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Social determinants of health (SDOH) associated with the risk of all-cause mortality and life expectancy in US adults with cardiovascular-kidney-metabolic syndrome: a NHANES 2001–2018 cohort study



Qihang Yang^{1†}, Pengfei Shi^{2*†}, Lanxia Pan³ and Zongqiang Huang^{1*}

Abstract

Objectives Social determinants of health (SDOH) contributed to preventable health inequities. However, association between SDOH and mortality in populations with cardiovascular-kidney-metabolic (CKM) syndrome remain still unclear. This study aims to investigate this association and the influence of SDOH on life expectancy in CKM syndrome populations.

Study design A cohort study using data from the 2001–2018 National Health and Nutrition Examination Survey (NHANES). Participants with incomplete data were excluded.

Methods CKM stages 1–4 were considered as CKM syndrome according to American Heart Association's suggestions. Ten measures of SDOH were assessed, and the combined score of SDOH were calculated as the sum of the weighted scores for each SDOH. Participants were then categorized into 3 groups according to SDOH tertiles. After adjustment for confounders, cox regression models were fitted to investigate the association between SDOH and all-cause mortality. Restricted cubic splines (RCS), subgroup analysis, and interaction analysis were also constructed.

Results During a median follow-up of 7.33 years (IQR 4.17–10.58), a total of 10,040 participants with CKM syndrome were enrolled. The linear positive association between SDOH and the risk of all-cause mortality was observed. Results were consistent in subgroup analysis and several sensitivity analyses, and interaction analysis showed that this association can be modified by drinking. We also found that unfavorable SDOH correlated with shorter life expectancy compared to favorable SDOH.

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Page 2 of 10

Conclusion Unfavorable SDOH associated with higher risk of all-cause mortality and shorter life expectancy in populations with CKM syndrome, addressing the importance of integrating SDOH into the management of CKM syndrome.

Clinical trial number Not applicable.

Keywords Social determinants of health, SDOH, Cardiovascular-kidney-metabolic syndrome, NHANES, CKM syndrome, Health related social needs

Introduction

Cardiovascular-kidney-metabolic (CKM) syndrome, as recently introduced by the American Heart Association (AHA), refers to the pathophysiological interplay between cardiovascular system, renal system, and metabolic risk factors (obesity, diabetes, and so on), and is further divided by a staging system ranging from stage 0 to stage 4 [1]. Recent studies have revealed that almost nine in ten US adults met the diagnostic criteria for CKM stage 1 or higher between 2011 and 2020, with notable disparities in prevalence stratified by sex, age, and socioeconomic status [2, 3]. There was a higher prevalence of advanced CKM stages (stages 3 or 4) in men than in women, in the elderly (aged ≥ 65 years) than in younger adults (aged 20-44 years), in unfavorable socioeconomic status than in the favorable [2, 3]. Poor CKM health is a key determinant of all-cause mortality and places a substantial strain on public health systems, indicating the urgent need for prevention, treatment, and management of CKM syndrome [4].

Social determinants of health (SDOH), which refers to nonmedical risk factors that affect health outcomes and quality-of-life outcomes, can be as important as medical healthcare or lifestyle choices in influencing health [5]. A framework with five domains was introduced in the Healthy People 2030 to evaluate comprehensive SDOH: financial circumstances, education access and quality, healthcare access and quality, neighborhood and built environment, and social and community context [5]. Disadvantaged SDOH was shown to be associated with increased risk of higher stage of CKM syndrome and poor cardiovascular health [6, 7]. However, associations between SDOH and mortality in CKM syndrome populations remain still unclear, and it is critical to understand the influence of SDOH among populations with CKM syndrome. The AHA has also emphasized the importance of integrating SDOH into the management of CKM syndrome [1]. Additionally, the definition and scope of SDOH differed across studies, and previous studies evaluated different individual SDOH (i.e. employment status, food security) as having the same contribution to combined SDOH [6, 7, 8], which was not fully rigorous. Previous studies using NHANES data only evaluated marital status in domain of social and community contexts [6, 7,

8], which might not fully capture this domain or differentiate between low and high SDOH.

