



OPEN Dietary intake of live microbes mitigates the mortality risk associated with sedentary behavior in US hypertensive individuals

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To investigate the association between dietary microbes intake and sedentary behavior with mortality risk in hypertensive adults in the United States. This study uses data from hypertensive individuals included in the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2018. The relationship between live-microbe intake, sedentary time, and mortality risk among hypertensive individuals is preliminarily explored using Kaplan–Meier curves. Cox proportional hazards models are employed to analyze the associations separately and jointly, followed by subgroup analyses and sensitivity analysis to assess model stability. The study enrolled 10,036 participants with hypertension, among whom 1599 deaths occurred, including 512 cardiovascular disease-related deaths. Initial Kaplan–Meier curve analysis revealed that hypertensive individuals with both low intake of dietary live microbes and prolonged sedentary time had significantly higher mortality risk. Subsequent Cox proportional hazards model analysis demonstrated that high dietary microbial intake combined with reduced sedentary time were associated with lower mortality risk in hypertensive patients. Joint effect analysis suggested that maintaining proper dietary microbial eating habit may mitigate the adverse health effects of chronic sedentary behavior in this population. Subgroup and sensitivity analyses confirmed the stability of these findings across most examined conditions. The mortality risk in hypertensive individuals due to low intake of dietary live microbes and prolonged sedentary behavior is cumulative. Consuming foods rich in dietary microbes may help reduce the mortality risk associated with sedentary behavior in hypertensive populations.

Keywords Dietary live microbes, Sedentary behavior, Mortality risk, Cross-sectional study, NHANES

Abbreviations

NCHS	National Center for Health Statistics
BMI	Body Mass Index
PIR	Price-to-income ratio
SB	Sedentary behavior
CKD	Chronic kidney disease
NHANES	National Health and Nutrition Examination Survey
CVD-cause	Cardiovascular disease-caused mortality
ALL-cause	All reasons-caused mortality
HR	Hazard ratios
CI	Confidence intervals

Hypertension is one of the most common chronic diseases worldwide, significantly impacting both quality of life and life expectancy for affected populations¹. Epidemiological data indicate that the prevalence of hypertension continues to rise due to lifestyle changes and population aging. According to the World Health Organization (WHO), approximately 1.3 billion people globally suffer from hypertension, with around 10 million deaths each year attributed to hypertension and its complications². Reducing mortality risk among hypertensive individuals

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has therefore become a pressing issue in public health. In this context, sedentary behavior and live-microbe dietary intake are increasingly recognized as lifestyle factors that may exacerbate or improve hypertension prognosis.

In the development process of modern society today, sedentary behavior has already evolved into an extremely common lifestyle pattern. Especially in the contexts of daily work and leisure activities, the daily sedentary duration of most individuals significantly exceeds their activity time^{3,4}. Numerous studies have shown that this prolonged sedentary state is regarded as a high-risk factor for a series of chronic diseases such as cardiovascular diseases, diabetes, and cancer^{5,6}, and there exists a close and complex internal relationship with the overall health outcomes of the population. Some research reports have pointed out that prolonged and continuous sedentary behavior can lead to the impairment of vascular endothelial function. Under the sedentary state, the normal metabolism and functional regulation of vascular endothelial cells are disrupted, resulting in the imbalance of the synthesis and release of vasoactive substances. The release of vasodilatory substances such as nitric oxide decreases, while the secretion of vasoconstrictive substances such as endothelin-1 relatively increases, thereby causing the impairment of vascular dilation function^{7,8}. At the same time, sedentary behavior can significantly enhance insulin resistance, interfere with glucose and lipid metabolism, and trigger metabolic syndrome^{9–11}, further accelerating the process of atherosclerosis and exacerbating the progression of hypertension. In addition, under the sedentary state, the sympathetic nerve remains in a relatively excited state continuously, and the vascular tension increases, thus further raising the blood pressure and increasing the pressure load on the cardiovascular system^{12,13}. Given the numerous adverse effects of the above-mentioned sedentary behavior on patients with hypertension, reducing sedentary time has been widely and unanimously recommended as one of the key components of lifestyle interventions for patients with hypertension. By changing this unhealthy lifestyle habit, it is expected to improve the vascular function, metabolic status, and blood pressure control of patients with hypertension, and thus enhance their overall health level.

Enhancing the dietary intake of live microorganisms has emerged as another noteworthy lifestyle intervention in recent years, demonstrating unique potential in modulating gut microbiota and promoting cardiovascular health¹⁴. Dietary microorganisms are microbes consumed via food or supplements that can positively impact human health, such as probiotics and other functional microorganisms. They can be categorized into colonizing strains (such as *Bifidobacterium longum* and *Lactiplantibacillus plantarum*) and non-colonizing strains (including *Lactobacillus delbrueckii* subsp. *bulgaricus* and *Bacillus subtilis* var. *natto*) based on their intestinal colonization capacity^{15–17}. For hypertensive patients, these two microbial categories exert synergistic therapeutic effects through distinct but complementary mechanisms. Colonizing strains persistently adhere to the intestinal epithelium, competitively inhibiting the proliferation of pro-inflammatory bacteria like *Escherichia* and *Proteus*, while stimulating the production of neuroactive and anti-inflammatory metabolites such as short-chain fatty acids (SCFAs) and polysaccharide A. These microbial-derived molecules not only enter systemic circulation to improve vascular endothelial function, but also act as key signaling molecules in the gut-brain axis. By modulating enteric nervous system activity and vagal afferent pathways, colonizing strains indirectly influence central regulation of blood pressure^{18–21}. Transient gut microbes exert dual health benefits: Their metabolites can cross the blood-brain barrier or activate enteroendocrine cells to regulate neurotransmitter (serotonin, dopamine, acetylcholine) synthesis, thereby fine-tuning autonomic nervous function for physiological regulation like blood pressure control. Simultaneously, they transiently improve the gut microenvironment (pH modulation, mucus secretion) to create favorable niches for beneficial commensals, amplifying their health-promoting effects. These transient interactions yield sustained benefits even post-clearance^{22,23}. Notably, in sedentary hypertensive patients, these microbial strains demonstrate synergistic effects in preserving intestinal ecosystem homeostasis while improving metabolic health. They enhance motility in hypokinetic intestines induced by sedentarism, prevent dysbiosis-related barrier impairment, and reduce endotoxin translocation^{24,25}. By modulating gut microbiota locally and extending to systemic metabolic and neural regulation, dietary microorganisms collectively improve glucose homeostasis, uric acid balance, and lipid profiles, thereby mitigating sedentarism-aggravated metabolic syndrome components contributing to hypertension pathogenesis^{26–28}.

