Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Life's Essential 8 Health Behaviors and All-Cause Mortality Across CKM Stages: Accounting for Construct Overlap in NHANES 2005–2014

Yang Zhang
Third Clinical College, Liaoning University of Traditional Chinese Medicine

Yanyuan Wu
Zhejiang Cancer Hospital

Hongxi Zhang
Third Clinical College, Liaoning University of Traditional Chinese Medicine

Xiaochen Liu
liuxiaochen@cmu.edu.cn

Third Clinical College, Liaoning University of Traditional Chinese Medicine

Article

Keywords: cardiovascular-kidney-metabolic syndrome, Life's Essential 8, health behaviors, all-cause mortality, NHANES, complex survey

Posted Date: September 21st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10628515/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Cardiovascular-kidney-metabolic (CKM) syndrome staging and Life's Essential 8 (LE8) share several metabolic and cardiovascular constructs. We evaluated stage-specific associations of the LE8 health behavior score with all-cause mortality and compared their magnitude with associations for total LE8. Using NHANES 2005–2014 linked to the 2019 public-use mortality files, we included 5,949 participants aged 30–79 years (893 deaths) and applied complex survey-weighted Cox models, global Wald and stage-interaction tests, restricted cubic splines, and marginal standardization. Per 10-point higher behavior score, adjusted hazard ratios were 0.807 (95% CI, 0.724–0.900), 0.952 (0.835–1.086), and 0.831 (0.787–0.877) for CKM stages 0–2, 3, and 4, respectively. The global Wald, stage-interaction, and nonlinearity P values were 9.36×10^{-10}, 0.0484, and 1.18×10^{-7}. Corresponding standardized 5-year mortality risk differences were − 0.300, − 0.589, and − 1.885 percentage points; the stage 3 interval was wide. The global comparison of stage-specific slopes between the behavior and total LE8 scores yielded P = 0.094 (Holm-adjusted P = 0.120 for stage 3). Higher behavior scores were associated with lower mortality in stages 0–2 and 4. These observational findings support joint interpretation of relative and absolute risks and require validation in independent cohorts.

Introduction

Cardiovascular-kidney-metabolic syndrome places obesity, metabolic risk factors, chronic kidney disease, and clinical cardiovascular disease within a continuous staging framework that describes the accumulation of multisystem risk [1–3]. Life's Essential 8 (LE8) assesses cardiovascular health across eight domains: diet, physical activity, nicotine exposure, sleep, body weight, blood lipids, blood glucose, and blood pressure [4]. Because both CKM staging and LE8 integrate metabolic and cardiovascular information, analyses combining them must distinguish genuine stage-specific associations from mechanical gradients created by shared constructs.

Cohort evidence supports an association between more advanced CKM stages and higher mortality risk [5, 6]. Studies of populations with CKM stages 0–3 and advanced CKM have associated higher LE8 or health behavior scores with lower mortality [7–10], and studies spanning CKM stages 0–4 or cardiovascular events have extended this observation [11–13]. Associations of LE8 with mortality and life expectancy have generally been directionally consistent in general-population and young-adult cohorts [14–17]. Findings in chronic kidney disease, diabetes, and metabolic syndrome also support lower risk at higher scores [18–20], with similar patterns reported in high-risk populations such as people with previous cardiovascular disease [21–23]. Two systematic reviews and meta-analyses provide pooled evidence [24, 25]. Although this literature establishes the broad direction of association, joint CKM–LE8 analyses still require a systematic hierarchy for evaluating shared constructs, within-stage associations, and between-stage heterogeneity, together with absolute risks, nonlinear patterns, and the stability of results to score components and missing-data selection.

To reduce construct overlap, we specified the four-component health behavior score—diet, physical activity, nicotine exposure, and sleep—as the primary exposure and total LE8 and the health factor score as prespecified comparators, without treating the behavior score as fully independent of CKM. In the NHANES 2005–2014 adult cohort, we estimated stage-specific associations between the health behavior score and all-cause mortality within CKM stages 0–2, 3, and 4; tested stage heterogeneity and nonlinearity; quantified absolute changes in 5-year mortality risk; and compared the association strengths of the health behavior and total LE8 scores. The analysis plan anticipated that the sample size and compositional heterogeneity of CKM stage 3 could produce wide intervals, and stage-localizing findings were interpreted in relation to global tests and multiplicity adjustment.

Results

Participant characteristics

The primary analysis included 5,949 participants and 893 deaths. Across the original five CKM stages, stages 0, 1, 2, 3, and 4 included 512, 1,216, 2,162, 493, and 1,566 participants, with 9, 42, 162, 155, and 525 deaths, respectively. Because the number of deaths in stage 0 was below the prespecified minimum of 20 events per primary stratum, the primary model used the prespecified combined stages 0–2 group. After grouping, CKM stages 0–2, stage 3, and stage 4 included 3,890, 493, and 1,566 participants, representing 70.6%, 5.7%, and 23.7% of the complex survey-weighted population, respectively. Weighted mean behavior scores were 73.45, 69.55, and 62.92 (Table 1).

Table 1
Sample characteristics by CKM stage and stage group

Classification	Level	Participants	Deaths	Weighted proportion (%)	Mean behavior score (SE)
CKM staging	Stage 0	512	9	10.6	76.75 (0.68)
CKM staging	Stage 1	1,216	42	23.8	73.08 (0.47)
CKM staging	Stage 2	2,162	162	36.1	72.73 (0.34)
CKM staging	Stage 3	493	155	5.7	69.55 (0.77)
CKM staging	Stage 4	1,566	525	23.7	62.92 (0.49)
CKM stage group	Stages 0–2	3,890	213	70.6	73.45 (0.26)
CKM stage group	Stage 3	493	155	5.7	69.55 (0.77)
CKM stage group	Stage 4	1,566	525	23.7	62.92 (0.49)

Note: Weighted proportions and mean behavior scores account for the NHANES complex survey design. SE, standard error.

Health behavior score and all-cause mortality

The global Wald test of the three stage-specific slopes being jointly equal to zero yielded P = 9.36×10^{-10}, indicating a statistical association between the health behavior score and all-cause mortality in at least one CKM stage group. Per 10-point higher score, the adjusted HR was 0.807 (95% CI, 0.724–0.900) for CKM stages 0–2, 0.952 (0.835–1.086) for stage 3, and 0.831 (0.787–0.877) for stage 4 (Fig. 2 and Table 2). The confidence intervals for stages 0–2 and stage 4 were entirely below HR = 1, corresponding to relative risk reductions of approximately 19.3% and 16.9%, respectively. The stage 3 estimate was less precise; therefore, the principal stage-specific information came from stages 0–2 and stage 4.