In this study, we constructed a weighted combined SDOH to investigate its relationship with all-cause mortality and life expectancy in CKM syndrome (stage 1–4) populations using NHANES 2001–2018. And we also constructed a more complex combined SDOH in our sensitivity analysis.

Methods

The data used in this study are publicly accessible and can be retrieved from the NHANES website (https://www.cd c.gov/nchs/nhanes/index.html). Since the study relied on publicly available anonymized databases, it was exempt from ethical review. All participants provided consent to participate in the NHANES data collection.

Study population

NHANES uses advanced multiperiod probability-based sampling techniques to obtain nationally representative samples. All NHANES protocols have received approval from the National Center for Health Statistics Research Ethics Review Board, and written informed consent was obtained from all participants. Data from NHANES 2001–2018 was utilized for this cohort study and after excluding ineligible participants, 10,040 participants with CKM syndrome were finally involved (Figure S1 shows the flowchart of this study).

Assessment of cardiovascular-kidney-metabolic (CKM) syndrome

For each participant, we assigned a CKM syndrome stage according to the criteria introduced by AHA [1]: stage 0 (no CKM risk factors), stage 1 (excess or dysfunctional adiposity), stage 2 (additional metabolic risk factors or moderate- to high-risk chronic kidney disease), stage 3 (very high-risk chronic kidney disease or high predicted 10-year cardiovascular disease risk), and stage 4 (established cardiovascular disease). We utilized the 2021 raceand ethnicity-free Chronic Kidney Disease Epidemiology Collaboration creatinine equation to calculate the estimated glomerular filtration rate [9]. The 10-yr CVD risk was estimated by the PREVENT Eqs. [10, 11]. Detailed definition of the CKM stage, adapted to the data available in NHANES, are provided in the Supplement materials

Characteristic	Overall	Favorable (n=3387)	Medium (<i>n</i> = 3313)	Unfavorable (n=3340)	p ¹
sex, n (%)					< 0.001
Female	4,779 (48%)	1,458 (45%)	1,606 (50%)	1,715 (51%)	
Male	5,261 (52%)	1,929 (55%)	1,707 (50%)	1,625 (49%)	
Age, years, Median (IQR)	49.00 (35.00, 61.00)	53.00 (41.00, 64.00)	46.00 (31.00, 61.00)	41.00 (28.00, 55.00)	< 0.001
Age strata, n (%)					< 0.001
20–45	4,188 (44%)	1,067 (33%)	1,385 (49%)	1,736 (57%)	
46–65	3,630 (38%)	1,411 (45%)	1,049 (31%)	1,170 (35%)	
over 65	2,222 (18%)	909 (21%)	879 (20%)	434 (8.4%)	
Race, n (%)					< 0.001
White	4,574 (70%)	2,099 (84%)	1,447 (67%)	1,028 (48%)	
Black	1,973 (9.7%)	318 (3.0%)	672 (10%)	983 (21%)	
Other	3,493 (20%)	970 (13%)	1,194 (23%)	1,329 (31%)	
BMI, Median (IQR)	28.50 (25.30, 32.90)	28.00 (25.20, 32.10)	28.90 (25.41, 33.10)	29.00 (25.20, 33.99)	0.002
Obesity status, n (%)					< 0.001
Normal weight	2,241 (23%)	816 (23%)	698 (21%)	727 (23%)	
Overweight	3,706 (37%)	1,341 (40%)	1,235 (36%)	1,130 (33%)	
Obesity	4,093 (40%)	1,230 (36%)	1,380 (43%)	1,483 (44%)	
Smoke status, n (%)					< 0.001
current	2,032 (20%)	332 (11%)	572 (18%)	1,128 (39%)	
former	2,624 (27%)	1,063 (32%)	907 (27%)	654 (19%)	
never	5,384 (53%)	1,992 (57%)	1,834 (55%)	1,558 (42%)	
Alcohol use, n (%)	7,666 (81%)	2,681 (83%)	2,470 (78%)	2,515 (80%)	0.002
Diet, n (%)					< 0.001
Unhealthy	3,347 (34%)	892 (27%)	1,089 (35%)	1,366 (43%)	
Moderate	3,346 (33%)	1,066 (32%)	1,155 (35%)	1,125 (33%)	
Healthy	3,347 (34%)	1,429 (41%)	1,069 (31%)	849 (24%)	
Physical activity, n (%)					< 0.001
inactive	3,843 (35%)	1,152 (32%)	1,321 (36%)	1,370 (38%)	
active	6,197 (65%)	2,235 (68%)	1,992 (64%)	1,970 (62%)	
Hypertension, n (%)	5,228 (48%)	1,793 (49%)	1,774 (49%)	1,661 (45%)	0.021
Diabetes, n (%)	1,885 (14%)	548 (12%)	683 (15%)	654 (16%)	0.004
Cardiovascular disease, n (%)	1,106 (9.1%)	329 (8.4%)	349 (9.0%)	428 (11%)	0.027
Cancer, n (%)	941 (9.8%)	450 (13%)	304 (8.8%)	187 (5.0%)	< 0.001
CKMS [#] stage, n (%)					0.003
1	2,062 (23%)	754 (24%)	636 (21%)	672 (23%)	
2	4,277 (41%)	1,457 (43%)	1,443 (42%)	1,377 (37%)	
3	2,595 (27%)	847 (25%)	885 (29%)	863 (29%)	
4	1,106 (9.1%)	329 (8.4%)	349 (9.0%)	428 (11%)	