However, most of the current studies are derived from animal experiments. The actual effects and mechanisms of dietary microorganisms on the health of hypertensive individuals in the human population are still unclear. Moreover, due to the similarities and differences in the gut microbiota between animals and humans, as well as the completely different living habits between humans and animals, the research results are also limited in terms of promotion and application²⁹. Therefore, there is still a lack of large-scale population studies to confirm the long-term effectiveness of different live-microbe dietary intakes and reducing sedentary time intervention in the management of hypertension. Meanwhile, the comprehensive impact of the two on the mortality risk of hypertensive individuals is still unclear, and the relevant clinical research data are relatively limited. To address this issue, this study conducts research through the large-scale clinical data of the NHANES database, systematically evaluating the comprehensive impact of sedentary behavior and differential intake of dietary live microbes on the health of patients with hypertension, in order to deepen the understanding of the roles of sedentary behavior and dietary microorganisms in the mortality risk of hypertensive individuals, provide a scientific basis for the lifestyle management of patients with hypertension, and offer a reference for formulating more targeted public health intervention strategies.

Materials and methodology

This study utilizes data from the NHANES database, conducted by the National Center for Health Statistics (NCHS) in the United States. NHANES is a comprehensive survey designed to collect representative information on the health and nutrition of the U.S. civilian population, including demographics, socioeconomic factors, diet, and health-related issues. To ensure sample diversity, NHANES employs a stratified, multistage sampling method to select participants from across the nation. The study protocol received approval from the NCHS Research Ethics

Review Board of the Centers for Disease Control and Prevention, and all participants provided written informed consent. Further details are available on the NHANES website.

Inclusion and exclusion criteria for participants

This study utilized participant data from 1999 to 2018, available on the NHANES website. Hypertensive patients were identified based on self-reported responses to questions about a physician's diagnosis of hypertension, the use of antihypertensive medications, and the average of three blood pressure measurements (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg). A total of 15,008 hypertensive individuals were initially identified. Participants under the age of 20, those lacking data on sedentary behavior, dietary intake, survival status, or key covariates were excluded. Ultimately, 10,036 eligible participants were included in the study. The screening process is detailed in Fig. 1.

Assessment of live-microbe dietary intake and sedentary behavior

Previous studies have indicated that sterile or pasteurized foods contain very low levels of live microorganisms, unpeeled fresh fruits and vegetables contain moderate levels, and unprocessed fermented foods generally contain high levels of live microorganisms. Thus, this study estimated dietary intake of live microbes using 24-h dietary recall data. Foods were categorized by microbial content as low (10^4 CFU/g), moderate (10^4 – 10^7 CFU/g),

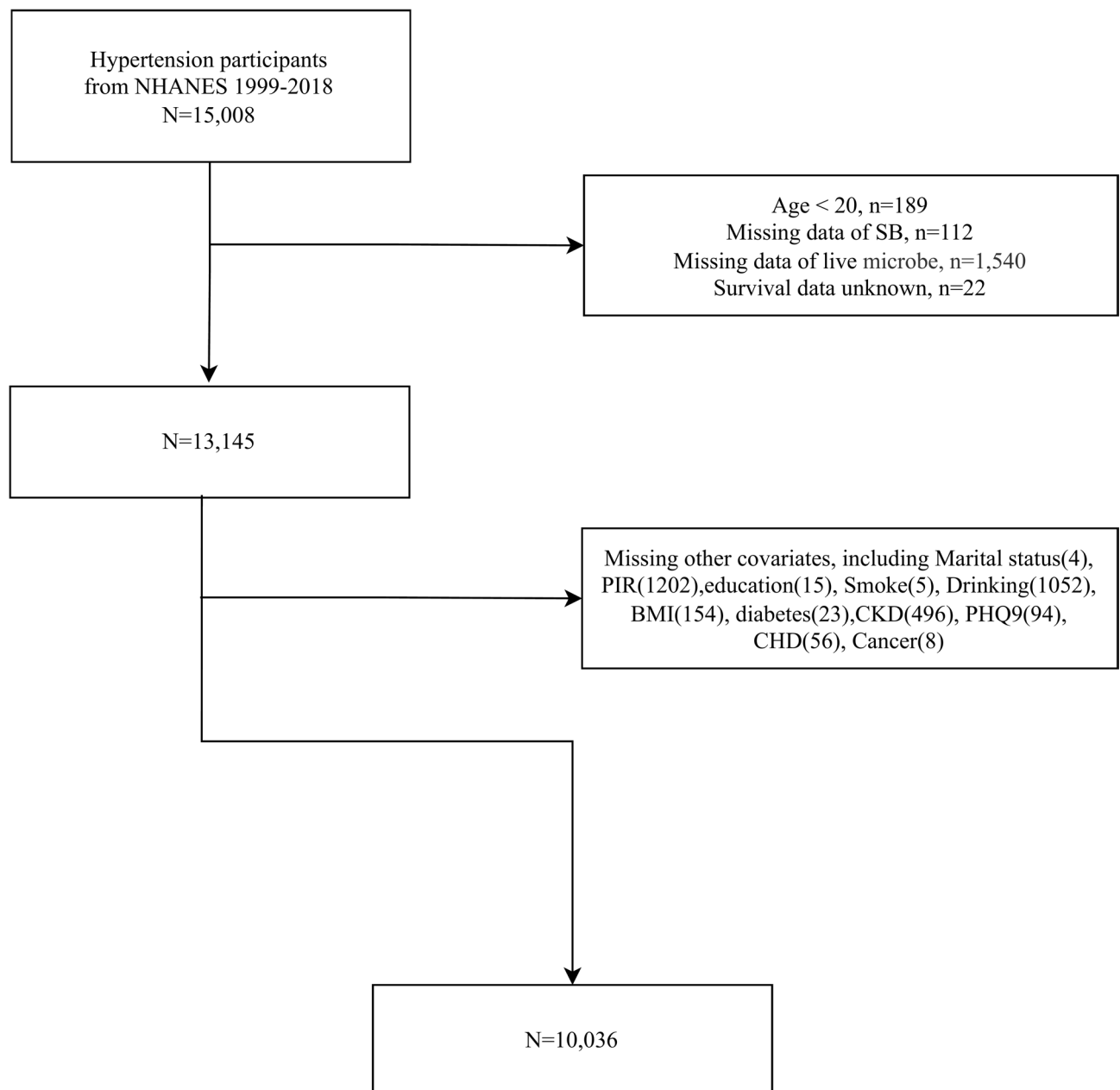


Fig. 1. Flow diagram illustrating the participant selection process.

or high ($> 10^7$ CFU/g) levels of dietary microbes. Based on food consumption, participants were divided into three groups: a low live-microbe dietary intake group (all foods with low levels of live microbes), a moderate live-microbe dietary intake group (foods including moderate levels of live microbes, excluding high levels), and a high live-microbe dietary intake group (foods including high levels of live microbes). This classification approach has been reported and applied in several studies^{30–32}.