Table 2
Primary Cox model of the LE8 health behavior score and all-cause mortality within CKM stage groups

Analysis	Effect estimate or statistic	95% CI	P value	Holm-adjusted P value	Model sample size/deaths
3-df global Wald test	F = 20.04	—	9.36×10^{-10}	—	5,949/893
CKM stages 0–2	HR 0.807	0.724–0.900	0.000107	0.000214	5,949/893
CKM Stage 3	HR 0.952	0.835–1.086	0.463	0.463	5,949/893
CKM Stage 4	HR 0.831	0.787–0.877	1.57×10^{-11}	4.71×10^{-11}	5,949/893
CKM stage group×behavior score interaction	F = 3.15	—	0.0484	—	5,949/893

Note: HRs are reported per 10-point higher health behavior score. The three stage-specific HRs were obtained from the same complex survey-weighted Cox model containing a CKM stage group×behavior score interaction and adjusted for prespecified covariates. The sample size/death count shown is the total for the model, not the count within each stage.

The interaction test between CKM stage group and behavior score yielded P = 0.0484, suggesting some heterogeneity in slopes across stages. Together with the stratified estimates, this result showed stable inverse associations in stages 0–2 and stage 4, whereas the interval for stage 3 was wide. The restricted cubic spline test for nonlinearity yielded P = 1.18×10^{-7}, indicating that the association with mortality risk varied across score levels (Fig. 3). Figure 2 presents the stage-specific HRs from the primary linear model, whereas Fig. 3 shows nonlinear curves across the score range.

5-year absolute risk

After increasing the behavior score by 10 points within the same CKM stage group, the covariate-standardized absolute changes in 5-year mortality risk were − 0.300 percentage points (95% CI, − 0.461 to − 0.140), − 0.589 percentage points (− 2.022 to 0.844), and − 1.885 percentage points (− 2.364 to −

1.405) for stages 0–2, stage 3, and stage 4, respectively (Supplementary Fig. S1 and Supplementary Table S2). The risk-difference intervals for stages 0–2 and stage 4 were below zero, with the largest absolute decrease in stage 4; the interval for stage 3 was wide. Figure 3 presents nonlinear curves on the relative hazard scale, whereas Supplementary Fig. S1 presents the standardized 5-year absolute risk differences.

When described by behavior-score tertile, 5-year cumulative mortality risks in the low, middle, and high groups were 3.84%, 1.68%, and 0.45% for CKM stages 0–2 and 14.64%, 9.77%, and 7.71% for stage 4, decreasing as the score increased. Corresponding estimates for stage 3 were 10.61%, 21.37%, and 7.47%, showing a nonmonotonic pattern. In conjunction with the cell-specific sample sizes and interval widths, the nine-cell analysis further highlighted consistent risk gradients in stages 0–2 and stage 4 (Supplementary Fig. S2).

Construct-overlap comparison of the health behavior and total LE8 scores

The global test comparing the three stage-specific slopes of the health behavior and total LE8 scores yielded P = 0.094. Expressed as differences in log HRs, the values were 0.087 (95% CI, − 0.069 to 0.243), 0.220 (0.010 to 0.430), and 0.029 (− 0.088 to 0.147) for CKM stages 0–2, stage 3, and stage 4, respectively (Table 3). For stage 3, the unadjusted P value was 0.040 and the Holm-adjusted P value was 0.120. Considering the global test and multiplicity adjustment together, the overall association strengths of the two scores were similar, and the nominal stage-specific difference did not alter the overall comparative conclusion.

Table 3
Stage-specific differences between the health behavior and total LE8 score slopes

Analysis	Difference in log HR	95% CI	Unadjusted P value	Holm-adjusted P value	Model sample size/deaths
3-df global difference test	—	—	0.094	—	5,118/677
CKM stages 0–2	0.087	−0.069 to 0.243	0.276	0.552	5,118/677
CKM Stage 3	0.220	0.010–0.430	0.040	0.120	5,118/677
CKM Stage 4	0.029	−0.088 to 0.147	0.627	0.627	5,118/677

Note: Positive values indicate that the log HR for the health behavior score was higher than that for the total LE8 score. Stage-specific differences were obtained from the same comparative model, and the sample size/death count shown is the model total. The global test yielded P = 0.094, and the stage 3 localizing comparison yielded Holm-adjusted P = 0.120; together, the results indicate similar overall association strengths for the two scores.

Sensitivity analyses

After excluding deaths within 2 years of baseline, HRs were 0.801, 0.966, and 0.836 for CKM stages 0–2, stage 3, and stage 4, respectively; using attained age as the time scale produced corresponding HRs of 0.804, 0.936, and 0.821. Under alternative eGFR/CKM rules, inverse-probability missingness weighting, multiple imputation, and a nonignorable-missingness stress test, HRs remained below 1 in stages 0–2 and stage 4, whereas stage 3 estimates fluctuated around HR = 1 with wide intervals (Supplementary Tables S3–S5). Global-test conclusions remained stable after each of the five survey cycles was omitted in turn (Supplementary Fig. S4). The global Schoenfeld residual test yielded χ^2=46.69 with 22 degrees of freedom (P = 0.00161), indicating overall deviation from the proportional hazards assumption; P values were 0.000977 for the behavior-score term and 0.0516 for the CKM stage group×behavior-score term. In the prespecified, triggered exploratory analysis of 5-year restricted mean survival time, a 10-point higher score corresponded to standardized mean differences of 0.0068, 0.0140, and 0.0453 years in stages 0–2, stage 3, and stage 4, respectively; all were positive, with the largest difference in stage 4. These point estimates were directionally consistent with the primary analysis. Because the available RMST variance implementation did not fully account for uncertainty from model-parameter estimation and the complex survey design, this analysis provided directional support only (Supplementary Tables S5 and S9).

After exclusion of the nicotine component, HRs in the three CKM stage groups were 0.880, 0.972, and 0.844. After exclusion of diet, physical activity, or sleep in turn, HRs in stages 0–2 and stage 4 generally remained below 1. These findings indicate that the primary associations in stages 0–2 and stage 4 were not driven by a single behavior component and were stable across component definitions. In stage 3, excluding diet or physical activity produced relative changes in the log effect that exceeded the prespecified threshold, indicating greater dependence on score composition; interpretation of this stage should therefore emphasize the global test and the stable stratified findings (Supplementary Fig. S3). Results for missing data, model assumptions, cycle robustness, and staging-algorithm validation are provided in Supplementary Tables S4–S6.

