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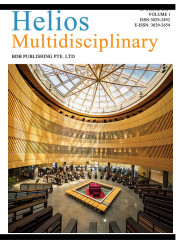

Yuanyuan Wu[1#] , Xinming Jia [2#], Chao Li[3#], Wending Zhong[2], Can Xie[2], Haiyang Chi[2], Yushuang Peng[4], Lihua Di[5], Yangxi Huang[6], Shuo Wu[7], Chanyuan Sun[8*], Jia Zhou[9*], Xiaobing Zhai[2*]

[1] Luoyang Orthopedic Hospital of Henan Province (Orthopedic Hospital of Henan Province), Zhengzhou 450000, China
[2] Faculty of Applied Sciences, Macao Polytechnic University, Macao SAR 999078, China
[3] Guang Ming District Center for Disease Control and Prevention, Shenzhen, Guangdong Province, China
[4] Hubei Provincial Center for Disease Control and Prevention, Hubei province 430000, China
[5] Chenghua District Center for Disease Control and Prevention, Chengdu 610000, China
[6] School of Nursing, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR 999077, People's Republic of China
[7] Shuo Wu Medical school, WuHan University of Science and Technology
[8] Chanyuan Sun Department of Oncolog, Wuhan NO.1 hospital
[9] Chongqing Yubei Maternal and Child Health Hospital, Chongqing 401120, China

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ABSTRACT

Background: There is limited understanding of the effect of salt types on the progression of cardiovascular disease (CVD) and their longevity, due to previous evidence from cross-sectional studies. The purpose of this study was to evaluate the association of type of salt with CVD and all-cause mortality in the American population by using a prospective design.

Methods: The National Health and Nutrition Examination Survey (NHANES) is a large, complex, public health survey of the US population. Weighted Cox proportional hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated to evaluate the association of type of salt with CVD and all-cause mortality, using data from NHANES 2006-2018 linked with mortality data obtained in December 31, 2019.

Results: Among 29416 participants (aged ≥20 years, 47.53% male), 2562 deaths were recorded (717 from CVD) during a median follow-up of 7.6 years. In multivariable-adjusted models, ordinary salt decreased the risk of CVD and all-cause mortality by 25% and 10%, compared with no using salt. HRs (95% CIs) were 0.75 (0.64 - 0.89) and 0.90 (0.81, 0.99), respectively. Similarly, compared to no using salt, salt substitute was negatively associated with CVD and all-cause mortality, decreasing risk of CVD and all-cause mortality by 55% and 28%. HRs (95% CIs) were 0.45 (0.22 - 0.93) and 0.72 (0.52, 0.98), respectively. The stratification analyses showed association of ordinary salt and salt substitutes with CVD and all-cause mortality depend on irreversible age, unhealthy habits, and pre-existing chronic diseases.

Conclusions: Moderate dietary salt intake was essential to alleviate CVD and all-cause mortality, and supported adding appropriate salt to food to meet human needs. Although salt is essential to an organism's survival, excessive salt intake significantly impacts individual and population health. Salt substitute should be promoted appropriately as a strategic healthcare program.

[*] *Corresponding author: Xiaobing Zha; Jia Zhou; Chanyuan Sun*
Email address: zhaixbwh@163.com; zhoujj0706@163.com; sunchanyuan2024@163.com
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1. Introduction

Cardiovascular disease (CVD) is one of the major causes of death and disability worldwide (Sacco et al., 2016). In recent years, although CVD mortality decreased from 1980 to 2015, CVD remains the leading cause of death in the United States (Global et al., 2016). According to the report by the American Heart Association, about one-third of Americans suffered from one or more CVDs in 2013 (Mozaffarian et al., 2016). Additionally, 8.4 million people in Brazil, Russia, India, China, and South Africa (BRICS countries) died of cardiovascular diseases in 2016 (Global et al., 2018).

Previous studies have shown that healthy lifestyles are positively associated with lower cardiovascular disease (CVD) events and mortality (Zhang et al., 2021), supporting the critical role of healthy lifestyles in improving quality of life and reducing the burden of disease. Salt, as a necessity of life, is often added during cooking or at the table, influenced by preferences or habits, which may contribute to high sodium intake. For instance, a study from the Million Veteran Program in the United States reported that participants with high sodium intake had a 9% higher risk of CVD compared to those with low sodium intake (Wang et al., 2022). In China, reducing population salt intake by 1 g/day could lower the risk of ischemic heart disease by about 4% and stroke by about 6% (Tan et al., 2022). Similarly, data from the UK Biobank indicated that individuals who always added salt at the table had a 21% increased risk of CVD events and a 19% increased risk of CVD death compared to those who never or rarely added salt (Li et al., 2022).

