

RESEARCH LETTERS

Association of Cardiovascular Health Measures With Cardiovascular Disease and Mortality in CKD: A UK Biobank Study



To the Editor:

CKD is a serious global public health issue associated with high morbidity and mortality.¹ In 2010, the American Heart Association developed Life's Simple 7 (LS7), a composite score including 4 lifestyle factors (smoking, BMI, diet, physical activity) and 3 metabolic factors (cholesterol level, BP, and glycemic status) to reflect cardiovascular health.² Several studies have shown that adherence to combined lifestyle factors may reduce the risk of CVD and mortality among patients with CKD³⁻⁵; however, evidence regarding associations of LS7 score with future cardiovascular outcomes and mortality among patients with CKD is scarce.

Thus, we prospectively examined the associations of LS7 score with incident CVD events, ischemic heart disease (IHD), heart failure (HF), and all-cause mortality among patients with CKD using data from the UK Biobank Study, a large prospective cohort study.⁶

The current analysis included 21,071 patients with CKD after excluding individuals with incomplete information on any LS7 factor (n = 6,537), prevalent CVD

cases (n = 7,334), or indications of kidney replacement therapy (n = 52; Fig S1). Participants were considered to have CKD if they had eGFR <60 mL/min/1.73 m², albuminuria (UACR >30 mg/g), or a CKD diagnosis based on ICD-10 (N18) via linkage with electronic health records.

To account for the competing risk of death, we used multivariable-adjusted Fine-Gray subdistribution hazard models to estimate the associations of LS7 score with risks of incident CVD and subtypes of CVD events. For all-cause mortality, multivariable-adjusted Cox regression models were used. HRs were adjusted for age, sex, ethnicity, education, Townsend deprivation index (TDI), alcohol intake, sleep duration, family history of CVD, and baseline eGFR.

At recruitment, among 21,071 CKD patients (mean age, 59.0 years; 9,363 men [44.4%]), 28.0%, 29.4%, 24.0%, 13.0%, and 5.7% had 0-1, 2, 3, 4, and ≥5 LS7 factors at ideal levels, respectively. Table 1 shows participants with higher scores were more likely to be younger, women, higher educated, less deprived, non-daily drinkers, with lower levels of BMI, BP, cholesterol, and HbA_{1c}. Further, they tended to have higher baseline eGFR and lower UACR. Participants included in the current analyses were more likely to be men, White, higher educated, less deprived, daily drinkers, and have higher BMI than those who were excluded owing to missing values (absolute standardized differences >10%; Table S1).

Table 1. Baseline Characteristics According to LS7 Score Among Patients With CKD in the UK Biobank Study (N = 21,071)

Characteristic	LS7 Score				
	≤1	2	3	4	≥5
No. of participants	5,899 (28.0%)	6,187 (29.4%)	5,046 (24.0%)	2,730 (13.0%)	1,209 (5.7%)
Age, y	60.4 ± 7.0	59.3 ± 7.5	58.8 ± 7.9	57.8 ± 8.2	54.8 ± 8.8
Male sex	3,427 (58.1%)	2,882 (46.6%)	1,949 (38.6%)	834 (30.6%)	271 (22.4%)
College or university degree	544 (9.2%)	619 (10.0%)	583 (11.6%)	355 (13.0%)	188 (15.6%)
White descent	5,498 (94.7%)	5,761 (94.5%)	4,719 (94.5%)	2,580 (95.5%)	1,142 (95.3%)
TDI	-0.80 ± 3.27	-1.19 ± 3.12	-1.42 ± 3.00	-1.55 ± 2.97	-1.71 ± 2.81
Sleep duration of 7-8 h/d	3,675 (62.3%)	4,043 (65.4%)	3,421 (67.8%)	1,884 (69.0%)	871 (72.0%)
Daily drinker	1,344 (22.8%)	1,303 (21.1%)	974 (19.3%)	469 (17.2%)	177 (14.6%)
Family history of CVD	3,522 (59.7%)	3,710 (60.0%)	2,940 (58.3%)	1,581 (57.9%)	618 (51.1%)
BMI, kg/m ²	31.3 ± 5.2	29.3 ± 5.0	27.3 ± 4.8	25.1 ± 4.3	23.0 ± 3.0
Systolic BP, mm Hg	148.2 ± 19.5	147.8 ± 20.1	145.0 ± 21.7	141.2 ± 22.5	129.1 ± 22.1
Diastolic BP, mm Hg	86.1 ± 10.9	86.7 ± 11.0	85.0 ± 11.3	82.7 ± 11.2	77.3 ± 11.3
Antihypertension medication	3,370 (57.1%)	2,629 (42.5%)	1,721 (34.1%)	678 (24.8%)	164 (13.6%)
Total cholesterol, mg/dL	213.5 ± 51.5	223.5 ± 46.5	223.3 ± 44.4	217.7 ± 43.7	203.5 ± 40.0
Lipid-lowering medication	2,944 (49.9%)	1,760 (28.5%)	889 (17.6%)	302 (11.1%)	60 (5.0%)
HbA _{1c} , mmol/mol	44.5 ± 13.9	37.8 ± 8.8	35.8 ± 6.7	34.7 ± 4.3	33.7 ± 3.3
Diabetes medication	1,357 (23.0%)	416 (6.7%)	119 (2.4%)	17 (0.6%)	1 (0.1%)
Baseline eGFR category					
<45 mL/min/1.73 m ²	308 (5.2%)	289 (4.7%)	179 (3.6%)	90 (3.3%)	25 (2.1%)
45-60 mL/min/1.73 m ²	1,397 (23.7%)	1,597 (25.8%)	1,302 (25.8%)	619 (22.7%)	250 (20.7%)
≥60 mL/min/1.73 m ²	4,194 (71.1%)	4,301 (69.5%)	3,565 (70.7%)	2,021 (74.0%)	934 (77.3%)
UACR, mg/g ^a	49.8 [32.9-99.0]	45.9 [32.7-84.9]	45.3 [33.1-82.0]	46.3 [33.9-80.4]	47.1 [34.2-83.7]

