scientific reports

Check for updates

OPEN

Effect of dietary probiotics intake on cancer mortality: a cohort study of NHANES 1999–2018

Yang Yang[1,2], Mengshu Pan[1], Xi Xia[2], Jiajing Liang[3], Xiangxiang Yin[2], Qian Ju[2] & Jiqing Hao[1]✉

Limited research has explored the connection between consuming dietary probiotics in the diet and cancer-related deaths. This study aimed to examine how the intake levels of three different groups of dietary probiotics are associated with the risk of dying from cancer in a representative sample of adults in the United States. Using data from the USDA Food Survey Nutrient Database, researchers categorized foods based on their microbial levels as low (10^4 CFU/g), medium (10^4–10^7 CFU/g), or high (> 10^7 CFU/g). They then used Cox proportional risk regression models to assess the risk of cancer-specific death, with follow-up periods until December 31, 2019. The study included 36,894 participants aged 20 and older, representing 148,639,331 U.S. citizens. After adjusting for various factors, the results showed that low and moderate intake of probiotics significantly reduced the risk of cancer mortality, with no significant association found for high probiotic intake. The findings suggest a notable link between dietary probiotics and cancer-specific mortality, highlighting the potential impact of dietary choices on cancer survival and indicating areas for healthcare interventions.

Sensible dietary patterns have been widely associated with various health benefits, including the positive effects of appropriate microbial exposure on managing complex diseases such as obesity and diabetes[1]. Experimental studies demonstrate that microbial changes contribute to metabolic endotoxemia, inflammation, and associated diseases, suggesting that the intestinal microbiota may set the threshold for metabolic disorders[2]. Certain strains of these microorganisms can colonize the human gut, potentially modulating the gut microbiota composition, stabilizing immune function, and reducing the risk of inflammatory infections[3–5]. Despite these insights, the relationship between dietary probiotic consumption and cancer mortality risk remains largely underexplored.

Cancer remains one of the leading causes of premature mortality worldwide, with its incidence expected to rise due to demographic shifts. This growing burden underscores the importance of identifying factors that may reduce cancer mortality risk[6]. Prior studies have confirmed that lifestyle interventions such as regular physical activity, smoking cessation, and weight management can improve cancer prognosis[7–9]. Among these factors, dietary influences on cancer mortality have gained increasing attention, with research suggesting that dietary changes may extend cancer patient survival by modulating the body's inflammatory response[10]. Microorganisms, in particular, are believed to play a crucial role in the relationship between diet and cancer prognosis. However, the specific role of dietary probiotics in enhancing cancer survival remains largely unclear[11].

The National Health and Nutrition Examination Survey (NHANES) is a population-based study that provides comprehensive health and nutrition data for adults and children in the U.S., updated biennially since 1999. Using the Sanders classification system for dietary probiotics and NHANES data from 1999 to 2018, we examined the association between dietary probiotics intake and cancer mortality risk[12].

Results

Baseline characteristics of the study population

In this study, we analyzed data from 111,066 NHANES participants aged 20 and older, spanning from 1999 to 2018. Of these, 54,813 participants (49%) were excluded due to incomplete dietary probiotic intake data, and a further 19,359 participants were excluded due to missing baseline characteristic information. Ultimately, 36,894 participants were included, representing a total of 148,639,331 non-institutionalized U.S. residents, as illustrated in eFigure. The demographic results presented in Table 1 indicate that the average age of participants was 46.99 ± 0.20 years, with the largest racial group being non-Hispanic Whites (47.33%, 17,463 individuals). A higher proportion of participants had completed high school (24.94%, 9,202 individuals) compared to those who

[1]Department of Oncology, The First Affiliated Hospital of Anhui Medical University, 218 Jixi Road, Hefei, China. [2]Department of Oncology, The Second Affiliated Hospital of Anhui Medical University, 678 Furong Road, Hefei, China. [3]Department of Clinical Nutrition, The Second Affiliated Hospital of Anhui Medical University, 678 Furong Road, Hefei, China. ✉email: haojiqing2023@163.com

had not (75.06%, 27,692 individuals). Non-smokers comprised 53.39% of the cohort (19,698 individuals), and mild alcohol consumption was reported by 33.65% (12,415 individuals). Most participants had a normal BMI (61.71%, 22,766 individuals), and a significant proportion did not have diabetes (75.46%, 27,840 individuals) or hypertension (57.71%, 21,293 individuals), although a notable number had hyperlipidemia (72.36%, 26,696 individuals), with few reporting coronary heart disease (4.14%, 1,527 individuals).