Discussion

The principal findings concern differences across CKM stages and effect scales. The global test supported an overall association between the health behavior score and all-cause mortality, and stage-specific estimates in CKM stages 0–2 and stage 4 showed lower mortality risk per 10-point higher score. On the absolute scale, stage 4 had the largest standardized decrease in 5-year mortality risk. The interaction test and restricted cubic splines showed that both stage heterogeneity and nonlinearity affected interpretation. The relative-effect and absolute-risk intervals for stage 3 were wide, indicating that larger samples are needed to characterize this stage more precisely. The global comparison of the health behavior and total LE8 scores showed that their overall association strengths were similar.

Recent studies in populations with CKM stages 0–3 and advanced CKM have associated higher LE8 or health behavior scores with lower mortality [7–10], and studies spanning stages 0–4 and cardiovascular

events have reported findings in the same direction [11–13]. General-population and young-adult cohorts have further linked LE8 with mortality risk and life expectancy [14–17]. Studies in chronic kidney disease, diabetes, and metabolic syndrome support the presence of this association across different metabolic-risk settings [18–20], and findings in high-risk populations such as people with previous cardiovascular disease are broadly consistent [21–23]. Two systematic reviews and meta-analyses provide pooled evidence [24, 25]. The contribution of the present study is not simply to repeat that higher scores are associated with lower risk, but to treat shared CKM–LE8 constructs as a design constraint; separately quantify within-stage associations, between-stage heterogeneity, standardized absolute risk, and differences in score structure; and incorporate the precision of stage 3 estimates into prespecified evidence boundaries.

In this study, the relative HRs per 10-point higher score were similar in CKM stages 0–2 and stage 4, but the standardized absolute reduction in 5-year risk was larger in stage 4. This pattern illustrates how higher stage-specific baseline risk can amplify differences on the absolute scale despite similar relative associations. Previous research has linked diet, physical activity, nicotine exposure, and sleep with pathways involving inflammatory burden, insulin sensitivity, blood-pressure regulation, lipid metabolism, and functional reserve [26–28], providing biological context for the observed direction. We did not directly measure longitudinal changes in these pathways; mechanistic interpretations therefore remain contextual rather than demonstrated by this study. CKM stage 3 is jointly defined by subclinical cardiovascular risk, kidney status, and a prediction threshold, and the stage 3 sample was relatively small. These features may together account for the wide intervals and can be evaluated in future studies with larger samples and more detailed characterization of stage 3 composition.

The construct-overlap sensitivity analyses directly inform the credibility of the primary findings. CKM staging and total LE8 share information on body weight, blood pressure, blood glucose, and blood lipids, while PREVENT risk inputs also overlap with the nicotine domain [1–4]. The four-component health behavior score reduces direct overlap with health factors, but shared causes, correlated measurement, and mathematical coupling within the staging algorithm may remain. After each component was removed, HRs remained below 1 in CKM stages 0–2 and stage 4, indicating that associations in these groups were not driven by a single behavior component. Stage 3 was more sensitive to removal of diet and physical activity, indicating greater dependence on score composition. Together with the global comparison of the health behavior and total LE8 scores, the evidence supports focusing the main conclusion on cross-component stable associations in stages 0–2 and stage 4, while treating stage 3 as a heterogeneous stage requiring further decomposition and validation.

Before analysis, we distinguished the global association test from the stage-interaction test, reported both relative effects and standardized 5-year absolute risks, and used variance estimation and Rao–Wu resampling that accounted for the complex survey design. Component deletion, alternative staging, time-scale, missing-data, and leave-one-cycle-out analyses assessed stability from different perspectives; all numerical results were generated under the prespecified analysis plan and underwent consistency

checks. The principal limitations arise from possible residual confounding and reverse causation inherent in the observational design. Diet, physical activity, and sleep were largely self-reported, and a single baseline assessment may not represent long-term change. Complete-case requirements may introduce selection bias, whereas multiple imputation and inverse-probability complete-case weighting rely on their respective modeling assumptions. CKM stage 0 included only nine deaths; the primary analysis therefore prespecified combining stages 0–2 and could not separately estimate differences among stages 0, 1, and 2. The stage 3 sample and some cells of the nine-cell stratification were small, limiting precision. Cardiovascular mortality, subgroup analyses, and some sensitivity analyses were exploratory. Leave-one-cycle-out stability indicates internal robustness within NHANES, but external validation in independent cohorts remains necessary.

From a public-health perspective, the health behavior score provides within-stage risk-stratification information in CKM stages 0–2 and stage 4, and the standardized absolute-risk findings further show larger observable risk differences in the higher-risk stage. These results define population-level association strengths and risk distributions and provide quantitative evidence for subsequent studies of intervention effects. Future research could reproduce the same CKM grouping, behavior score, and global testing framework in independent populations; use repeated behavior measurements to assess temporal change; characterize stage 3 composition in larger samples; and evaluate the relation between improvements in health behavior and changes in clinical outcomes using appropriate causal designs or intervention studies.

In the NHANES 2005–2014 adult cohort, higher LE8 health behavior scores were associated with lower all-cause mortality risk in CKM stages 0–2 and stage 4, with the largest standardized absolute reduction in 5-year risk in stage 4; estimates for stage 3 were less precise. The stage-interaction and nonlinear analyses indicate that a single overall linear effect does not adequately summarize all CKM stages. The overall association strengths of the health behavior and total LE8 scores were similar. In view of the observational design, construct overlap, measurement error, and residual confounding, these findings define the evidence boundaries of stage-specific associations and provide explicit targets for replication in independent cohorts, longitudinal measurement, and intervention research.

Methods

Study design and data sources

This observational cohort study used the complex survey sample of the US National Health and Nutrition Examination Survey (NHANES) across five cycles from 2005–2006 through 2013–2014, linked to the National Center for Health Statistics 2019 public-use mortality files [29, 30]. Reporting followed the STROBE statement [31].

Study population

The initial demographic sample comprised 50,965 participants. Because classification of CKM stage 3 incorporates the PREVENT 10-year total cardiovascular disease risk equation, which applies to adults aged 30–79 years [3], we restricted the study to this age range. Sequential requirements for valid mortality follow-up, complex survey design variables, CKM stage, and all four health behavior components produced 6,418 eligible participants before screening for completeness of the primary adjustment covariates. Requiring complete primary adjustment covariates yielded a primary analytic sample of 5,949 participants. The sequence of exclusions and numbers at each step are shown in Fig. 1 and Supplementary Table S1. The target population was noninstitutionalized US adults represented by NHANES; all estimates accounted for sampling weights, strata, and clusters.