Table 1 Baseline characteristics of participants according to combined SDOH^{*}

*SDOH, social determinants of health; SDOH was grouped into tertiles: the bottom tertile represented the favorable, the middle tertile represented the medium, and the top tertile represented the unfavorable

Data are presented as weighted median (IQR) for continuous variables and unweighted frequencies (weighted percentages) for categorical variables; BMI, body mass index

#CKMS, Cardiovascular-Kidney-Metabolic Syndrome

¹chi-squared test with Rao & Scott's second-order correction; Wilcoxon rank-sum test for complex survey samples

(supplementary methods). Individuals at CKM stage 1-4 were defined as having CKM syndrome.

Assessment of social determinants of health (SDOH)

Information was collected using a standardized questionnaire administered through face-to-face interviews. All determinants were selected based on the Healthy People 2030 objectives and prior studies from NHANES [5, 6, 12]. According to the framework with 5 domains introduced by the Healthy People 2030 objectives [5], we included 10 measures of SDOH: household income (evaluated by family income-to-poverty ratio), employment, food security (evaluated by questions from the food security survey module [13]), education attainment, access to healthcare, health insurance, accommodation stability, psychosocial problems, race or ethnicity, and marital P for trend

p < 0.001

< 0.001

	Crude model		Model 1		Model 2	
Characteristic	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	
SDOH (per 1 point increase)	1.10 (1.06, 1.14)	< 0.001	1.26 (1.21, 1.32)	< 0.001	1.20 (1.15, 1.25)	
SDOH strata						
Favorable	_		_		_	
Medium	1.63 (1.33, 2.00)	< 0.001	1.94 (1.60, 2.35)	< 0.001	1.73 (1.43, 2.09)	
Unfavorable	1.33 (1.06, 1.68)	0.015	2.87 (2.27, 3.61)	< 0.001	2.13 (1.71, 2.66)	

Table 2 Association between combined SDOH and all-cause mortality in CKMS population

SDOH, social determinants of health; CKMS, Cardiovascular-Kidney-Metabolic Syndrome; HR, hazard ratio

SDOH was grouped into tertiles: the bottom tertile represented the favorable, the middle tertile represented the medium, and the top tertile represented the unfavorable

< 0.001

Crude model was adjusted none; Model 1 included adjustments for age (continuous) and sex. Model 2 was further adjusted for smoke, alcohol use, diet (Healthy Eating Index 2020 score), physical activity, BMI (continuous), hypertension, diabetes, cardiovascular diseases, and cancer. All models were survey-weighted Test for trend based on variables containing median value for each tertile

status [12]. and we dichotomized these factors using conventional cutoff points for analysis (details in Table S1).