Sedentary behavior was assessed through the Global Physical Activity Questionnaire (GPAQ), conducted by trained interviewers at a mobile examination center. Participants were asked, “How much time do you spend sitting each day during work, home, commuting, or social activities? This includes time at a desk, in a car or on public transportation, reading, playing cards, watching television, or using a computer.” Based on responses, and in line with previously published studies, sedentary time was temporarily classified into three levels: < 5 h/day, $5–8$ h/day, and > 8 h/day^{33,34}. Subsequent studies will utilize statistical algorithms to adjust sedentary time thresholds for specific population subgroups based on individualized health risk profiles.

Assessment of mortality

The NCHS linked NHANES data with NDI data using identifiers such as Social Security numbers and birth dates to obtain survival status information, with follow-up ending on December 31, 2019. If no match was found in the NDI, the participant was considered to be alive. The causes of death for survivors were classified according to the International Classification of Diseases, 10th Revision (ICD-10). Cardiovascular-related mortality in this study included rheumatic heart disease, hypertensive heart disease, ischemic heart disease, pulmonary heart disease, cardiomyopathy, endocarditis, as well as cerebral hemorrhage and cerebral infarction, with relevant ICD codes I00–I09, I11, I13, I20–I51, I60–I69.

The covariates included in this study

This study accounted for multiple covariates that could influence the relationship between dietary live microbes, sedentary behavior, and risks of cardiovascular and all-cause mortality. These variables encompassed a range of demographic characteristics within the study population, including age, gender, race, education level, income-to-poverty ratio, and BMI, as well as lifestyle factors such as smoking and alcohol consumption, and health conditions such as diabetes, coronary heart disease, depression, kidney disease, and cancer. Demographic characteristics and lifestyle habits were collected via questionnaires, while disease diagnoses were based on physician diagnosis, laboratory tests, and relevant medication use. Depression was diagnosed using a PHQ-9 score greater than 10. In the sensitivity analysis, the consumption amount of salt, the intake of dietary fiber, the usage of probiotics within 30 days, and the Healthy Eating Index (HEI)³⁵ were also analyzed.

Statistical analyses

The statistical analysis in this study strictly adhered to the design methodology recommended by the NHANES database, applying appropriate weights for each study parameter. Continuous variables with a normal distribution were expressed as mean \pm standard deviation, while non-normally distributed continuous variables were represented by the median, and categorical variables were presented as percentages. Initially, the Kaplan–Meier method was used to explore the preliminary effects of dietary live microbe intake and sedentary time on all-cause and cardiovascular mortality among hypertensive participants. Subsequently, Cox proportional hazards regression models were employed to further assess the specific impact of dietary live microbes and sedentary behavior on all-cause and cardiovascular mortality, with results presented as hazard ratios (HR) and 95% confidence intervals (CI). To examine the nonlinear relationship between sedentary time and mortality risk among hypertensive individuals, we used a restricted cubic spline (RCS) model, determining critical inflection points through segmented stepwise fitting. Based on these inflection points, participants were grouped for combined analysis according to sedentary time and levels of dietary live microbe intake. Three regression models were constructed for this analysis: Model 1, unadjusted for confounding factors; Model 2, adjusted for demographic characteristics, including age, gender, race, education level, PIR, and marital status; and Model 3, further adjusted for health-related variables, including BMI, alcohol consumption, smoking, diabetes, coronary heart disease, chronic kidney disease, cancer, and depression. Subgroup analyses and Sensitivity analysis were conducted to confirm the robustness and consistency of the findings within specific populations. In the sensitivity analysis, the consumption amount of salt, the intake of dietary fiber, the usage of probiotics within 30 days, and the HEI were also analyzed. For missing covariate data, the primary approach was complete case deletion. All statistical analyses were conducted using R software (version 4.3.1), with a two-sided $P < 0.05$ considered statistically significant.

Results

Demographic and clinical attributes of participants

After screening, this study ultimately included 10,036 hypertensive participants from the NHANES 1999–2018 data, comprising 5091 men and 4945 women, with 1599 cases of all-cause mortality and 512 cases of cardiovascular mortality. According to the study objectives, participants were divided into three groups based on the level of dietary live microbes. It was observed that individuals with high live-microbe dietary intake tended to have higher incomes, lower BMI, higher educational attainment, and lower risks of diabetes, kidney disease, heart disease, depression, and cancer. Additionally, those with high live-microbe dietary intake had lower risks of cardiovascular and all-cause mortality. However, we also observed that hypertensive individuals with prolonged sedentary behavior tended to consume diets high in live microbes (see Table 1).