In response, the World Health Organization (WHO) set an interim global target of reducing population salt intake by 30% by 2025 and recommends that adults reduce their salt intake to less than 5 g/day (WHO, 2013). Numerous studies confirm the association between high salt or sodium intake and CVD (Vega-Solano et al., 2021).

However, limited evidence suggests that no salt intake or excessively low sodium intake may also be associated with increased CVD incidence and mortality (Mente et al., 2016; O'Donnell et al., 2011). Prolonged sodium deficiency can lead to symptoms such as swelling, muscle spasms, headaches, nausea, diarrhea, lethargy, cerebral edema, microvascular spasm, and even death (Moran et al., 2014; Aleksandrowicz & Kozniewska, 2022; Hoorn & Zietse, 2017; Nagler et al., 2014). Excessive salt intake is also harmful. Thus, salt substitutes or light salt might offer a solution, ensuring adequate sodium intake while reducing high sodium consumption.

This study aimed to examine the associations of salt type with CVD and all-cause mortality among adults (aged ≥ 20 years) using data from the National Health and Nutrition Examination Survey (NHANES) and to provide recommendations for optimizing the population's health benefits.

2. Materials and Methods

2. 1 Study population

This prospective cohort study included US subjects aged ≥ 20 years from the complex, comprehensive, multistage sampling design National Health and Nutrition Examination Survey (NHANES) 2005 to 2018, and followed-up for a median of 7.6 years.

The NHANES data are an ongoing, independent, nationally representative sample of civilian, community-dwelling members of the US population conducted by the National Center for Health Statistics (NCHS) every two years. More details about NHANES have been described elsewhere (Ahluwalia et al., 2016). After a series of data purges (Figure 1), a total of 29,416 adults and older adults were included in the final analysis. Data used in this study were derived from a de-identified and public database (https://www.cdc.gov/nchs/nhanes/index.htm). The NHANES is approved by the National Center for Health Statistics Research Ethics Review Board, and all participants provided written consent.