0.002

A weighted combined SDOH score was constructed to account for the varying magnitudes of associations between different individual measures of SDOH and health outcomes, following a commonly used approach in epidemiological analyses [12, 14]. Each individual SDOH was dichotomized into advantaged and disadvantaged levels, and β coefficients for each SDOH (comparing the disadvantaged to the advantaged level) were estimated using Cox regression models for all-cause mortality, adjusted for age, sex, smoke, alcohol use, diet, physical activity, BMI, hypertension, diabetes, cardiovascular diseases, and cancer (β coefficients for each SDOH were displayed in Table S2). The weighted combined SDOH score was calculated as follows: each binary SDOH (0 or 1) was multiplied by its respective β coefficient, the products were summed, then divided by the total sum of all the β coefficients, and finally multiplied by 10 (the number of measures of SDOH). The SDOH score of the specific domain was calculated as follow: each binary SDOH in that specific domain (i.e. financial circumstances domain includes 3 measures: household income, employment, and food security) was multiplied by its respective β coefficient, summed up, then divided by the total sum of all the β coefficients, and finally

Table 3 Association between each part of SDOH and all-cause mortality in CKMS population

Characteristic	HR (95% CI) ¹	р
Financial circumstances	1.32 (1.21, 1.43)	< 0.001
Education attainment	1.50 (1.14, 1.97)	0.003
Healthcare access and quality	1.44 (1.16, 1.77)	< 0.001
Accommodation stability	1.50 (1.24, 1.81)	< 0.001
Social and community context	1.44 (1.28, 1.62)	< 0.001

SDOH, social determinants of health; CKMS, Cardiovascular-Kidney-Metabolic Syndrome; HR, hazard ratio

Survey-weighted cox regression was fully adjusted (age (continuous), sex, smoke, alcohol use, diet, physical activity, BMI (continuous), hypertension, diabetes, cardiovascular diseases, and cancer)

multiplied by 10. The sum of the five domain-specific SDOH scores equal to the total SDOH score. In sensitivity analysis, we also used unweighted combined SDOH and a more complex weighted combined SDOH (multiclassification). Details of these methods are in Supplementary materials (supplementary methods). Compared to equal weighting, weighting by β coefficients allows us to estimate the relative importance of each SDOH factor while accounting for their effects on mortality risk. It also provided a more direct reflection of the actual impact of each SDOH factor on the mortality risk in our sample. Principal component analysis (PCA) was not used since it may mask individual associations despite its reduction of dimensionality. The weighted combined SDOH ranged from 0 to 10 and higher SDOH scores indicate less favorable SODH. Participants were divided into tertiles: the bottom tertile represented the favorable SDOH group, the middle tertile represented the moderate SDOH group, and the top tertile represented the unfavorable SDOH group.

< 0.001

Assessment of mortality

To determine mortality status in the follow-up population, we used the NHANES public-use linked mortality file, updated through December 31, 2019, which was linked to the National Death Index (NDI) by the NCHS using a probability matching algorithm.

Assessment of other covariates

Demographic covariates in this study included sex (male and female) and age (continuous). Self-reported lifestyle factors included smoking (current, former, never), physical activity (inactive, active), current alcohol drinker (Yes, No), and diet (the Healthy Eating Index-2020 (HEI-2020) [15, 16]; ranged from 0 to 100 and derived from the first 24-hour dietetic recall interview completed during the NHANES mobile examination center visit). Self-reported physical activity (PA) was converted to metabolic equivalent (MET) minutes of moderate to vigorous PA per





Fig. 1 Restricted cubic spline (RCS) of the association between SDOH and the risk of all-cause mortality in populations with CKM syndrome. A linear association between SDOH and the risk of all-cause mortality was found (P for nonlinearity = 0.322). Predicted values (solid lines) and 95% CI (blue areas) were adjusted for sex, age (continuous), smoke, alcohol use, diet (Healthy Eating Index 2020 score), physical activity, BMI (continuous), hypertension, diabetes, cardiovascular diseases, and cancer. CKM: cardiovascular-kidney-metabolic syndrome; SDOH: social determinants of health