CKM staging

Following the American Heart Association CKM framework, participants were classified according to the highest stage whose criteria they met [1, 2]. Stage 4 was defined by self-reported coronary heart disease, myocardial infarction, angina, heart failure, or stroke. Stage 3 required no clinical cardiovascular disease, fulfillment of at least stage 1 or stage 2 criteria, and a PREVENT 10-year total cardiovascular disease risk ≥ 20%. Stage 2 was defined by hypertension, diabetes, or chronic kidney disease. Stage 1 was defined by BMI ≥ 25 kg/m², waist circumference ≥ 102 cm in men or ≥ 88 cm in women, or prediabetes, in the absence of stage 2–4 criteria. All remaining participants were classified as stage 0. Because NHANES lacks subclinical imaging data, stage 3 was identified only through the high-risk PREVENT pathway.

Hypertension was defined as mean systolic blood pressure ≥ 130 mmHg, mean diastolic blood pressure ≥ 80 mmHg, or current antihypertensive medication use. Diabetes was defined by self-reported diabetes, glucose-lowering medication use, HbA1c ≥ 6.5%, or fasting plasma glucose ≥ 126 mg/dL. Prediabetes was defined, among participants without diabetes, as HbA1c 5.7%–6.4% or fasting plasma glucose 100–125 mg/dL. Chronic kidney disease was defined as eGFR < 60 mL/min/1.73 m² or UACR ≥ 30 mg/g. PREVENT used the base model for 10-year total cardiovascular disease risk on a 0–1 scale, applicable at ages 30–79 years, with inputs for age, sex, systolic blood pressure, antihypertensive treatment, total cholesterol, HDL cholesterol, statin treatment, diabetes, current smoking, eGFR, and BMI. When a required input was missing, stage 3 classification was recorded as unknown and was not automatically reassigned to stage 2. Clinical cardiovascular disease took priority as stage 4. Before outcome analysis, the primary analysis prespecified grouping participants as stages 0–2, stage 3, and stage 4, with at least 20 deaths required in each primary stratum; this grouping does not imply complete clinical homogeneity among stages 0, 1, and 2. Kidney function was estimated using the race-free 2021 CKD-EPI creatinine equation, and staging was recalculated using the 2009 CKD-EPI equation in a sensitivity analysis [32]. Full operational definitions are provided in Supplementary Table S7.

LE8 health behavior score

The primary exposure was the four-component LE8 health behavior score, comprising diet, physical activity, nicotine exposure, and sleep. The diet component was the Healthy Eating Index 2015 (HEI-2015) total score (0–100). Participants were included only if both 24-hour dietary recalls were valid and WTDR2D > 0; arithmetic means of the two days of Food Patterns Equivalents Database amounts and nutrient intakes were calculated before scoring the 13 HEI-2015 components. Physical activity was standardized to moderate-intensity-equivalent minutes per week (moderate-intensity minutes + 2×vigorous-intensity minutes) and assigned scores of 0, 20, 40, 60, 80, 90, and 100 for 0, 1–29, 30–59, 60–89, 90–119, 120–149, and ≥ 150 min/week, respectively.

Nicotine exposure was scored as 0, 25, 50, 75, and 100 for current smoking, smoking cessation < 1 year, cessation 1 to < 5 years, cessation ≥ 5 years, and never smoking, respectively; the primary score across all five cycles did not deduct points for secondhand smoke exposure. Sleep duration was scored as 0, 20, 40, 70, 100, 90, and 40 for < 4, 4 to < 5, 5 to < 6, 6 to < 7, 7 to < 9, 9 to < 10, and ≥ 10 h/night, respectively. When all four components were complete, their equally weighted mean yielded the health behavior score on a 0–100 scale. Total LE8 was the equally weighted mean of the four health behaviors and four health factors—BMI, non-HDL cholesterol, blood glucose, and blood pressure—and the health factor score was the equally weighted mean of the latter four components. Because PREVENT includes current smoking, a three-component score excluding nicotine and leave-one-component-out analyses were prespecified. Full variable definitions, cross-cycle harmonization procedures, and scoring rules are provided in Supplementary Table S8.

Outcome and follow-up

The primary outcome was all-cause mortality, with vital status and follow-up time determined from the 2019 public-use linked mortality files [30]. PERMTH_EXM records the number of follow-up months from the Mobile Examination Center (MEC) examination date. Follow-up extended from the baseline examination to death or December 31, 2019; participants presumed alive were censored on that date. Primary relative effects used the full follow-up period, whereas absolute effects were uniformly estimated as 5-year mortality risks. Cardiovascular mortality was considered only as a secondary, exploratory outcome and was not used to strengthen the primary conclusions.

Covariates

The primary adjustment set included age, sex, race and ethnicity, educational attainment, family income-to-poverty ratio, and NHANES survey cycle. Age was modeled using restricted cubic splines with boundary knots at 32 and 75 years and internal knots at 47 and 60 years; survey cycle was modeled as a fixed effect. This adjustment set was frozen before examination of outcome results. On the basis of construct boundaries, BMI, blood pressure, blood glucose, blood lipids, chronic kidney disease, and cardiovascular disease status were not included in the primary adjustment set to avoid duplicate adjustment for information that contributes to CKM staging or LE8.

Statistical analysis

Complex survey-weighted Cox proportional hazards models estimated associations between each 10-point higher health behavior score and all-cause mortality within the three CKM stage groups [33–35]. The sole primary significance test was a 3-degree-of-freedom Wald test of the three stage-specific slopes being jointly equal to zero. A separate 2-degree-of-freedom interaction test between CKM stage group and behavior score assessed stage heterogeneity. Stage-specific HRs and 95% CIs were reported, and the three localizing P values were adjusted using the Holm method [36]. All tests were two-sided with prespecified $\alpha = 0.05$. The primary global test, interaction test, and multiplicity-adjusted localizing comparisons addressed overall association, stage heterogeneity, and localization to specific stages, respectively, and were not treated as substitutes for one another. The proportional hazards assumption was evaluated using Schoenfeld residual tests. An exploratory analysis of 5-year restricted mean survival time was prespecified to be triggered when the global P value was < 0.01; the Cox model remained the primary analysis.

Nonlinearity was evaluated using restricted cubic splines [37]. Boundary knots for the behavior score were 37.202 and 92.190, and internal knots were 64.407 and 81.972, corresponding to the weighted 5th, 35th, 65th, and 95th percentiles. Reference values were 77.898, 72.531, and 63.254 for CKM stages 0–2, stage 3, and stage 4, respectively. Nonlinearity was assessed using a joint Wald test of the corresponding nonlinear spline terms. Five-year absolute risks were obtained by model-based marginal standardization: each participant's behavior score was increased by 10 points within the same CKM stage group and truncated at 100, then compared with the observed-score scenario. Uncertainty in risk differences and in differences between the health behavior and total LE8 score slopes was estimated using 500 Rao–Wu complex survey bootstrap replicates with complete model refitting [38]. The health behavior versus total LE8 comparison used a separate 3-degree-of-freedom global test; localizing comparisons in the three stage groups were Holm-adjusted and interpreted in conjunction with the global result to determine the evidence hierarchy.