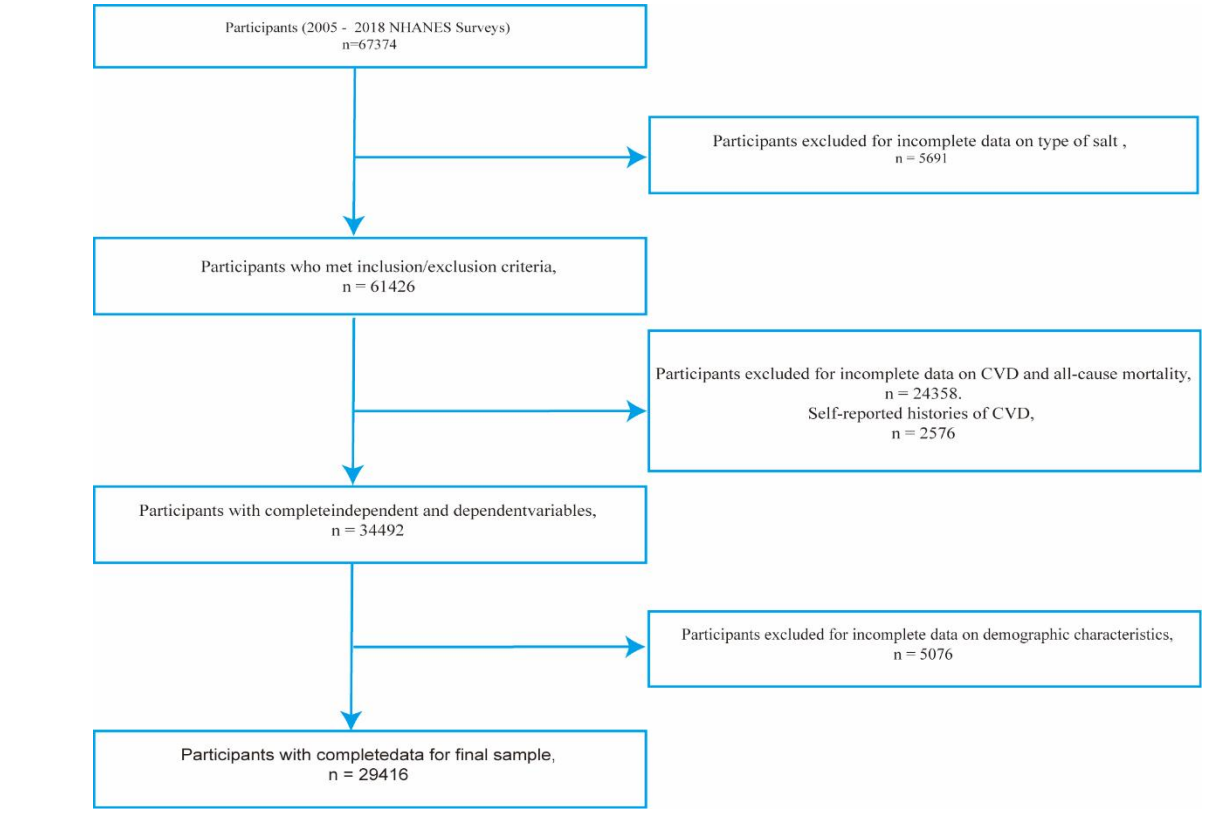

Figure 1 Flowchart of the study

2.2 Exposure assessment

No using salt referred to no salt used or adding at the table and in food preparation in household. Ordinary salt includes regular iodized salt, sea salt and seasoning salts made with regular salt, indicating using or adding these kinds of salt at the table or while cooking. Other salt indicated the lite salt or salt substitute at the table or while cooking. All subjects were asked to list all food and beverages consumed in the 24-h period from midnight to midnight on the day before the interview. At the end of the dietary recall, participants were asked questions about discretionary salt use. The questions are: "(Did {you/SP} add any salt to {your/her/his} food at the table yesterday? Salt includes ordinary or seasoned salt, lite salt, or a salt substitute).

2.3 Covariates

A series of covariates were adjusted in this study, including age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and others), education (< high school, high school, and >high school), marital status (married, single, widowed, and divorced) (Rong et al., 2019), body mass index (BMI), drinking status (never drinkers, moderate drinkers, and heavy drinkers), smoking status (never smoker, former smoker, and current smoker), history of hypertension, history of diabetes, and history of cancer. These were collected using standardized questionnaires during interviews (Ahluwalia et al., 2016).

2.3.1 Covariates

Age, sex, race/ethnicity, education, marital status, body mass index (BMI), drinking status, smoking status, history of hypertension, history of diabetes, and history of cancer were collected using standardized questionnaires during interviews. Race/ethnicity was defined as non-Hispanic white, non-Hispanic black, Mexican American, and others. Education was classified as less than high

school, high school, and more than high school. Marital status was defined as married, single (never married and separated), widowed, and divorced. BMI was calculated as weight in kilogram divided by height in meters squared and was categorized as <25.0 kg/m2, 25.0-29.9 kg/m2, and ≥ 30.0 kg/m2. Current alcohol intake was categorized as none (0 g/day), moderate drinking (0.1to 27.9 g/day for men and 0.1 to 13.9 g/day for women), and heavy drinking. Drinking status for each participant was grouped into never drinkers, moderate drinkers, and heavy drinkers. Smoking status was classified as never smoker, former smoker, and current smoker using two inquiries: "Smoked at least 100 cigarettes in life and Do you now smoke cigarettes?". Histories of hypertension, diabetes mellitus, and cancer were obtained by self- reported or being diagnosed previously.

2.4 Mortality ascertainment and follow-up

National Center for Health Statistics mortality was determined using a probabilistic record match between NHANES participants and National Death Index (NDI) death certificate data. Through December 31, 2019, the NHANES-linked NDI public access data was used to identify the mortality status and cause of death. The NCHS classified mortality from heart diseases, including acute rheumatic fever and chronic rheumatic heart diseases (codes I00–I09), hypertensive heart disease (codes I11), hypertensive heart and renal disease (codes I13), ischemic heart diseases (codes I20–I25) and other heart diseases (codes I26–I51), and mortality from cerebrovascular disease (i.e., stroke) (codes I60–I69) according to ICD-10. This study defined deaths from CVD as death from either heart disease or cerebrovascular disease. Meanwhile, the follow-up time of this study was calculated from the examination date of NHANES 2005-2018 until the last known alive or censored date up to December 31, 2019. The data of each participant is linked with the National Death Index through probabilistic matching based on identifiers.

2.5 Statistical analysis

This study integrated sample weight that had been created in the NHANES analysis. Descriptive statistics were used to analyze the characteristics and distribution of the population. Weighted Cox proportional hazard models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) to identify the association of type of salt with CVD and all-causes mortality. Unadjusted model was type of salt. Adjusted model was further adjusting age, sex, education level, race/ethnicity, drinking status, smoking status, BMI, history of hypertension, history of diabetes mellitus, and history of cancer based on unadjusted model.