	Total	Low	Middle	High	P-value
Age, year	56.788 ± 0.224	54.849 ± 0.387	58.459 ± 0.327	56.688 ± 0.355	< 0.0001
PIR	3.028 ± 0.039	2.692 ± 0.051	3.090 ± 0.045	3.359 ± 0.056	< 0.0001
BMI	31.260 ± 0.105	31.776 ± 0.202	31.181 ± 0.146	30.730 ± 0.203	0.004
SB, hours	6.435 ± 0.053	6.349 ± 0.080	6.268 ± 0.077	6.799 ± 0.099	< 0.001
Fiber, g	16.550 ± 0.160	13.951 ± 0.181	17.833 ± 0.276	17.871 ± 0.252	< 0.0001
sodium, mg	3519.074 ± 23.890	3406.863 ± 41.764	3481.936 ± 37.340	3717.139 ± 50.032	< 0.0001
HEI2015	51.010 ± 0.269	45.925 ± 0.320	53.618 ± 0.300	53.448 ± 0.385	< 0.0001
Prebiotic					0.439
No	9824(97.469)	3692(97.945)	4068(97.259)	2064(97.189)	
Yes	212(2.531)	60(2.055)	101(2.741)	51(2.811)	
Sex					< 0.0001
Male	5091(50.829)	2054(55.611)	2046(49.029)	991(47.542)	
Female	4945(49.171)	1698(44.389)	2123(50.971)	1124(52.458)	
Race					< 0.0001
Mexican American	1221(5.770)	403(5.810)	617(7.135)	201(3.641)	
Non-hispanic black	2508(12.432)	1241(18.382)	927(11.269)	340(6.700)	
Non-hispanic white	4546(71.565)	1474(64.360)	1899(71.930)	1173(80.091)	
Other hispanic	913(4.156)	325(4.531)	376(4.037)	212(3.866)	
Other Race	848(6.077)	309(6.916)	350(5.629)	189(5.702)	
Marital status					< 0.0001
No-single	5931(65.044)	2021(59.411)	2566(66.584)	1344(69.799)	
Single	4105(34.956)	1731(40.589)	1603(33.416)	771(30.201)	
Education level					< 0.0001
< High school	1108(5.307)	480(7.138)	477(5.442)	151(2.792)	
High school	3915(35.951)	1677(43.707)	1580(34.907)	658(27.761)	
> high school	5013(58.742)	1595(49.155)	2112(59.651)	1306(69.447)	
Smoke					< 0.0001
Never	5031(50.215)	1742(46.576)	2200(52.227)	1089(51.738)	
Former	3130(31.881)	1081(28.529)	1342(33.410)	707(33.779)	
Now	1875(17.904)	929(24.894)	627(14.363)	319(14.483)	
Drinking					< 0.0001
Never	1471(10.941)	571(12.119)	658(12.220)	242(7.507)	
Former	2050(16.879)	867(18.859)	822(16.989)	361(14.216)	
Mild	3592(39.506)	1144(33.761)	1560(41.096)	888(44.330)	
Moderate	1335(15.537)	477(14.485)	551(14.823)	307(17.953)	
Heavy	1588(17.136)	693(20.776)	578(14.871)	317(15.995)	
Diabetes					0.002
No	6859(73.764)	2568(74.216)	2790(71.671)	1501(76.383)	
Yes	3177(26.236)	1184(25.784)	1379(28.329)	614(23.617)	
CKD					0.037
No	6991(74.794)	2584(74.737)	2873(73.190)	1534(77.309)	
Yes	3045(25.206)	1168(25.263)	1296(26.810)	581(22.691)	
CVD					0.079
No	9283(93.233)	3478(93.831)	3835(92.347)	1970(93.829)	
Yes	753(6.767)	274(6.169)	334(7.653)	145(6.171)	
Depression					< 0.0001
No	8977(90.237)	3259(87.418)	3790(91.756)	1928(91.476)	
Yes	1059(9.763)	493(12.582)	379(8.244)	187(8.524)	
Cancer					< 0.0001
No	8568(84.436)	3284(87.539)	3517(82.694)	1767(83.176)	
Yes	1468(15.564)	468(12.461)	652(17.306)	348(16.824)	
ALL-cause death					< 0.001
Continued					

	Total	Low	Middle	High	P-value
No	8437(88.094)	3115(87.064)	3487(87.232)	1835(90.707)	
Yes	1599(11.906)	637(12.936)	682(12.768)	280(9.293)	
CVD-cause death					0.008
No	9524(96.257)	3537(95.750)	3966(96.421)	2021(96.648)	
Yes	512(3.743)	215(4.250)	203(3.579)	94(3.352)	

Table1. Demographic and clinical characteristics of participants by dietary live microbes. SB: sedentary behavior; BMI: Body Mass Index; PIR: Price-to-Income Ratio; CKD: Chronic Kidney Disease; CVD: Cardiovascular disease; CVD-cause: Cardiovascular disease-caused mortality; ALL-cause: All reasons-caused mortality.

The Kaplan–Meier curves between live-microbe dietary intake and sedentary behavior with mortality

To preliminarily explore the clinical significance of live-microbe dietary intake and sedentary time in the prognosis of hypertensive individuals, this study used Kaplan–Meier analysis to assess the association between these factors and all-cause and cardiovascular mortality. Based on prior research, dietary live microbes eating habits were categorized into three levels: low, medium, and high. Sedentary time was also divided into three levels: < 5 h/day, 5–8 h/day, and > 8 h/day. Results indicated a significant association between live-microbe dietary intake and all-cause and cardiovascular mortality in hypertensive individuals. Those with low live-microbe dietary intake had a higher risk of all-cause ($P_{ALL}=0.001$) and cardiovascular ($P_{CVD}=0.020$) mortality, while those with high eating habit showed lower mortality risks. Additionally, sedentary behavior impacted long-term prognosis, with individuals who sat for less than 5 h/day having the lowest mortality risk ($P_{ALL}<0.001$). However, those with 5–8 h/day and > 8 h/day sedentary time displayed similar survival curves, suggesting that the current sedentary classification may not be optimally accurate for hypertensive populations. Detailed results are shown in Fig. 2.

Cox proportional hazards regression analysis of live-microbe dietary intake and sedentary behavior with mortality

To further investigate the impact of live-microbe dietary intake and sedentary behavior on long-term prognosis, we employed Cox proportional hazards models to examine these factors separately. Results revealed that both sedentary behavior and live-microbe dietary intake remained closely associated with mortality risk in hypertensive individuals. Specifically, sedentary duration was significantly related to mortality risk: for each additional unit of sedentary time, all-cause and cardiovascular mortality risks increased by 6% and 6.5%, respectively. Compared to individuals with less than 5 h of sedentary time, those with over 8 h had significantly higher mortality risks ($P_{ALL}<0.0001$, $P_{CVD}=0.013$). Using individuals with low live-microbe dietary intake as a reference, those with medium and high microbe intake showed significantly lower mortality risks ($P_{middle-ALL}<0.001$, $P_{high-ALL}=0.019$, $P_{middle-CVD}=0.002$). Details are provided in Tables 2 and 3.

The nonlinear relationship between sedentary time and mortality risk

After performing K–M and Cox proportional hazard analyses, we identified a potential nonlinear relationship between sedentary duration and mortality, suggesting that the current sedentary behavior classifications may not be optimal for hypertensive populations. Therefore, we utilized RCS curves to depict the nonlinear association between sedentary time and mortality risk in hypertensive individuals. After adjusting for relevant covariates, a “U-shaped” relationship was observed between sedentary duration and all-cause mortality risk, while no nonlinear association was found with cardiovascular mortality (see Fig. 3 for details). Using segmented stepwise fitting to calculate the inflection point between sedentary time and mortality risk, we identified 4.1 h as the threshold for both cardiovascular and all-cause mortality. Different effect values for all-cause mortality were observed before and after this 4.1-h threshold (P for interaction <0.011), with mortality risk progressively increasing for individuals with sedentary time exceeding 4.1 h. Furthermore, a linear relationship may exist between sedentary time and cardiovascular mortality risk, with a statistically significant effect becoming more pronounced after 4.1 h (see Table 4 for details).