The primary analysis used the 2-day dietary weight WTDR2D divided by five. Sampling units and strata were made unique across survey cycles in a nested design, and lonely primary sampling units were handled using a conservative adjustment. Leave-one-cycle-out analyses divided the weight by four; other subsets of cycles were rescaled by the number of included cycles.

The primary analysis used complete cases with complete CKM stage, all four health behaviors, mortality status, follow-up, complex survey design variables, and primary adjustment covariates. Missing covariates were addressed using multiple imputation by chained equations in a sensitivity analysis; mortality, follow-up, survey design variables, CKM stage, and behavior score were not imputed [39]. Stabilized inverse-probability complete-case weights were also used to evaluate selection arising from missing primary adjustment covariates [40], and prespecified delta scenarios were used in a nonignorable-missingness stress test. Other prespecified sensitivity analyses excluded deaths within 2

years of baseline, used alternative eGFR/CKM rules, used attained age as the time scale, removed each behavior component in turn, used a three-component score excluding nicotine, restricted absolute-risk analyses to the region of common support, and omitted each survey cycle in turn. All tests were two-sided. Outside the prespecified primary testing family, secondary and exploratory analyses were interpreted according to their purpose and were not used to expand conclusions on the basis of nominal significance.

Statistical analyses were performed in R version 4.6.0, primarily using survey 4.5, survival 3.8-6, and mice 3.19.0.

Ethics approval

The protocols for each NHANES cycle were approved by the National Center for Health Statistics Research Ethics Review Board, and all participants provided written informed consent. This study was a secondary analysis of publicly available, de-identified NHANES survey data and public-use linked mortality data and involved no new recruitment, direct participant contact, or research intervention. All analyses were conducted in accordance with relevant guidelines and regulations.

Declarations

Additional information

Competing interests:

The authors declare no competing interests.

Author Contribution

Yang Zhang and Yanyuan Wu jointly contributed to conceptualization, data curation, formal analysis, methodology, visualization, and writing—original draft. Hongxi Zhang and Xiaochen Liu jointly contributed to conceptualization, methodology, supervision, project administration, funding acquisition, and writing—review and editing. All authors contributed to interpretation of the results, approved the final version of the manuscript, and agreed to be accountable for all aspects of the work. Yang Zhang and Yanyuan Wu are joint first authors; Hongxi Zhang and Xiaochen Liu are joint corresponding authors.

Acknowledgements

This work was supported by the Liaoning Provincial Science and Technology Joint Program (General Program of the Natural Science Foundation, 2025-MSLH-470; XCL), the Natural Science Foundation of Zhejiang Province (LQN26H050003; WYY), the Zhejiang Traditional Chinese Medicine Science and

Technology Program (2025ZR081; WYY), and the Youth Research Fund of Zhejiang Cancer Hospital (PY2023032 and QN202308; WYY).

Data Availability

NHANES survey data, survey methods, and the 2019 public-use linked mortality files are publicly available through the National Center for Health Statistics [29,30]. In the 2019 public-use linked mortality files, PERMTH_EXM records follow-up months from the MEC examination date, with administrative follow-up ending on December 31, 2019. This study used publicly available, de-identified data and generated no new restricted-access individual-level data. The data sources, variable definitions, staging and scoring algorithms, and statistical methods required for replication are described in the main text and Supplementary Information.The specific datasets used in this analysis (NHANES 2005–2014) can be accessed at the following URL: https://wwwn.cdc.gov/nchs/nhanes/Default.aspx.

References

1. Ndumele, C. E. et al. Cardiovascular-kidney-metabolic health: a Presidential Advisory from the American Heart Association. *Circulation* **148**, 1606–1635. https://doi.org/10.1161/CIR.0000000000001184 (2023).
2. Ndumele, C. E. et al. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic syndrome: a Scientific Statement from the American Heart Association. *Circulation* **148**, 1636–1664. https://doi.org/10.1161/CIR.0000000000001186 (2023).
3. Khan, S. S. et al. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a Scientific Statement from the American Heart Association. *Circulation* 148, 1982–2004 (2023). https://doi.org/10.1161/CIR.0000000000001191
4. Lloyd-Jones, D. M. et al. Life's Essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a Presidential Advisory from the American Heart Association. *Circulation* **146**, e18–e43. https://doi.org/10.1161/CIR.0000000000001078 (2022).
5. Zhu, R. et al. Prevalence of cardiovascular-kidney-metabolic syndrome stages by social determinants of health. *JAMA Netw. Open.* **7**, e2445309. https://doi.org/10.1001/jamanetworkopen.2024.45309 (2024).
6. Li, N. et al. Association between different stages of cardiovascular-kidney-metabolic syndrome and the risk of all-cause mortality. *Atherosclerosis* **397**, 118585. https://doi.org/10.1016/j.atherosclerosis.2024.118585 (2024).
7. Yin, S. et al. Association between Life's Simple 7 and Life's Essential 8 with all-cause and cardiovascular mortality in cardiovascular-kidney-metabolic syndrome population. *Diabetes Res. Clin. Pract.* **231**, 113064. https://doi.org/10.1016/j.diabres.2025.113064 (2026).