Data given as mean ± SD, median [interquartile range], or number (%). Abbreviations: BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA_{1c}, hemoglobin A_{1c}; UACR, urinary albumin-creatinine ratio.

^aAvailable for 16,346 patients. A total of 12,784 CKD patients were defined based on UACR ≥30 mg/g only.

Table 2. HRs and PAFs for Incident CVD and Mortality According to LS7 Score

	Categorical Analysis by LS7 Score					P for Linear Trend	Continuous Analysis, per Each LS7 Factor	PAF% ^b (<4 vs ≥4 LS7 Factor)
	≤1	2	3	4	≥5			
Incident CVD								
Cases/person-year	1,798/55,467	1,464/61,234	997/51,412	420/28,607	136/12,999		4,815/209,728	
HR (95% CI) ^a	1.00 (reference)	0.84 (0.78-0.90)	0.74 (0.69-0.81)	0.62 (0.55-0.69)	0.54 (0.45-0.64)	<0.001	0.87 (0.85-0.89)	
Incident IHD								
Cases/person-year	870/59,651	651/64,999	397/54,298	154/29,859	43/13,435		2,115/222,243	
HR (95% CI) ^a	1.00 (reference)	0.80 (0.72-0.89)	0.65 (0.58-0.73)	0.51 (0.43-0.60)	0.38 (0.28-0.52)	<0.001	0.82 (0.79-0.85)	34.6 (27.3-41.2)
Incident HF								
Cases/person-year	383/62,633	268/67,406	159/55,696	73/30,432	13/13,584		896/229,750	
HR (95% CI) ^a	1.00 (reference)	0.77 (0.66-0.91)	0.63 (0.52-0.76)	0.59 (0.46-0.76)	0.30 (0.17-0.52)	<0.001	0.81 (0.77-0.86)	29.5 (16.8-40.3)
All-cause mortality								
Cases/person-year	839/61,938	581/66,155	383/54,341	155/29,612	55/13,158		2,013/225,204	
HR (95% CI) ^a	1.00 (reference)	0.76 (0.69-0.85)	0.68 (0.60-0.77)	0.56 (0.47-0.66)	0.57 (0.43-0.75)	<0.001	0.84 (0.81-0.87)	28.7 (19.3-37.0)

Abbreviations: HR, hazard ratio; PAF, population attributable fraction.

^aAdjusted for age at recruitment (continuous, years), sex, ethnicity (White, non-White), TDI (continuous), and education (college or university degree, other professional qualifications, A/AS levels or equivalent or O levels/GCSEs, none of the above), alcohol intake (never/special occasions, monthly to weekly, daily), sleep duration (<7, 7-8, >8 h/d), family history of CVD, and baseline eGFR.

^bTheoretically estimates the proportion of each outcome in this study population that could have been prevented if the population had ≥4 LS7 factors at ideal levels.

There were 4,815 composite CVD, 2,115 IHD, and 896 HF events, along with 2,013 total deaths. Comparing LS7 score ≥5 with 0-1, the adjusted HRs were 0.54 (95% CI, 0.45-0.64) for total CVD, 0.38 (95% CI, 0.28-0.52) for IHD, 0.30 (95% CI, 0.17-0.52) for HF, and 0.57 (95% CI, 0.43-0.75) for all-cause mortality. The adjusted PAFs for incident CVD and mortality associated with LS7 score <4 were 25.2 (95% CI, 20.0-30.0) and 28.7 (95% CI, 19.3-37.0), suggesting that 25.2% and 28.7% of these cases would not have happened if all participants had ≥4 ideal LS7 factors (Table 2).

The results were consistent in subgroup analyses stratified by age, sex, TDI, and baseline eGFR; no significant effect modifications were observed (Fig S2). The results were also largely unchanged when we excluded cases within 2 years of follow-up (Table S2), performed the analyses among CKD patients defined by baseline eGFR only (Table S3), or additionally adjusted for both eGFR and UACR (n = 16,346) (Table S4).