Joint association of live-microbe dietary intake and sedentary behavior with mortality

To explore the combined impact of live-microbe dietary intake and sedentary behavior on hypertensive individuals, we further divided sedentary behavior into two groups: those with sedentary time greater than 4.1 h and those with less than 4.1 h. Similarly, dietary live microbe intake was classified into low, medium, and high intake groups for joint analysis. Using the group with sedentary time above 4.1 h and the lowest dietary microbe intake as the reference (highest mortality risk), we found that hypertensive individuals with sedentary time under 4.1 h had significantly lower mortality risk, regardless of their level of dietary microbe intake, compared to those with sedentary time above 4.1 h. Moreover, both medium and high levels of dietary microbes were associated with lower mortality risk for both sedentary and non-sedentary hypertensive individuals, with nearly universal improvement observed across all subgroups in the non-sedentary population. In the sedentary group, dietary microbe intake significantly reduced cardiovascular mortality ($HR_{CVD}: 0.717 [0.566, 0.909]$). Although statistical significance for dietary microbe intake improving overall sedentary mortality risk was not observed in

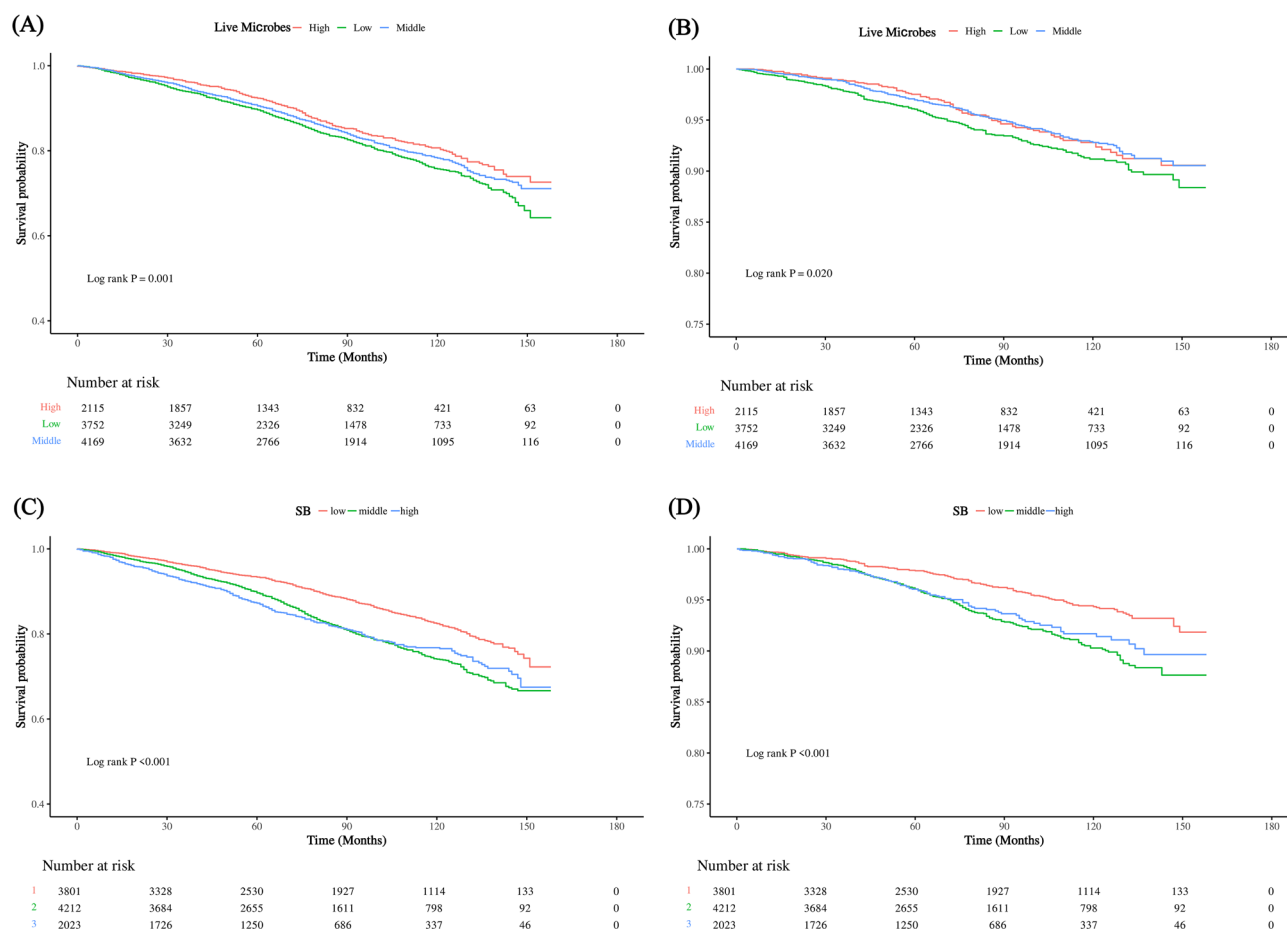


Fig. 2. Kaplan–Meier analysis of the impact of live-microbe dietary intake and sedentary behavior on mortality in hypertensive patients: (A) live-microbe dietary intakes and ALL-cause mortality risk (B) live-microbe dietary intakes and CVD-cause mortality risk (C) Sedentary behavior and ALL-cause mortality risk (D) Sedentary behavior and CVD-cause mortality risk.

Death	Sedentary	Model 1		Model 2		Model 3	
		HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
ALL	SB hours	1.049(1.029,1.069)	<0.0001	1.077(1.056,1.097)	<0.0001	1.060(1.040,1.080)	<0.0001
	<5 h	ref	ref	ref	ref	ref	ref
	5 h–8 h	1.391(1.179,1.642)	<0.0001	1.247(1.059,1.470)	0.008	1.142(0.962,1.355)	0.129
	>8 h	1.355(1.122,1.637)	0.002	1.702(1.448,2.000)	<0.0001	1.500(1.275,1.764)	<0.0001
CVD	SB hours	1.063(1.029,1.099)	<0.001	1.090(1.055,1.127)	<0.0001	1.065(1.030,1.101)	<0.001
	<5 h	ref	ref	ref	ref	ref	ref
	5 h–8 h	1.635(1.250,2.138)	<0.001	1.425(1.096,1.854)	0.008	1.300(0.991,1.706)	0.058
	>8 h	1.499(1.049,2.141)	0.026	1.857(1.332,2.588)	<0.001	1.534(1.096,2.147)	0.013

Table 2. Association between sedentary behavior and mortality across Cox proportional hazards models. Model 1: No-adjust; Model 2: Age, Sex, Race, PIR, marital status, educational level; Model 3: Model 2, smoke, drinking, BMI, diabetes, CKD, CHD, depression, cancer.

the remaining groups, a trend toward reduced mortality risk was evident (P for trend < 0.05). Detailed results are presented in Table 5, and Fig. 4 illustrates the effect relationship between each group and mortality risk.