week in accordance with the WHO analysis guide [17]. PA (MET-min/wk) = MET \times weekly frequency \times duration of each PA. The participants were classified based on whether they met the American PA guideline (<600 MET-min/wk defined as inactive, otherwise active) [18]. Body mass index (BMI) was calculated as weight in kg divided by height in m [2]. For subgroup, participants were further classified into three obesity status: normal (BMI < 25), overweight $(25 \le BMI < 30)$, and obesity (BMI \geq 30). Diet was grouped into three: healthy (top tertile), moderate (middle tertile), and unhealthy (bottom tertile) base on HEI-2020 score tertiles. Medical conditions include hypertension (Yes, No), diabetes (Yes, No), cardiovascular diseases (Yes, No), and cancer (Yes, No). Hypertension was defined as a medical diagnosis of hypertension, or average systolic blood pressure (SBP) > 130 mmHg, or average diastolic blood pressure (DBP)>85 mmHg. Average blood pressure was calculated as the mean of first two measures of blood pressure. Diabetes was defined as a medical diagnosis of diabetes or hemoglobin A1c \geq 6.5% or fasting plasma glucose (FPG)≥126 mg/dL. Cardiovascular diseases include coronary heart disease, angina, heart attack, heart failure, and stroke. Medication use includes diabetes medication (insulin or diabetic pills), antihypertensive drug, and statin use.

Statistical analysis

The data were analyzed according to analytical guidelines, using the recommended survey weights for NHANES. All analyses were performed using R version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria). Two-sided statistical tests were conducted, with statistical significance set at P < 0.05.

Baseline characteristics were summarized using unweighted frequencies with weighted percentages for categorical variables, and weighted medians and interquartile ranges (IQRs) for continuous variables. Participants were grouped according to the weighted combined SDOH tertiles and compared using the chi-squared test with Rao & Scott's second-order correction for categorical variables and the weighted Wilcoxon rank-sum test for continuous variables.

Survey-weighted cox regressions were fitted to investigate the associations between the SDOH (either continuous or categorized) with the all-cause mortality. The crude model was adjusted for none. Model 1 was adjusted for sex (female and male) and age (continuous). Model 2 was further adjusted for smoke (current, former never), current alcohol use (Yes, No), diet (HEI-2020 scores), physical activity (inactive, active), BMI (continuous), hypertension (Yes, No), diabetes (Yes, No), cardiovascular diseases (Yes, No), and cancer (Yes, No). We tested for linear trends (p for trend) by using the median value of each SDOH group as a continuous variable in the models. Additionally, restricted cubic spline regressions (RCS) were used to examine the potential nonlinear relationship between continuous SDOH and all-cause mortality in the overall population and within each CKM stage (stage 1, 2, 3, 4). Nonlinearity was assessed using the likelihood ratio test which compared the linear regression with the nonlinear regression.

For subgroup analysis, SDOH was considered as a continuous variable and we stratified the data by sex, age (20–45, 46–65, >65), race (White, Black, Other), smoking status (current, former, never), physical activity (inactive, active), diet (unhealthy, moderate, healthy), BMI (normal weight, overweight, obese), current alcohol consumption (Yes, No), diabetic status (normal, pre-diabetes, diabetes), hypertension (Yes, No), and CKM stage (stage 1, 2, 3, 4). Interaction analysis was performed by the likelihood ratio test.

Years of life lost were the difference in residual life expectancy, which is estimated using survival models with age as the time scale. First, residual life expectancy was calculated as the area under the survival curve up to age 95, conditional on survival between ages 45 and 95 (at 1-year intervals). Second, years of life lost of were calculated as the difference in residual life expectancy between medium or unfavorable group with the reference favorable group [19]. All analyses were fully adjusted for