This is among the first studies to investigate the association of LS7 score with risks of a wide range of CVD events and all-cause mortality among patients with CKD. Several limitations should be considered. First, self-reported, 1-time assessment of LS7 factors may result in some misclassification bias. Second, chronicity data for eGFR and UACR were not available. Third, UACR was only available among a subset population (n = 156,595), so selection bias may exist. Fourth, some baseline characteristics of participants included and excluded from the analysis owing to missing information on LS7 factors were slightly different, which may lead to selection bias. Fifth, a lack of ethnic diversity (94.7% White) may limit generalizability to other populations. Finally, owing to the observational design, residual confounding cannot be completely ruled out.

In conclusion, our findings suggest that higher LS7 score is associated with a substantially lower risk of CVD events and mortality among patients with CKD, which has important public health implications and clinical relevance. Our data support that primary prevention should be promoted among patients with CKD. Additionally, the observed dose-response relationship indicates physicians should encourage patients that their cardiovascular health could benefit by adopting even 1 additional ideal LS7 factor.

Tingting Geng, PhD, Yan-Bo Zhang, MBBS, Qi Lu, MBBS, Zhenzhen Wan, MPH, An Pan, PhD and Gang Liu, PhD

Supplementary Material

Supplementary File (PDF)

Figures S1-S2; Item S1; Tables S1-S4.

Article Information

Authors' Affiliations: Department of Nutrition and Food Hygiene, Hubei Key Laboratory of Food Nutrition and Safety, Ministry of Education Key Lab of Environment and Health, and State Key

Laboratory of Environmental Health (Incubating), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (TG, QL, ZW, GL); and Department of Epidemiology and Biostatistics, Ministry of Education Key Laboratory of Environment and Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (TG, YBZ, AP).

Address for Correspondence: Gang Liu, PhD (email: liugang026@hust.edu.cn) or An Pan, PhD (email: panan@hust.edu.cn), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, 13 Hangkong Rd, Wuhan 430030, China.

Authors' Contributions: Study concept and design: TG, GL, AP; data acquisition: GL; data analysis/interpretation: TG, Y-BZ, QL, ZW, GL; supervision or mentorship: GL, AP. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated, and resolved, including with documentation in the literature if appropriate.

Support: GL was funded by grants from National Natural Science Foundation of China (82073554), the Hubei Province Science Fund for Distinguished Young Scholars (2021CFA048), and the Fundamental Research Funds for the Central Universities (2021GCRC076). AP was supported by grants from National Natural Science Foundation of China (81930124, 82021005) and the Fundamental Research Funds for the Central Universities (2021GCRC075). TG is funded by grants from the China Postdoctoral Science Foundation (2021M691129). Funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Financial Disclosure: The authors declare they have no other relevant financial interests.

Acknowledgements: We are grateful to all UK Biobank participants and all involved in building the UK Biobank study.

Data Sharing: This research was conducted using the UK Biobank Resource under Application Number 68307. The UK Biobank data are available on application to the UK Biobank (www.ukbiobank.ac.uk/).

Peer Review: Received September 7, 2021. Evaluated by 2 external peer reviewers, with direct editorial input from a Statistics/Methods Editor, an Associate Editor, and the Editor-in-Chief. Accepted in revised form January 21, 2022.

Publication Information: © 2022 by the National Kidney Foundation, Inc. Published online March 18, 2022 with doi [10.1053/j.ajkd.2022.01.432](https://doi.org/10.1053/j.ajkd.2022.01.432)

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The Modified CKiD Study Estimated GFR Equations for Children and Young Adults Under 25 Years of Age: Performance in a European Multicenter Cohort



To the Editor:

The CKiD creatinine- and cystatin C–based glomerular filtration rate (GFR) estimating equations have recently been modified by incorporation of continuous age- and sex-dependent k values to yield less biased internal validation results in chronic kidney disease (CKD) patients aged under 25 years.¹ Here we report an external validation of these CKiDU25 equations in the European Kidney

Table 1. Patient Characteristics of the Cohorts

	Children With Creatinine and Cystatin C Measured (N = 2,293)	Young Adults (N = 1,816)	
		With Creatinine Measured (n = 1,816)	With Cystatin C Measured (n = 348)
Age, y	11.9 (2.3-17.8)	20.0 (18.0-24.6)	18.9 (18.0-24.1)
Female sex	949 (41%)	846 (47%)	144 (41%)
Body mass index, kg/m ²	18 (14-29)	21 (16-31)	22 (15-35)
Body surface area, m ²	1.29 (0.54-2.05)	1.68 (1.29-2.14)	1.73 (1.33-2.36)
Plasma/serum creatinine, μmol/L	52 (19-155)	75 (41-191)	78 (38-196)
Plasma/serum cystatin, mg/L	0.96 (0.61-2.72)	–	0.96 (0.62-2.39)
mGFR, mL/min/1.73 m ²	97 (28-169)	92 (31-141)	91 (30-134)
mGFR <75 mL/min/1.73 m ²	503 (22%)	543 (30%)	95 (27%)

Children defined as aged 2.0-17.9 years; young adults as 18.0-24.9 years. Continuous variables given as median (2.5 and 97.5 percentiles).