Subgroup analysis

To assess the stability of the prognostic impact of sedentary behavior and dietary microbe intake on hypertensive individuals across different populations, we conducted a subgroup analysis. The results showed no significant interaction effects across different genders, BMI categories, ages, lifestyle habits, cardiovascular, and depression status, indicating that our findings remain consistent across various populations. Further subgroup analyses on

Death	Dietary microbes	Model 1		Model 2		Model 3	
		HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
ALL	Low	ref	ref	ref	ref	ref	ref
	Middle	0.919(0.803,1.053)	0.223	0.807(0.709,0.920)	0.001	0.804(0.709,0.912)	<0.001
	High	0.743(0.611,0.905)	0.003	0.771(0.625,0.950)	0.015	0.788(0.646,0.961)	0.019
CVD	Low	ref	ref	ref	ref	ref	ref
	Middle	0.787(0.628,0.986)	0.037	0.703(0.561,0.880)	0.002	0.708(0.571,0.878)	0.002
	High	0.819(0.573,1.169)	0.271	0.896(0.614,1.306)	0.567	0.928(0.643,1.339)	0.69

Table 3. Association between live microbes intake and mortality across Cox proportional hazards models. Model 1: No-adjust; Model 2: Age, Sex, Race, PIR, marital status, educational level; Model 3: Model 2, smoke, drinking, BMI, diabetes, CKD, CHD, depression, cancer.

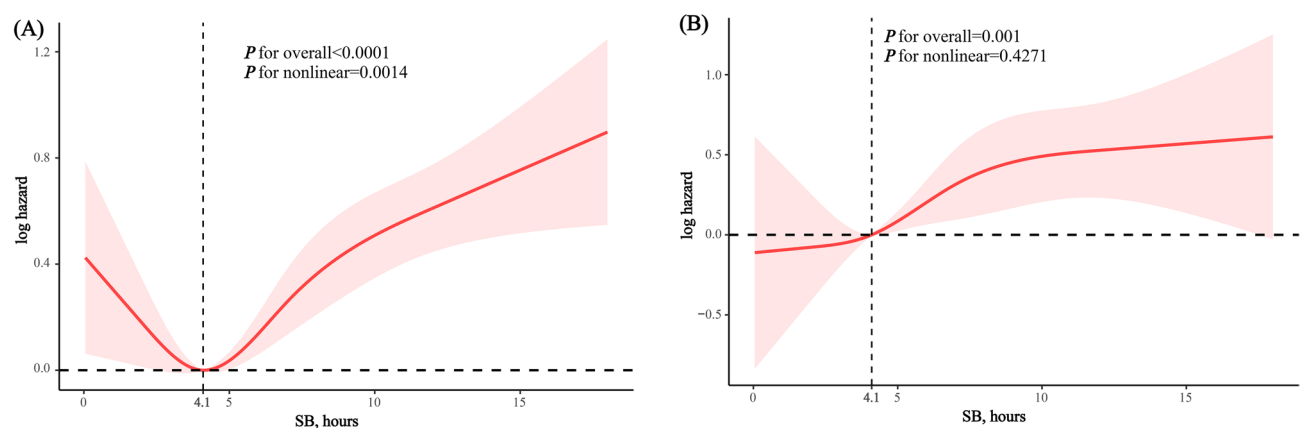


Fig. 3. Nonlinear relationship between sedentary time and mortality risk in hypertensive population: (A) The relationship between sedentary behavior and ALL-cause mortality (B) The relationship between sedentary behavior and CVD-cause mortality.

Death	Sedentary	HR (95% CI)	P	P for interaction
ALL	< = 4.1	0.940(0.827,1.067)	0.337	0.011
	> 4.1	1.082(1.054,1.112)	0.0001	
CVD	< = 4.1	1.151(0.845,1.567)	0.373	0.715
	> 4.1	1.058(1.011,1.108)	0.016	

Table 4. Threshold effect analysis of sedentary duration and mortality risk in hypertensive population.

live-microbe dietary intake and sleep disorders, along with detailed subgroup analysis results, can be found in Tables S1 and S2.

Sensitivity analysis

Considering the potential impacts of salt, dietary fiber, probiotics, and healthy eating habits on the long-term prognosis of sedentary individuals with hypertension, this study conducted relevant sensitivity analyses. The key adjustments included the daily salt intake, dietary fiber intake, the use of probiotic supplements in the past 30 days, and the Healthy Eating Index (HEI). The results showed that even after adjusting for these covariates, the dietary habit with intake of dietary microorganisms could still reduce the mortality risk of sedentary individuals with hypertension. Therefore, the research findings are still very robust. Detailed results are presented in Table 6.

Discussion

This study analyzed data from 10,036 hypertensive participants (5,091 males and 4,945 females) collected by NHANES between 1999 and 2018, including 1,599 all-cause deaths and 512 cardiovascular deaths. Preliminary Kaplan–Meier analysis of sedentary behavior and dietary live microbe intake revealed that both factors were significantly associated with mortality risk in this population. Specifically, prolonged sedentary time correlated with higher mortality risk, while participants with low dietary microbial intake also demonstrated elevated mortality. To further investigate the long-term prognostic impact of these lifestyle factors, we employed Cox proportional