Subgroup		HR (95% CI)	р	p for interaction
Overall	H	1.20 (1.15 to 1.25)	<0.001	
Sex				0.64
Female		1.19 (1.12 to 1.27)	<0.001	
Male		1.19 (1.12 to 1.26)	<0.001	
Age				0.06
20-45		1.10 (0.97 to 1.26)	0.134	
46-65		1.26 (1.16 to 1.37)	<0.001	
over 65		1.10 (1.03 to 1.18)	0.005	
Race and ethnicity				0.48
White		1.23 (1.16 to 1.31)	<0.001	
Black		1.16 (1.05 to 1.28)	0.002	
Other		1.14 (1.05 to 1.24)	0.002	
Smoke status				0.19
current		1.21 (1.10 to 1.32)	<0.001	
former		1.20 (1.11 to 1.29)	<0.001	
never		1.14 (1.07 to 1.23)	<0.001	
Physical activity		, , , , , , , , , , , , , , , , , , ,		0.73
inactive		1.20 (1.13 to 1.28)	<0.001	
active		1.20 (1.12 to 1.28)	<0.001	
Diet		,		0.36
Unhealthy		1.27 (1.19 to 1.35)	<0.001	
Moderate		1.19 (1.09 to 1.30)	<0.001	
Healthy		1.16 (1.07 to 1.24)	< 0.001	
BMI		,		0.54
Normal weight		1.25 (1.16 to 1.35)	<0.001	
Overweight		1.14 (1.07 to 1.22)	< 0.001	
Obesity		1.21 (1.13 to 1.30)	< 0.001	
Alcohol use				0.01
Yes	-	1.23 (1.17 to 1.29)	<0.001	
No		1.09 (0.99 to 1.19)	0.064	
Diabetic status	_			0.83
Normal		1.23 (1.11 to 1.37)	<0.001	
Pre diabetes		1.23 (1.15 to 1.31)	< 0.001	
Diabetes		1.14 (1.06 to 1.22)	< 0.001	
Hypertension	_		01001	0.83
Yes		1 19 (1 14 to 1 25)	<0.001	
No		1 22 (1 12 to 1 33)	<0.001	
CKMS stage		1.22 (1.12 to 1.00)	-0.001	0 72
stage 1		1.26 (1.09 to 1.46)	0.001	
stage 2		1 22 (1 14 to 1 30)	<0.001	
stage 3		1 16 (1 05 to 1 20)	0.004	
stage 4		1 15 (1 07 to 1 24)	<0.001	
			0.001	
0.9 Hazar	n 1.1 1.2 1.3 1.4 1 d Ratio	.5		

Fig. 2 Subgroup analysis of the association between SDOH and the risk of all-cause mortality. SDOH was considered as continuous in regressions. Each stratification was adjusted for sex, age, smoke, alcohol use, diet, physical activity, BMI, hypertension, diabetes, cardiovascular diseases, and cancer. CKMS: cardiovascular-kidney-metabolic syndrome; SDOH: social determinants of health

confounders (demographic, lifestyle, and medical conditions) [20].

Several sensitivity analyses were conducted. First, the unweighted SDOH were utilized instead. Second, a more complex SDOH score (multi-classification SDOH) was constructed and utilized to test the robustness of our study. Third, participants with cancer were excluded. Fourth, we excluded participants with a follow-up time of less than or equal to two years. Fifth, given that medication use may mediate the associations between SDOH and mortality, we excluded those with incomplete data on medication use (diabetes medications, antihypertensive medications, and statin use) and added a new model that further adjusted for medication use.

Results

Baseline characteristics

From NHANES 2001–2018, we finally identified 10,040 participants aged 20 years or older with CKM syndrome (median age 49.00 years [IQR 35.00–61.00]), among which 48% were woman (Table 1). Participants in the unfavorable SDOH group were more likely to be woman, younger, and non-White race, to have higher BMI, more unhealthy lifestyles, higher prevalence of diabetes, cardiovascular diseases, CKM syndrome stage 3 and stage 4.

Associations between SDOH and all-cause mortality

During a median follow-up of 7.33 years (IQR 4.17-10.58), there was totally 892 deaths. In the fully adjusted model 2, as shown in Table 2, the hazards ratio (HR) for all-cause mortality per 1 point increase of SDOH was 1.20 (95%CI, 1.15–1.25, p<0.001), and compared with the favorable SDOH group, the HR for all-cause mortality for medium group was 1.73 (95%CI, 1.43-2.09) and for unfavorable group was 2.13 (95%CI, 1.71-2.66). Table 3 shows that each domain of SDOH was positively associated with all-cause mortality (all HR>1, all p < 0.05), and HR per 1 point increase of each domain was very nearly the same due to our weighted SDOH calculation method. Restricted cubic spline (RCS) shows that there were linear positive associations (p for nonlinearity>0.05) between SDOH and the risk of all-cause mortality in all participants (Fig. 1), and in participants with different stages of CKM syndrome (Figure S2).

