0.77 (0.37–1.61)
Healthy Lifestyle Score										
0	29	37.9	1.00 (reference)	1.00 (reference)	1.00 (reference)	44	50.7	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	142	27.7	0.74 (0.50–1.11)	0.71 (0.47–1.06)	0.73 (0.48–1.09)	192	33.8	0.65 (0.47–0.90)	0.61 (0.44–0.86)	0.65 (0.47–0.91)
2	126	19.1	0.53 (0.35–0.80)	0.57 (0.38–0.86)	0.58 (0.38–0.88)	145	20.4	0.41 (0.29–0.58)	0.42 (0.30–0.60)	0.46 (0.32–0.65)

	Atherosclerotic Cardiovascular Events					All-Cause Mortality				
	No. of Events	Event Rate (/ 1,000 person-y)	Model 1 *	Model 2 [†]	Model 3 [‡]	No. of Events	Event Rate (/ 1,000 person-y)	Model 1 *	Model 2 [†]	Model 3 [‡]
3	52	20.8	0.60 (0.38–0.95)	0.80 (0.50–1.28)	0.84 (0.52–1.34)	52	18.9	0.40 (0.27–0.60)	0.47 (0.31–0.72)	0.51 (0.34–0.77)
4	6	15.1	0.44 (0.18–1.07)	0.78 (0.32–1.91)	0.75 (0.30–1.86)	4	9.2	0.21 (0.08–0.60)	0.31 (0.11–0.87)	0.32 (0.11–0.90)

Note: Unless otherwise indicated, values are given as hazard ratio (95% confidence interval).

Abbreviations: BMI, body mass index; CCID, clinical center identification.

* Model1: Stratified by CCID

[†]Model 2: Stratified by CCID and adjusted for demographic (age, sex, race/ethnicity, education) and clinical variables (diabetes, dyslipidemia, hypertension, any cardiovascular disease, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker)

[‡]Model 3: Stratified by CCID and adjusted for variables in model 2 + estimated glomerular filtration rate and proteinuria. Models with BMI as main predictor were also adjusted for serum albumin and waist circumference.

** There was a significant interaction between physical activity and age (p=0.0008) for atherosclerotic cardiovascular events. The fully adjusted values are 0.62 (0.46–0.85) for ideal physical activity (vs. inactive) for individuals younger than 65 y and 1.35 (0.89–2.06) for participants aged 65 y or older.