Death	Sedentary	Live microbes	Model 1		Model 2		Model 3	
			HR(95%CI)	P	HR(95%CI)	P	HR(95%CI)	P
ALL	> 4.1	Low	Ref	Ref	Ref	Ref	Ref	Ref
		Middle	0.947 (0.830, 1.081)	0.4206	0.868 (0.758,0.993)	0.0388	0.904(0.790,1.035)	0.1430
		High	0.788 (0.667, 0.931)	0.0051	0.851 (0.717,1.010)	0.0643	0.891(0.751,1.058)	0.1885
	≤ 4.1	Low	0.720 (0.611, 0.848)	0.0001	0.731 (0.620,0.863)	0.0002	0.801(0.678,0.946)	0.0090
		Middle	0.567 (0.481, 0.668)	0.0001	0.605 (0.512,0.714)	0.0001	0.682(0.576,0.807)	0.0001
		High	0.499 (0.390, 0.638)	0.0001	0.564 (0.440,0.724)	0.0001	0.661(0.515,0.849)	0.0012
CVD	> 4.1	Low	Ref	Ref	Ref	Ref	Ref	Ref
		Middle	0.743 (0.589, 0.937)	0.0121	0.683 (0.539,0.865)	0.0016	0.717(0.566,0.909)	0.0060
		High	0.764 (0.578, 1.009)	0.0579	0.843 (0.634,1.122)	0.2425	0.884(0.663,1.177)	0.3973
	≤ 4.1	Low	0.552 (0.410, 0.743)	0.0001	0.581 (0.430,0.783)	0.0004	0.645(0.477,0.872)	0.0044
		Middle	0.498 (0.375, 0.662)	0.0001	0.559 (0.419,0.745)	0.0001	0.634(0.474,0.847)	0.0021
		High	0.384 (0.243, 0.606)	0.0001	0.459 (0.290,0.728)	0.0009	0.527(0.332,0.838)	0.0068

Table 5. Association between the combined effects of live-microbe dietary intake and sedentary behavior on mortality across Cox proportional hazards models. Model 1: No-adjust; Model 2: Age, Sex, Race, PIR, marital status, educational level; Model 3: Model 2, smoke, drinking, BMI, diabetes, CKD, CHD, depression, cancer.

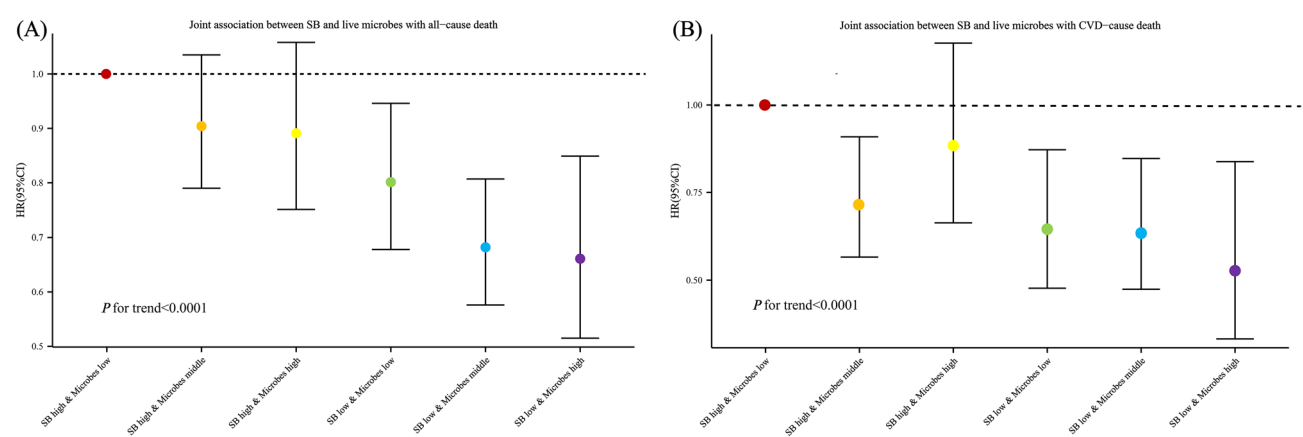


Fig. 4. Joint association of sedentary behavior and live-microbe dietary intake with mortality: (A) Relationship between sedentary behavior and live-microbe dietary intake with ALL-cause mortality (B) Relationship between sedentary behavior and live-microbe dietary intake with CVD-cause mortality.

Sedentary behavior	Dietary live microbes	ALL-cause mortality		CVD-cause mortality	
		HR (95%CI)	P	HR (95%CI)	P
> 4.1	Low	Ref	Ref	Ref	Ref
	Middle	0.922(0.789,1.076)	0.302	0.672(0.522,0.864)	0.019
	High	0.909(0.757,1.091)	0.306	0.986(0.692,1.405)	0.939
≤ 4.1	Low	0.755(0.611,0.933)	0.009	0.568(0.401,0.804)	0.001
	Middle	0.695(0.546,0.883)	0.003	0.591(0.400,0.872)	0.008
	High	0.655(0.460,0.932)	0.019	0.520(0.245,0.801)	0.023

Table 6. Sensitivity analysis of the combined effects of live-microbe dietary intake and sedentary behavior on long-term prognosis. Sensitivity Model: Further adjusted from Model 3 by including salt intake, dietary fiber intake, Healthy Eating Index (HEI), probiotic supplements.

hazards models, which confirmed their significant associations with clinical outcomes in hypertensive patients. Notably, joint analysis demonstrated that increased dietary microbial intake may attenuate the elevated mortality risk associated with sedentary behavior. Our findings suggest an intriguing protective strategy: hypertensive individuals with sedentary lifestyles may potentially reduce health risks through appropriate consumption of live microbe-rich foods.

While the combined effects of dietary microorganisms and sedentary behavior on hypertensive patients' prognosis require further investigation, current research has elucidated their potential interactions through complex metabolic, immunological, and neural regulatory networks, which substantiate our findings. The protective effects of dietary microorganisms on health are primarily manifested in the cardiovascular system and multiple other aspects. Firstly, natural ACE-inhibitory peptides in fermented foods (such as nattokinase and lactic acid bacteria metabolites) can specifically bind to angiotensin-converting enzyme, inhibiting the conversion of angiotensin I to angiotensin II while reducing bradykinin degradation, thereby significantly improving vascular function and exerting cardioprotective effects^{36,37}. Secondly, dietary patterns rich in microorganisms can promote the proliferation of beneficial gut microbiota (such as *Lactobacillus* and butyrate-producing bacteria)³⁸, which ferment dietary fibers to produce various SCFAs (including butyrate and propionate). These metabolites possess multi-level physiological regulatory functions: at the local vascular level, they can directly enhance the activity of nitric oxide synthase in vascular endothelial cells, thereby maintaining vasodilation³⁹; at the central nervous regulatory level, these short-chain fatty acids can modulate the activity of the hypothalamic–pituitary–adrenal axis through the bidirectional communication system of the gut–brain axis, suppressing excessive sympathetic excitation and reducing cardiac afterload^{40–42}. More importantly, these short-chain fatty acids can promote the synthesis of tight junction proteins in intestinal epithelial cells, enhancing the integrity of the intestinal barrier while improving intestinal motility, effectively preventing the entry of intestinal endotoxins and pro-inflammatory factors into the circulation, thereby alleviating systemic low-grade inflammation. This anti-inflammatory effect plays a crucial role in preventing vascular endothelial injury and the development of atherosclerosis^{43,44}.