Subgroup analysis and sensitivity analysis

In our subgroup analysis (Fig. 2), results showed that the positive associations between SDOH and the risk of all-cause mortality remained consistent in different subpopulations. A significant interaction was observed in subgroup of alcohol use, and among those who are current drinkers, the positive associations between SDOH and risk of death were stronger than that in those who are not current drinkers. In our several sensitivity

Fig. 3 Years of life lost for participants in the medium or unfavorable SDOH groups compared with participants in the favorable SDOH group among adults with CKM syndrome in NHANES cohort. Shaded areas represent 95% CIs. The bottom tertile represented the favorable SDOH group, the middle tertile represented the medium SDOH group, and the top tertile represented the unfavorable SDOH group. Model adjusted for sex, age (continuous), smoke, alcohol use, diet (Healthy Eating Index 2020 score), physical activity, BMI (continuous), hypertension, diabetes, cardiovascular diseases, and cancer. SDOH, social determinants of health. CKM: cardiovascular-kidney-metabolic syndrome. NHANES, National Health and Nutrition Examination Survey

analyses (Table S3-S7), we used different methods, as we introduced in our Methods section, to test the robustness of our study and results were consistent with the main analysis.

Life expectancy and years of life lost

As shown in Fig. 3, the mean life expectancy of participants was shorter in medium group and in unfavorable group compared with that in favorable group. At age 45 years, years of life lost (compare with the favorable group) were 1.65 years (95%CI, 0.54–2.77) in medium group and 2.65 years (95%CI, 1.56–3.73) in unfavorable group. Estimates of residual life expectancy at the age of 45, 55, 65 were shown in Table S8.

Discussion

Based on a nationally representative sample of US adults, we showed that unfavorable SDOH was associated with higher risk of mortality in populations with CKM syndrome, and this association was still significant in different stages of CKM syndrome. The results remained consistent in different subpopulations or using different methods to calculate SDOH, which proved the robustness of our study, and alcohol use can modify this association as a significant interaction was observed. We also showed that populations with an unfavorable SDOH



have shorter life expectancy than those with a favorable SDOH.

Previous studies have shown that SDOH or socioeconomic status was correlated with people's health across diverse populations. Bundy et al. found that unfavorable SDOH was associated with higher rates of premature death in the US adults [21]. Zhong et al. showed that among populations with type 2 diabetes, unfavorable SDOH contributed to increased risks of all-cause mortality and many adverse health outcomes (such as incident diabetes-related microvascular disease, dementia, and incident cancer) [12]. They found that life lost of unfavorable SDOH compared to favorable SDOH was about 3 years and our findings was 2.65 years. A cohort study showed that less favorable SDOH were significantly associated with an increased risk of cancer mortality using Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort [22]. Chen et al. found that disadvantaged SDOH was correlated with higher risks of mortality, higher incidence of liver-related events (LREs) and incident CVD in patients with steatotic liver disease [23]. It was also found that SDOH can significantly influence the burden of hypertension and depression, and that gender differences should not be ignored [24, 25, 26]. SDOH was also shown to be able to evaluate preoperative risk [27] and influence disparities in surgical outcomes in both children [28] and adults [29, 30]. After AHA recently introduced a staging system of CKM syndrome, Li et al. showed that less favorable SDOH was associated with increased risk of higher stage of CKM syndrome and higher odds of CKM multimorbidity [6]. In this study, we found that unfavorable SDOH was correlated with increased risk of all-cause mortality and shorter life expectancy among populations with CKM syndrome. All these results collectively underscored the importance of integrating SDOH into the management of healthcare.