In addition, stratification analyses were completed to assess the heterogeneity in the associations of type of salt with risk of CVD and all-causes mortality, including age groups (<60 and ≥60 years), sex (male and females), obesity (BMI <30 and BMI ≥30 kg/m2), smoking status (current and non-current smokers) and drinking status (current drinkers and non-current drinkers), history of hypertension (no and yes), history of diabetes (no and yes), and history of cancer (no and yes).

As sensitivity analyses, we excluded participants who died within first year of follow-up to minimize the possibility that deaths were due to an underlying health condition at baseline. In addition, we further adjusted sodium intake to reduce the impact of sodium intake on model. Finally, we repeated the weighted Cox proportional hazard analyses excluding participants with histories of hypertension, diabetes mellitus, and cancer to confirm the observed associations among healthy general US adult populations.

All analyses were performed using the SAS software version 9.4 and GraphPad Prism 8 software. Two-sided p values <0.05 were considered statistically significant.

3. Results

3.1 Baseline characteristics of participants

Table 1 shows baseline characteristics of all participants from NHANES. Among 29416 participants from NHANES (mean age 46.72 years, 47.53% men), 68.60% were non-Hispanic white, and 85.04% had at least a high school education. Only 8.35%, 29.71%, and 9.36% of this cohort had baseline diabetes, hypertension, and cancer, respectively. Participants were more likely to be married (67.74%). Current smoker and current drinker were 16.79% and 27.93%. Participants were more likely to be obese (36.67%).

Table 1 Baseline Demographic Characteristics of the Study Population, According to Type of Salt

Characteristic a	Total population	Type of Salt, No. (%)				
		No table salt	Ordinary salt	Lite salt	Salt substitute	P value
Total	29416	8984	19178	880	374	
Mean age, years	46.72 ± 0.10	48.81 ± 0.18	45.61 ± 0.12	50.85 ± 0.62	52.29 ± 0.87	<0.001
Male	13915(27.53)	4026(46.35)	9291(48.22)	422(42.99)	176(45.91)	<0.001
Race/ethnicity c						
Non-Hispanic white	12808(68.60)	3461(64.45)	8720(70.27)	383(68,69)	163(68.52)	<0.001
Non-Hispanic black	6050(10.47)	2186(13.20)	3523(9.17)	217(12.43)	124(17.09)	
Mexican American	4682(8.30)	1184(7.14)	3331(8.84)	127(8.04)	40(5.05)	
Other	5876(12.63)	2153(15.21)	3523(11.72)	153(10.84)	47(9.34)	
Education						<0.001
<High school	6888(14.96)	2127(15.26)	4454(14.75)	221(17.95)	86(13.04)	
High school	6681(22.91)	1882(21.30)	4473(23.36)	224(25.16)	102(29.43)	
>High school	15847(62.13)	4975(63.44)	10251(61.89)	435(56.89)	186(57.53)	
Marital status						<0.001
Married	17919(64.74)	5418(64.04)	11770(65.18)	514(60.63)	217(65.48)	
Widowed	2043(5.04)	792(7.37)	1123(4.31)	92(8.78)	36(7.05)	
Divorced	3118(10.08)	986(10.30)	2014(10.07)	76(8.97)	42(7.94)	
Single	6336(20.	1788(1	4271(20.	198(21.	79(19.52)	

	14())	9.29)	44)	62)		
BMI, kg/m2						
<25.0	8630(30.49)	2422(28.58)	5873(31.47)	254(29.14)	81(20.88)	<0.001
25.0~29.9	9701(32.84)	2933(32.74)	6374(33.01)	281(29.38)	113(33.83)	
≥30.0	11085(36.67)	3629(38.68)	6931(35.52)	345(41.47)	180(45.29)	
Current smoker	5006(16.79)	1117(12.51)	3727(18.71)	103(10.79)	59(19.13)	<0.001
Current drinker	7035(27.93)	1855(25.65)	4917(28.99)	201(26.86)	62(22.94)	
History of hypertension,	9724(29.71)	3539(35.35)	5600(26.59)	359(39.27)	226(56.76)	<0.001
History of diabetes	3331(8.35)	1269(10.50)	1867(7.30)	121(10.12)	74(15.38)	<0.001
History of cancer	2527(9.36)	852(10.27)	1528(8.75)	93(12.92)	54(15.68)	<0.001

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

[a] Percentages and means were estimated using US population weights.