8. Wang, Y., Dong, T., Wang, B. & Zhang, P. The association between Life's Essential 8 health behavior component score and all-cause and cardiovascular mortality among U.S. adults with cardiovascular-kidney-metabolic syndrome stages 0–3. *Prev. Med.* **202**, 108360. https://doi.org/10.1016/j.ypmed.2025.108360 (2026).
9. Zhang, J., Yin, L., Liu, Y., Xiao, X. & Shuai, P. Association between the Life's Essential 8 health behaviors score and mortality risk in US adults with cardiovascular-kidney-metabolic syndrome stage 0–3. *Diabetes Metab. J.* https://doi.org/10.4093/dmj.2025.0366 (2025).
10. Tan, S. et al. Association between the Life's Essential 8 health behaviors and prognosis in patients with advanced cardiovascular-kidney-metabolic syndrome. *Eur. J. Prev. Cardiol.* https://doi.org/10.1093/eurjpc/zwaf443 (2025).
11. Niu, R. et al. Life's Essential 8-defined cardiovascular health and mortality risk in cardiovascular-kidney-metabolic health stages 0–4: a cohort study. *J. Epidemiol. Glob Health*. **16**, 91. https://doi.org/10.1007/s44197-026-00590-3 (2026).
12. Tu, D., Zuo, X., Li, P. & Wang, J. Association between the Life's Essential 8 health behaviors score and all-cause mortality in cardiovascular-kidney-metabolic syndrome patients. *Front. Nutr.* **12**, 1612693. https://doi.org/10.3389/fnut.2025.1612693 (2025).
13. Li, M. et al. Life's Essential 8 cardiovascular health, cardiovascular-kidney-metabolic syndrome stages, and incident cardiovascular events: a nationwide 10-year prospective cohort study in China. *Cardiovasc. Diabetol.* **24**, 197. https://doi.org/10.1186/s12933-025-02735-3 (2025).
14. Yi, J., Wang, L., Guo, X. & Ren, X. Association of Life's Essential 8 with all-cause and cardiovascular mortality among US adults: a prospective cohort study from NHANES 2005–2014. *Nutr. Metab. Cardiovasc. Dis.* **33**, 1134–1143. https://doi.org/10.1016/j.numecd.2023.01.021 (2023).
15. Ma, H. et al. Cardiovascular health and life expectancy among adults in the United States. *Circulation* **147**, 1137–1146. https://doi.org/10.1161/CIRCULATIONAHA.122.062457 (2023).
16. Xing, A. et al. Life's Essential 8 cardiovascular health with premature cardiovascular disease and all-cause mortality in young adults: the Kailuan prospective cohort study. *Eur. J. Prev. Cardiol.* **30**, 593–600. https://doi.org/10.1093/eurjpc/zwad033 (2023).
17. Zhang, J. et al. Relation of Life's Essential 8 to the genetic predisposition for cardiovascular outcomes and all-cause mortality: results from a national prospective cohort. *Eur. J. Prev. Cardiol.* **30**, 1676–1685. https://doi.org/10.1093/eurjpc/zwad179 (2023).
18. Chen, H. et al. Life's Essential 8 and mortality in US adults with chronic kidney disease. *Am. J. Nephrol.* **54**, 516–527. https://doi.org/10.1159/000533257 (2023).
19. Li, W. et al. Life's Essential 8 in relation to cardiovascular disease and mortality in individuals with diabetes. *JACC Asia*. **4**, 456–464. https://doi.org/10.1016/j.jacasi.2024.03.007 (2024).
20. Zhou, D. C. et al. Adherence to higher Life's Essential 8 scores is linearly associated with reduced all-cause and cardiovascular mortality among US adults with metabolic syndrome: results from NHANES 2005–2018. *PLoS One*. **19**, e0314152. https://doi.org/10.1371/journal.pone.0314152 (2024).

21. Yang, Y. et al. Association of Life's Essential 8 with mortality among individuals with cardiovascular disease. *Sci. Rep.* **14**, 18520. https://doi.org/10.1038/s41598-024-69603-0 (2024).
22. Huang, L. et al. Life's Essential 8 and risk of all-cause mortality in individuals with cardiovascular diseases: a prospective community-based study. *Clin. Cardiol.* **47**, e24119. https://doi.org/10.1002/clc.24119 (2024).
23. Ni, G. et al. Association of Life's Essential 8 with abdominal aortic calcification and mortality among middle-aged and older individuals. *Diabetes Obes. Metab.* **26**, 5126–5137. https://doi.org/10.1111/dom.15854 (2024).
24. Sebastian, S. A., Shah, Y., Paul, H. & Arsene, C. Life's Essential 8 and the risk of cardiovascular disease: a systematic review and meta-analysis. *Eur. J. Prev. Cardiol.* **32**, 358–373. https://doi.org/10.1093/eurjpc/zwae280 (2025).
25. Li, G., Zhang, Y., Wu, Q., Shi, B. & Chen, D. A systematic review and meta-analysis of the association between cardiovascular health determined by Life's Essential 8 and risk of mortality and major non-communicable diseases. *Front. Cardiovasc. Med.* **12**, 1612056. https://doi.org/10.3389/fcvm.2025.1612056 (2025).
26. Piercy, K. L. et al. The Physical Activity Guidelines for Americans. *JAMA* **320**, 2020–2028. https://doi.org/10.1001/jama.2018.14854 (2018).
27. St-Onge, M. P. et al. Sleep duration and quality: impact on lifestyle behaviors and cardiometabolic health: a Scientific Statement from the American Heart Association. *Circulation* **134**, e367–e386. https://doi.org/10.1161/CIR.0000000000000444 (2016).
28. Krebs-Smith, S. M. et al. Update of the Healthy Eating Index: HEI-2015. *J. Acad. Nutr. Diet.* **118**, 1591–1602. https://doi.org/10.1016/j.jand.2018.05.021 (2018).
29. National Center for Health Statistics. NHANES survey methods and analytic guidelines. August (2026). https://wwwn.cdc.gov/nchs/nhanes/analyticguidelines.aspx (accessed 1.
30. National Center for Health Statistics. Public-Use Linked Mortality Files for NHANES 1999–2018. (2019). https://ftp.cdc.gov/pub/Health_Statistics/NCHS/datalinkage/linked_mortality/ (accessed 1 August 2026).
31. von Elm, E. et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann. Intern. Med.* **147**, 573–577. https://doi.org/10.7326/0003-4819-147-8-200710160-00010 (2007).
32. Inker, L. A. et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl. J. Med.* **385**, 1737–1749. https://doi.org/10.1056/NEJMoa2102953 (2021).
33. Cox, D. R. Regression models and life-tables. *J. R Stat. Soc. Ser. B Stat. Methodol.* **34**, 187–220. https://doi.org/10.1111/j.2517-6161.1972.tb00899.x (1972).
34. Lumley, T. Analysis of complex survey samples. *J. Stat. Softw.* **9**, 1–19. https://doi.org/10.18637/jss.v009.i08 (2004).
35. Therneau, T. M. & Grambsch, P. M. *Modeling survival data: extending the Cox model* (Springer, 2000). https://doi.org/10.1007/978-1-4757-3294-8

36. Holm, S. A simple sequentially rejective multiple test procedure. *Scand. J. Stat.* **6**, 65–70 (1979).
37. Durrleman, S. & Simon, R. Flexible regression models with cubic splines. *Stat. Med.* **8**, 551–561. https://doi.org/10.1002/sim.4780080504 (1989).
38. Rao, J. N. K. & Wu, C. F. J. Resampling inference with complex survey data. *J. Am. Stat. Assoc.* **83**, 231–241. https://doi.org/10.1080/01621459.1988.10478591 (1988).
39. White, I. R., Royston, P. & Wood, A. M. Multiple imputation using chained equations: issues and guidance for practice. *Stat. Med.* **30**, 377–399. https://doi.org/10.1002/sim.4067 (2011).
40. Robins, J. M., Hernán, M. A. & Brumback, B. Marginal structural models and causal inference in epidemiology. *Epidemiology* **11**, 550–560. https://doi.org/10.1097/00001648-200009000-00011 (2000).