The potential causal pathways are complex and interconnected. Patients with CKM syndrome may get worse due to limited access to high-quality healthcare and absence of health insurance. Limited healthcare access can exacerbate CKM progression by delaying diagnosis and treatment, while low educational attainment may limit individuals' ability to navigate healthcare systems effectively. Lower household income may influence health through factors like access to healthcare, health insurance, and food security. The health of people with poorer food security may get worse due to food insufficiency, and they may be more likely to eat unhealthy food and more likely to eat irregularly, which is bad for health. People with a higher level of education may have stronger awareness of protecting their health and more knowledge about health, while also having higher income. Previous study also showed that mental health mediated the associations between socioeconomic status and CVD [31],

and favorable SDOH may have better mental health thus have better health outcomes. To address these problems, we cannot only start from one aspect, but need to systematically intervene in all aspects related to SDOH, like public welfare, social financing, municipal organizations, psychosocial support systems and so on.

To the best of our knowledge, this is the first study to investigate the relationship between combined SDOH and all-cause mortality in populations with CKM syndrome. A higher stage of CKM syndrome correlated with a higher risk of all-cause mortality [32], and SDOH inequities in CKM syndrome have been well documented [3]. We constructed a combined weighted SDOH scoring system in this study, and we additionally included the psychosocial problems and race/ethnicity in the domain of social and community context compared with previous studies [3], [6, 7]. Mental health indicators were crucial for understanding CKM health outcomes and many indicators related to cardiovascular disease are also related to mental health [33], [34, 35]. Race/ethnicity disparities were found in cardiovascular diseases and SDOH [36], and racism may lead to injustice in health care which is the most shocking and inhumane of all the forms of inequality [36]. We also constructed a more complex weighted SDOH scoring system and classified individual SDOH into three or more levels (if possible), which can distinguish the level of SDOH with more preciseness. Of note, in our subgroup analysis, we found that SDOHmortality associations were stronger in current drinkers. The explanation may be that alcohol consumption may amplify stress related to unfavorable SDOH factors, such as financial insecurity or limited healthcare access [37]. Alcohol use may also interact with underlying health conditions, exacerbating the effects of SDOH on mortality [38].

However, several limitations should be acknowledged. First, the scope of the SDOH measures is limited. Several factors such as social support, social connecting, environment factors, community safety, and community engagement were not included in NHANES. Absence of these variables could potentially underestimate the impact of SDOH on mortality, and future research should aim to incorporate these additional factors. Second, participants in this study were all from the United States, future studies should better include participants from other countries and regions. Third, despite controlling for major confounders, residual confounding covariates such as genetic factors and healthcare quality could still bias the results. Fourth, the assessments of several variables are self-reported answers to questionnaire, which could be influenced by recall bias, social desirability bias, and the potential inaccuracies in self-reported health behaviors and conditions. Future studies should better use objective measures to supplement self-reported data.

Conclusion

In conclusion, based on the nationwide cohort study NHANES, unfavorable SDOH was associated with higher risk of all-cause mortality and shorter life expectancy in individuals with CKM syndrome. The results were consistent across populations with different stages of CKM syndrome, demographic, lifestyle, and medical conditions. It is essential to promote SDOH screening and integrate SDOH into the management of CKM syndrome.

Abbreviations

SDOH	Social determinants of health
CKMS	Cardiovascular-kidney-metabolic syndrome
CVD	Cardiovascular disease
AHA	American heart association
BMI	Body mass index
HEI-2020	Healthy eating index-2020
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
NHANES	National health and nutrition examination survey
IQRs	Interquartile ranges
HR	Hazard ratio

Supplementary Information

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Supplementary Material 1

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Author contributions

Q. Y. and P. S. designed the research, performed the data curation and statistical analysis, drafted and reviewed the manuscript. L. P. and Z. H. were responsible for the visualization, reviewed the manuscript and made critical revisions. All authors reviewed the manuscript.

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Data availability

This dataset used is publicly available from https://www.cdc.gov/nchs/nhane s/index.html.

Declarations

Ethics approval and consent to participate

The NHANES is a public-use dataset available through the Centers for Disease Control and Prevention (https://www.cdc.gov/nchs/nhanes/index.html). The NHANES protocol was approved by the institutional review board of the Centers for Disease Control and Prevention (https://www.cdc.gov/nchs/nh anes/about/erb.html). This study was in compliance with the Declaration of Helsinki (https://www.ema.net/policies-post/wma-declaration-of-helsinki /). Since the study relied on publicly available anonymized databases, it was exempt from ethical review. All participants provided consent to participate in the NHANES data collection.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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