[b] P values were computed separately for each covariate and indicate statistically significant differences between step groups if P < 0.05.

[c] Race/ethnicity was determined using preferred terminology from the National Center for Health Statistics as non-Hispanic white, non-Hispanic black, and Mexican American. Mexican American individuals were oversampled rather than broader groups of individuals from Latin America. Other includes Asian, other Hispanic, Alaskan native, and multiracial individuals.

3.2Association of type of salt with CVD and all-cause mortality

In NHANES, 2562 deaths were recorded (717 from CVD) during a median follow-up of 7.6 years. Overall, type of salt was significantly associated with CVD and all-cause mortality (Table 2). In unadjusted model, only ordinary salt was negatively associated with CVD mortality. HR (95% CI) was 0.53(0.45,0.62) compared with no using salt. In adjusted model, ordinary salt and salt substitute were negatively associated with CVD mortality, and HRs (95%CIs) were 0.75 (0.64-0.89) and 0.45 (0.22-0.93), compared with no using salt. As for all-cause mortality, ordinary salt and lite salt were associated with all-cause mortality compared with no using salt, and HRs (95%CIs) were 0.71(0.64,0.79) and 1.30(1.04,1.62) in unadjusted model. In addition, in adjusted model, ordinary salt and salt substitute were negative associated with all-cause mortality, and HRs (95%CIs) were 0.90(0.81,0.99) and 0.72(0.52,0.98), respectively.

Table 2 Associations of Type of Salt with Cardiovascular and All-Cause Mortality in U.S. Adults Aged at Least 20 Years

	Type of Salt			
	No using salt （n=8984）	Ordinary salt (n=19178)	Lite salt (n=880)	Salt substitute (374)
All-cause mortality				
Deaths, No. (%)	915(7.90)	1473(5.53)	118(10.63)	56(8.78)
Deaths/person-years	22706433/387241233	40948537/943495913	3157764/39624282	1068488/16589950
Unadjusted model	1.00 [Reference]	0.71(0.64,0.79)	1.30(1.04,1.62)	1.08(0.77,1.51)
P value		<0.001	0.023	0.665
Adjusted model	1 .00[Reference]	0.90(0.81,0.99)	1.00(0.81,1.23)	0.72(0.52,0.98)
P value		0.037	0.985	0.035
CVD mortality				
Deaths, No. (%) a	297(2.49)	371(1.30)	37(3.12)	12(1.77)
Deaths/person-years	7027818/387241233	10099754/943495913	1002249/39624282	166290/16589950
Unadjusted model	1.00 [Reference]	0.53(0.45,0.62)	1.20(0.80,1.81)	0.69(0.34,1.37)
P value		<0.001	0.373	0.285
Adjusted model	1 .00[Reference]	0.75(0.64,0.89)	0.90(0.61,1.33)	0.45(0.22,0.93)
P value		0.001	0.595	0.031

Values are n or hazard ratio (95% confidence interval). CVD = cardiovascular disease.
Unadjusted model: type of salt; Adjusted model: unadjusted model +age, gender, race/ethnicity, education, BMI, drinking status, smoking status, history of hypertension, history of diabetes mellitus, and history of cancer

3.3 Stratification analyses

Pre-specified stratification analyses were presented in Figure 2 and Figure 3. The associations between type of salt with CVD mortality varied by the levels of the stratifying factors, especially age≥60 years (HR: 0.71, 95% CI: 0.58-0.87 for ordinary salt ; HR: 0.39, 95% CI: 0.17-0.86 for salt substitute) , non-obesity (HR: 0.71, 95% CI: 0.58-0.85 for ordinary salt) and obesity (HR: 0.71, 95% CI: 0.58-0.81 for ordinary salt ; HR: 0.15, 95% CI: 0.04-0.57 for salt substitute), non-current smoker (HR: 0.79, 95% CI: 0.65-0.96 for ordinary salt), non-current drinker (HR: 0.73, 95% CI: 0.60-0.89 for ordinary salt), non-diabetes (HR: 0.75, 95% CI: 0.63-0.89 for ordinary salt), hypertension (HR: 0.74, 95% CI: 0.60-0.92 for ordinary salt), and non-cancer (HR: 0.75, 95% CI: 0.63-0.89 for salt substitute).

As for all-cause mortality, the associations between type of salt with all-cause mortality did not vary by the levels of the stratifying factors; except for current smoker (HR: 0.74, 95% CI: 0.56-0.99) non-current drinker (HR: 0.86, 95% CI: 0.77-0.97) for ordinary salt, obesity (HR: 0.47, 95% CI: 0.28-0.81) and hypertension (HR: 0.68, 95% CI: 0.48-0.97) for salt substitute.