Figures

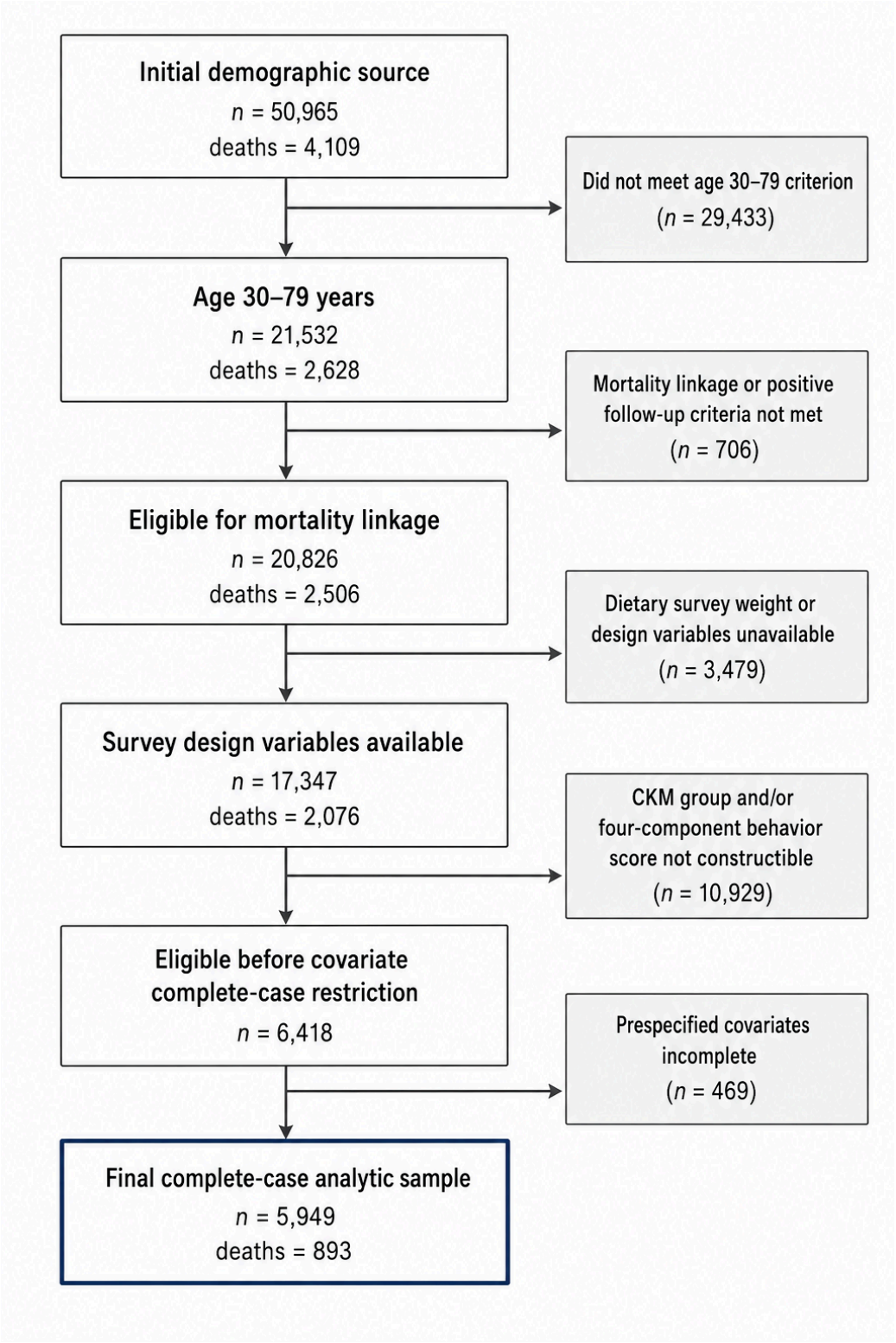


Figure 1

Participant inclusion flow. Across five NHANES cycles from 2005–2014, the initial demographic sample of 50,965 participants was sequentially screened for age, mortality follow-up, complex survey design variables, CKM stage and the four-component health behavior score, and completeness of the primary adjustment covariates, yielding a primary analytic sample of 5,949 participants with 893 deaths during follow-up. All counts are unweighted.