In contrast, sedentary behavior disrupts gut microbiota equilibrium and elevates cardiovascular risk through multiple mechanisms. Prolonged sitting slows intestinal motility and reduces blood circulation, leading to abnormal increases in intestinal oxygen partial pressure that suppress the proliferation of beneficial bacteria like *Bifidobacterium* and *Lactobacillus* while promoting overgrowth of opportunistic pathogens, thereby exacerbating gut dysbiosis^{45–49}. This microbial imbalance not only impairs short-chain fatty acid production^{50–52} but also compromises intestinal barrier integrity, allowing bacterial toxins and inflammatory factors to enter systemic circulation. This process triggers chronic low-grade inflammation, further activating the renin–angiotensin–aldosterone system (RAAS) and exacerbating insulin resistance, creating a vicious cycle of blood pressure elevation^{53,54}. Crucially, reduced muscle activity from sedentariness decreases secretion of specific myokines (particularly irisin, brain-derived neurotrophic factor) that normally enhance intestinal epithelial mitochondrial function to optimize anaerobic bacterial environments. These myokines also regulate rhythmic intestinal motility and mucus secretion via the enteric–vagal nerve axis, preventing pathogenic bacterial overcolonization^{55,56}. Additionally, lack of muscle contraction reduces anti-inflammatory myokine secretion (such as IL-10, IL-15) while visceral fat accumulation promotes macrophage infiltration, elevating proinflammatory factors like TNF- α and IL-1 β that aggravate vascular endothelial damage and disrupt blood pressure regulation^{57,58}. Collectively, this findings of this study are supported by numerous previous studies, demonstrating that combining dietary intake of live microbe-rich foods with reduced sedentary behavior produces synergistic health benefits for hypertensive patients. These results provide clinically actionable nutritional approaches for managing hypertension through targeted dietary modifications.

Nevertheless, several noteworthy findings in this study warrant further discussion. While high dietary microbial intake significantly reduced all-cause mortality risk in hypertensive patients when analyzed independently, restricted cubic spline (RCS) curve analysis stratified by sedentary status revealed a paradoxical pattern: sedentary individuals derived benefits from moderate microbial intake but showed no significant improvement with high intake. This complex phenomenon may involve multisystem interactions. For instance, prolonged sedentary behavior slows intestinal transit, while substantial supplementation with dietary microbe-rich foods may lead to excessive accumulation of microbial metabolites in the colon that surpass optimal physiological thresholds. This can result in altered pH, osmotic diarrhea, and erosion of the mucus layer, ultimately compromising intestinal barrier integrity^{59,60}. Furthermore, chronic sedentariness-induced low-grade inflammation and reduced microbial diversity impair the gut ecosystem's capacity to regulate high microbial loads, predisposing to dysbiosis⁴⁷. Intriguingly, our baseline data also showed that while all hypertensive participants averaged 6 h of daily sitting time, those in the high microbial intake group actually had the longest sedentary duration (6.8 h). This apparent contradiction may reflect compensatory dietary patterns among sedentary office workers who frequently consume probiotic beverages (specifically yogurt, kombucha, kefir)^{61–63}, potentially masking some sedentary risks. Furthermore, in wealthier participants exhibiting both prolonged sedentariness and high microbial intake, elevated salt consumption (may primarily stem from certain high-salt fermented food varieties such as salt-rich kimchi, high-sodium natto, or brine-pickled cucumbers)⁶⁴ appears to counteract microbial benefits, ultimately resulting in similar HEI scores across medium and high intake groups. Conversely, lower-income individuals showed more physical activity but poorer diets (relying on processed/canned foods with minimal fruit intake), yielding higher mortality risk despite less sedentarism, as evidenced by their lower Healthy Eating Index (HEI) scores^{65–67}. These counterbalancing effects likely contributed to the non-significant joint association between sedentarism and microbial intake on mortality outcomes. Based on these findings, we propose a dual intervention strategy for sedentary hypertensive patients: combining eating live microbe-containing foods with regular exercise to synergistically restore gut motility and microbial diversity (rather than solely increasing microbial intake). This integrated approach may optimize vascular function, suppress inflammatory cascades, and reestablish autonomic balance, offering a positive solution for long-term hypertension management.

In summary, our study possesses several notable strengths. We are the first to systematically investigate the combined effects of varying dietary live microbe intake levels and sedentary behavior on mortality risk in hypertensive populations, demonstrating an additive cumulative risk from both low microbial intake and

prolonged sedentariness. Importantly, our application of threshold analysis to redefine sedentary behavior thresholds offers improved characterization of activity patterns in this hypertensive population. Therefore, this study provides valuable insights for hypertensive individuals with sedentary occupations (such as office workers, programmers, truck drivers). It suggests that incorporating foods rich in dietary microbes such as yogurt, kimchi, and kefir may serve as an effective dietary intervention to complement their health management. However, several limitations must be acknowledged. First, while our classification of dietary live microbes follows established expert consensus cited in numerous studies, the lack of precise microbial quantification in food items may introduce classification bias. Second, the NHANES dietary data collection relies on self-reported questionnaires, which are susceptible to recall bias regarding both food intake and sedentary time estimation. These methodological constraints necessitate validation through subsequent studies. Furthermore, as our analysis focused on the U.S. population with distinct genetic, lifestyle, healthcare and socioeconomic characteristics compared to other regions, global generalization of these findings requires caution. While our results suggest potential benefits of dietary microbial supplementation for sedentary hypertensive individuals, more robust evidence is needed to conclusively establish the relationship between live microbe consumption, sedentary behavior and mortality risk.

Conclusion

The mortality risk in hypertensive individuals due to low intake of dietary live microbes and prolonged sedentary behavior is cumulative. Consuming foods rich in dietary microbes may help reduce the mortality risk associated with sedentary behavior in hypertensive populations.

Data availability

The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

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Declarations

Competing of interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics approval and consent to participate

The data supporting the results of this study are available in NHANES database. Our analysis was conducted on the basis of publicly available data, and previous subjects signed an informed consent form. Thus, our research does not require renewed informed consent from participants or ethical approval from the NCHS Research Ethics Review Board. More detailed information can be obtained from the official NHANES website. (<https://www.cdc.gov/nchs/nhanes/irba98.htm>).

Additional information

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