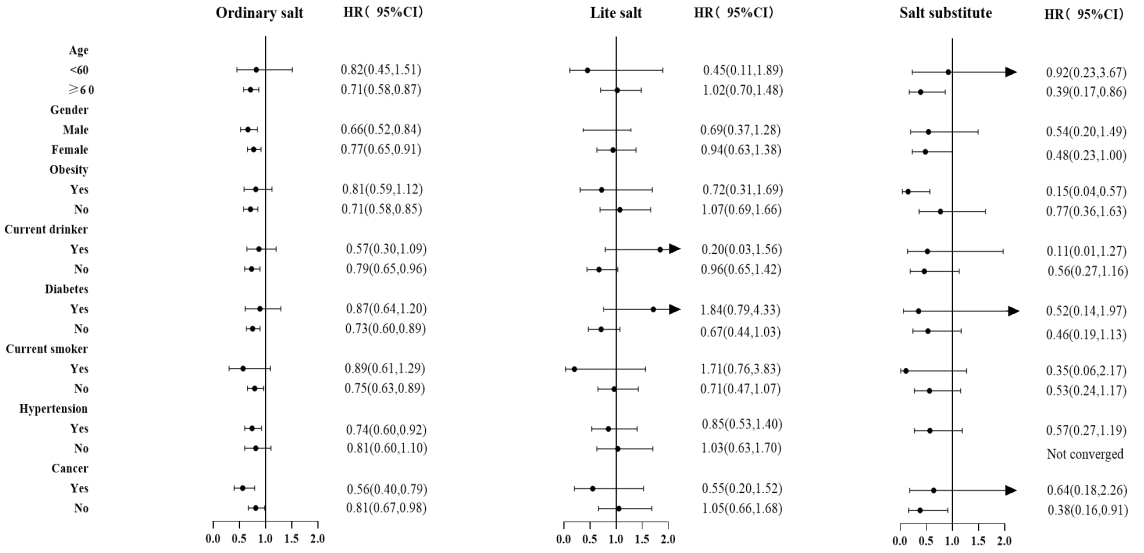

Figure 2 Associations of Type of Salt with CVD Mortality in Stratification Analyses

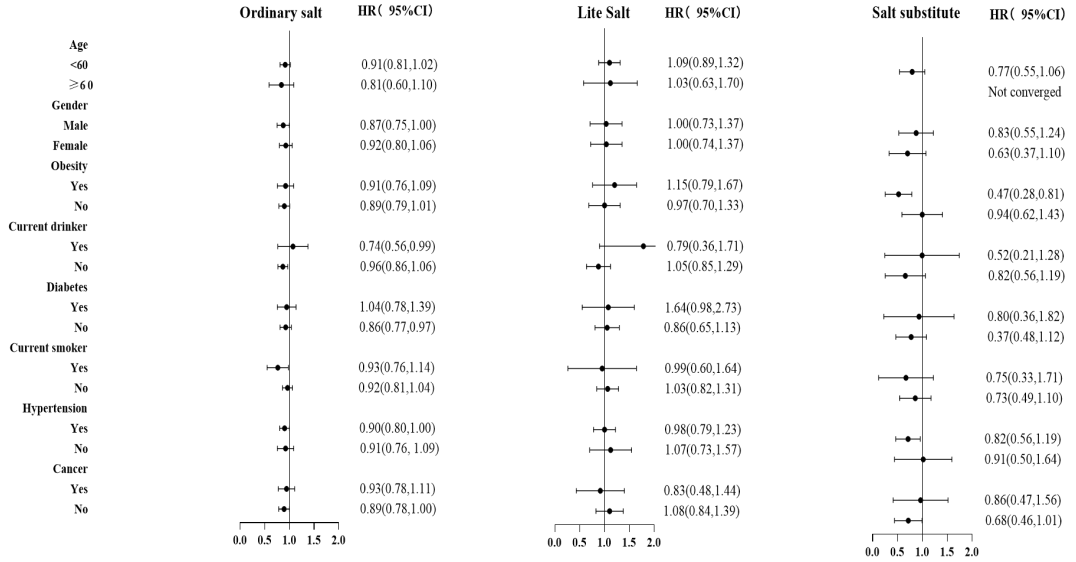

Figure 3 Associations of Type of Salt with All-Cause Mortality in Stratification Analyses

3.4 Sensitivity analysis

After excluding participants who died within first year of follow-up, ordinary salt and salt substitute were significantly associated with CVD and all-cause mortality, and results were similar to the whole sample population (Table S1). When the sodium intake was further adjusted, association of ordinary salt and salt substitute with CVD and all-cause mortality was not varied by adjusting sodium intake (Table S2). In addition, when participants with a history of diabetes, hypertension, or cancer were excluded from analyses, only ordinary salt was associated with CVD and all-cause mortality (Table S3).