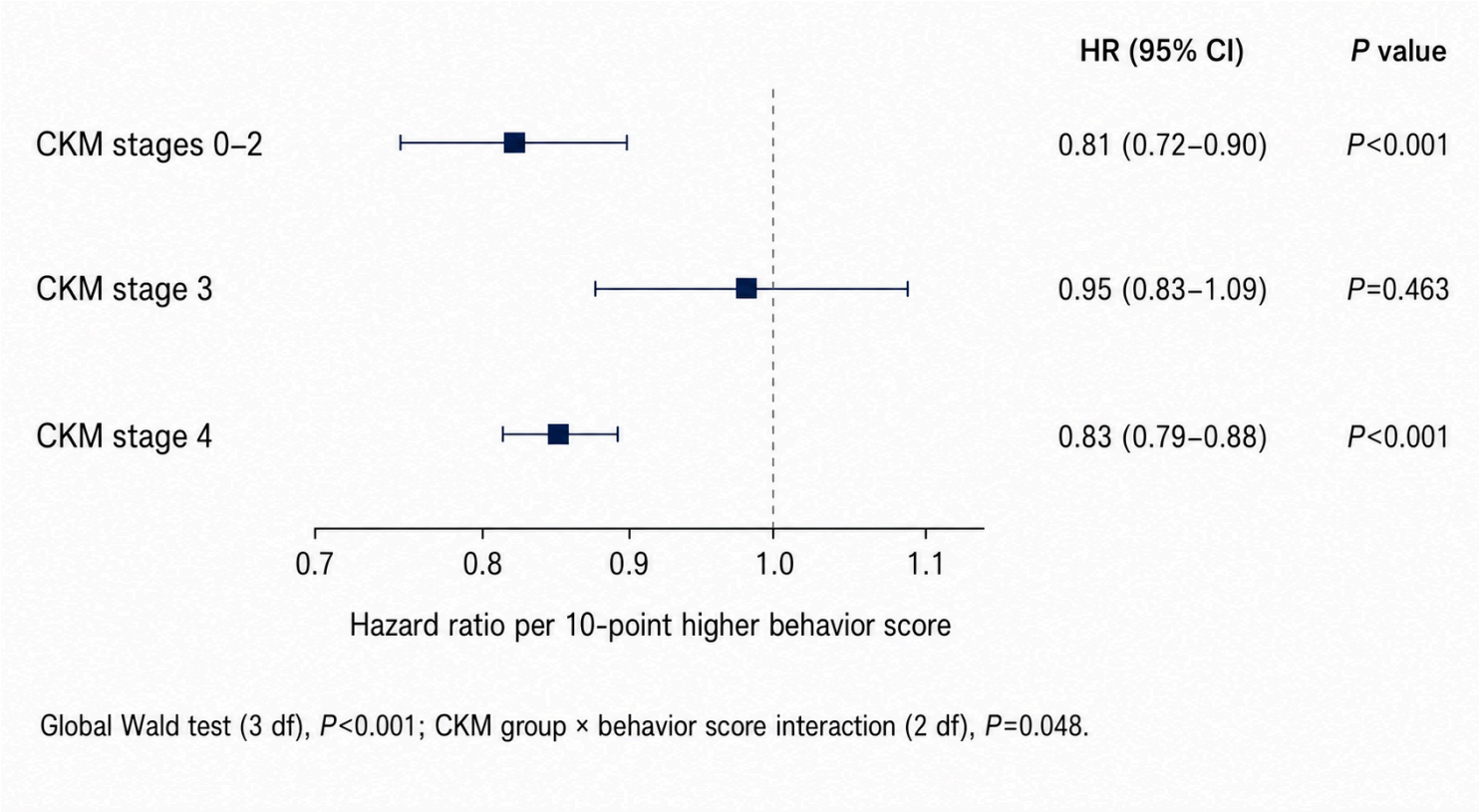


Figure 2

Association between the LE8 health behavior score and all-cause mortality within CKM stage groups. The forest plot shows adjusted HRs and 95% CIs per 10-point higher health behavior score among 5,949 participants with 893 deaths. Estimates were obtained from a complex survey-weighted Cox model containing an interaction between CKM stage group and the health behavior score and adjusted for age, sex, race and ethnicity, educational attainment, family income-to-poverty ratio, and NHANES survey cycle. The vertical line indicates HR=1.

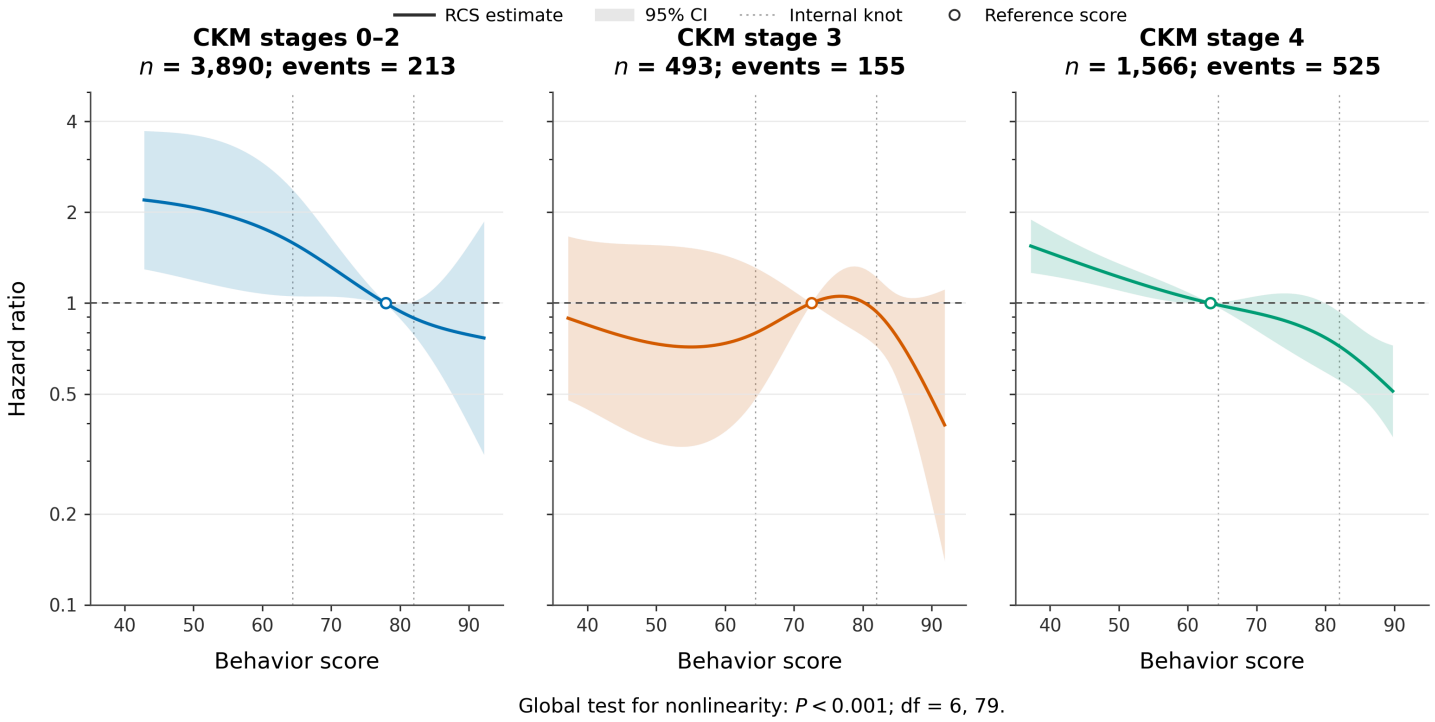


Figure 3

Nonlinear associations between the health behavior score and all-cause mortality across CKM stage groups. The curves show adjusted HRs and 95% CIs estimated using restricted cubic splines among 5,949 participants with 893 deaths. Models incorporated NHANES complex survey weights and adjusted for the same covariates as the primary model. Boundary knots for the behavior score were 37.202 and 92.190, and internal knots were 64.407 and 81.972. Reference values were 77.898, 72.531, and 63.254 for CKM stages 0–2, stage 3, and stage 4, respectively. The global test for nonlinearity yielded $P=1.18\times10^{-7}$.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 02SupplementaryInformation.docx
- SupplementaryFigureS1Standardized5YearRiskDifference.tiff
- SupplementaryFigureS2NineCell5YearRisk.tiff
- SupplementaryFigureS4LeaveOneCycleOut.tiff
- SupplementaryFigureS3ComponentDeletion.tiff