Table S1 Associations of Type of Salt with Cardiovascular and All-Cause Mortality with Excluding Participants who Died within First Year of Follow-up

	Type of Salt			
	No table salt	Ordinary salt	Lite salt	Salt substitute
	（n=8984）	(n=19178)	(n=880)	(374)
All-cause mortality				
Deaths, No. (%)	853(7.40)	1373(5.15)	112(9.98)	54(8.62)
Deaths/person-years	22543972/ 387078773	40662417 / 943209793	3137417/ 39603935	1067637/ 16589099
Adjusted model	1 .00[Reference]	**0.90(0.81,1.00)**	1.00(0.81,1.23)	0.75(0.54,1.03)
P value		0.045	0.963	0.076
CVD mortality				
Deaths, No. (%) [a]	272(2.30)	355(1.24)	34(2.89)	10(1.61)
Deaths/person-years	6963658/ 387078773	10053508 / 943209793	996375/ 39603935	165439/ 16589099
Adjusted model	1 .00[Reference]	**0.79(0.67,0.93)**	0.90(0.60,1.36)	**0.44(0.20,0.96)**
P value		0.005	0.623	0.039

Values are n or hazard ratio (95% confidence interval). CVD = cardiovascular disease.

Unadjusted model: type of salt; Adjusted model: unadjusted model +age, gender, race/ethnicity, education, BMI, drinking status, smoking status, history of hypertension, history of diabetes mellitus, and history of cancer

Table S2 Associations of Type of Salt with Cardiovascular and All-Cause Mortality Further Adjusting Sodium Intake

	Type of Salt			
	No table salt	Ordinary salt	Lite salt	Salt substitute
	（n=8984）	(n=19178)	(n=880)	(374)
All-cause mortality				
Deaths, No. (%)	915(7.90)	1473(5.53)	118(10.63)	56(8.78)
Deaths/person-years	22706433/387241233	40948537/943495913	3157764/39624282	1068488/16589950
Adjusted model	1 .00[Reference]	**0.90(0.82,1.00)**	1.00(0.81,1.24)	**0.72(0.52,0.98)**
P value		0.048	0.979	0.039
CVD mortality				
Deaths, No. (%)[a]	297(2.49)	371(1.30)	37(3.12)	12(1.77)
Deaths/person-years	7027818/387241233	10099754/943495913	1002249/39624282	166290/16589950
Unadjusted model	1.00 [Reference]	**0.53(0.45,0.62)**	1.20(0.80,1.81)	0.69(0.34,1.37)
P value		<0.001	0.373	0.285
Adjusted model	1 .00[Reference]	**0.75(0.64,0.89)**	0.90(0.61,1.33)	**0.45(0.22,0.93)**
P value		0.001	0.600	0.031

Values are n or hazard ratio (95% confidence interval). CVD = cardiovascular disease.

Unadjusted model: type of salt; Adjusted model: unadjusted model +age, gender, race/ethnicity, education, BMI, drinking status, smoking status, history of hypertension, history of diabetes mellitus, history of cancer, and sodium intake

Table S3 Associations of Type of Salt with Cardiovascular and All-Cause Mortality Further with Excluding Participants with Chronic Disease

	Type of Salt			
	No table salt (n=8984)	Ordinary salt (n=19178)	Lite salt (n=880)	Salt substitute (374)
All-cause mortality				
Deaths, No. (%)	915(7.90)	1473(5.53)	118(10.63)	56(8.78)
Deaths/person-years	22706433/387241233	40948537/943495913	3157764/39624282	1068488/16589950
Adjusted model	1 .00[Reference]	**0.90(0.82,1.00)**	1.00(0.81,1.24)	**0.72(0.52,0.98)**
P value		0.048	0.979	0.039
CVD mortality				
Deaths, No. (%)[a]	297(2.49)	371(1.30)	37(3.12)	12(1.77)
Deaths/person-years	1506230/ 228421778	3281058/ 642895804	257417/ 22340909	0/ 6533511
Unadjusted model	1.00 [Reference]	0.69(0.49,0.98)	1.20(0.55,2.62)	**Not converged**
P value		0.040	0.733	
Adjusted model	1 .00[Reference]	0.81(0.57,1.15)	0.83(0.40,1.73)	**Not converged**
P value		0.245	0.611	

Values are n or hazard ratio (95% confidence interval). CVD = cardiovascular disease.

Unadjusted model: type of salt; Adjusted model: unadjusted model +age, gender, race/ethnicity, education, BMI, drinking status, and smoking status

4. Discussion

In this large-scale prospective cohort, we found that type of salt on food was associated with CVD and all-cause mortality, compared with no using salt on food. In particular, individuals who consumed salt substitutes had a lower risk of CVD and all-cause mortality, dependent of irreversible age and sex, unhealthy habits, pre-existing chronic diseases.

It is well known that the main source of salt intake is seasoning or salt added at home. As an essential element of the body, sodium mainly comes from table salt. The content of sodium varies with different table salts (Brand et al., 2022; Bernabe-Ortiz et al., 2022). A large number of studies have shown that excessive salt or sodium intake is closely related to unhealthy outcomes, including kidney disease (Malta et al., 2018), diabetes (Casagrande & Cowie, 2017; Das, 2021), hypertension (Mu et al., 2022; Chakraborty et al., 2018), arterial stiffness (Brady et al., 2022), cardiovascular disease (CVD) (Poggio et al., 2015; Milajerdi et al., 2019), and all-cause mortality (Singer et al., 2014). Prevention of CVD has always been widely concerned. However, previous studies focused on the association between salt intake and CVD (Xie et al., 2022; Ma et al., 2022; Shima et al., 2020).

Intriguingly, both high and low salt intake have been shown to be associated with metabolic dysfunction, leading to insulin resistance (IR), leptin resistance, obesity, and metabolic syndrome (Mente et al., 2016; O'Donnell et al., 2011; Moran et al., 2014). For participants who do not use salt on food, a previous study reported that an excessively low-salt diet caused salt-sensitivity hypertension, as long-term low sodium intake might result in high sensitivity to salt in the human body (Vega-Solano et al., 2021). In addition, sodium plays a key role in maintaining the volume and osmotic pressure of extracellular fluid and in transmembrane transport, especially in mediating membrane potential and action potential through sodium/potassium exchange (Nagler et al., 2014; Hoorn & Zietse, 2017). Previous evidence has shown that salt deficiency elevates low-density lipoprotein, cholesterol, and triglyceride levels (Aleksandrowicz & Kozniewska, 2022), which are closely related to CVD and all-cause mortality (Rong et al., 2019; Ahluwalia et al., 2016).

In this study, we found that ordinary salt and salt substitutes were significantly negatively associated with CVD and all-cause mortality. The results of this study supported the beneficial effect of salt on the human body, due to the rich content of sodium in salt. In addition, another interesting phenomenon was that the relationships between salt substitutes and CVD and all-cause mortality were stronger than those of ordinary salt. The possible explanation is that salt substitutes are used to replace ordinary salt (100% sodium chloride), where a portion of sodium is replaced with potassium chloride (usually 25%-30%) and/or magnesium sulfate (10%-14%), thus reducing the intake of sodium (Li et al., 2022). Another possible explanation is that people may prefer the taste of ordinary salt to salt substitutes, and some people do not accept the taste of salt substitutes. Consequently, when they use ordinary salt, they might use a larger amount, resulting in high sodium intake (Tan et al., 2022), which may increase the risk of various deaths.

This study had several limitations as well. Firstly, we could not assess the effect of changes in the type of salt during the follow-up on all-cause or CVD mortality because information on type of salt in NHANES was collected at baseline only. Secondly, the Causes of deaths are identified in the NHANES Linked Mortality File through linkage to the National Death Index, which is based on death certificates. Although this method has been verified by the Center for Disease Control and Prevention and used in many centers for disease control and prevention reports or related published reports, we could not rule out the possibility of errors when classifying the causes of mortality. Finally, although we have adjusted the confounding factors, the lack of information on salt intake may lead to residual confounding, which requires further study on the antagonistic effect of salt intake.

5. Conclusions

This study evaluated the general impact on CVD and all-cause mortality of type of salt at a population level in US, and supported adding appropriate salt to food to meet human needs. Although salt is essential to an organism's survival, excessive salt intake significantly impacts individual and population health. Safe salt intake should be promoted appropriately as a strategic healthcare program. Salt substitute might be an accessible and effective method for reducing the risk of death caused by excessive sodium intake.

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Conflict of interest statement

The authors declare that they have no competing interests.

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