Intake of different dietary probiotic groups

All participants reported consuming low dietary probiotics, with a daily intake range from 33 to 18,281.03 g and a mean intake of $3,179.02 \pm 19.21$ g. Intake levels significantly varied across demographic groups (age, gender, race), lifestyle habits (e.g., smoking, alcohol use), and underlying health conditions (e.g., hypertension, diabetes, hyperlipidemia) ($p < 0.0001$). Moderate dietary probiotic intake was reported by 59.32% of participants (21,884 individuals), with an average of 104.98 ± 1.91 g/day, while 40.68% (15,010 individuals) reported no intake. Intake differences were statistically significant across demographics and lifestyle groups ($p < 0.0001$) but showed no significant variation across groups with underlying health conditions. For high dietary probiotics, 78.34% (28,904 individuals) reported no intake, while 21.66% (7,990 individuals) reported an average intake of 20.51 ± 0.53 g/day. Significant intake differences were noted across demographics, lifestyle habits, and health condition groups ($p < 0.0001$) (Tables 1, 2).

Relationship between intake of different dietary probiotics and cancer mortality

Table 3 shows the associations between baseline covariates, adjusted for age and gender using a Cox proportional hazards regression model, and cancer mortality. Specifically, the hazard ratio (HR) for cancer mortality rises progressively with age. Females (HR = 0.76; 95% CI: 0.65–0.88) and Mexican Americans (HR = 0.40; 95% CI: 0.32–0.49) exhibit lower cancer mortality risks. Other factors associated with reduced cancer mortality risk include higher education (HR = 0.48; 95% CI: 0.41–0.56) and being married (HR = 0.84; 95% CI: 0.74–0.96). In contrast, former smokers (HR = 2.86; 95% CI: 2.40–3.40), former alcohol consumers (HR = 2.28; 95% CI: 1.76–2.96), and individuals with diabetes (HR = 2.85; 95% CI: 2.38–3.40), hypertension (HR = 3.19; 95% CI: 2.76–3.69), hyperlipidemia (HR = 1.79; 95% CI: 1.50–2.15), self-reported cardiovascular diseases like coronary heart disease (HR = 4.36; 95% CI: 3.43–5.54), and lower levels of serum albumin (HR = 0.31; 95% CI: 0.25–0.39) show a significant association with increased cancer mortality risk.

In the multivariable Cox regression model presented in Table 4, low dietary probiotic intake was divided into quintiles, and in the crude model, cancer mortality risk gradually decreased with higher intake levels, demonstrating significant differences and a clear trend ($p < 0.0001$). After adjusting for age and gender, only the Q2–Q4 intake levels retained statistical significance. Upon adjusting for all covariates significantly associated with both cancer mortality and dietary probiotic intake, only a moderate intake of low dietary probiotics (Q2) remained significantly associated with a reduction in cancer mortality risk (HR = 0.82; 95% CI: 0.68–0.98). For medium dietary probiotics, compared to participants with no intake, any intake of medium dietary probiotics (HR = 0.81; 95% CI: 0.69–0.95) was associated with reduced cancer mortality risk after adjusting for all confounders ($p = 0.01$). When further categorized into three intake levels, a significant association with decreased cancer mortality risk was observed only at the highest dose level (Q3) (HR = 0.75; 95% CI: 0.61–0.92). Conversely, high dietary probiotics showed no significant association with cancer mortality across intake levels in all models.

To visualize these findings, Kaplan–Meier curves adjusted for multiple factors were generated based on dietary probiotic intake levels to illustrate cancer mortality outcomes (Fig. 1). To explore dose–response patterns between different types of dietary probiotics and cancer mortality risk, dose–response curves were fitted (Fig. 2). Consistent with Table 4 results, low dietary probiotics displayed a "U"-shaped curve, with cancer mortality risk decreasing as intake rose at lower levels, then increasing once intake surpassed 2,676.953 g per day. Medium dietary probiotics showed an approximately linear inverse association with cancer mortality, while high dietary probiotics presented an inverted "U"-shaped curve, with risk initially decreasing and then increasing with rising intake levels.

Stratified analysis

A fully adjusted stratified analysis was performed according to age, gender, race, poverty level, BMI, smoking and alcohol consumption status, hypertension, and hyperlipidemia. Results in eTable 1 demonstrate a significant and consistent trend linking low-dose dietary probiotics intake with a reduced cancer mortality risk in individuals aged 40–79. Among those aged 80 and older, only a high intake (Q3) of medium and high dietary probiotics was significantly associated with a lower cancer mortality risk. Low dietary probiotic intake correlated significantly with decreased cancer risk across genders, while medium probiotic intake showed no significant association (eTable 2). However, high dietary probiotic intake was linked to a lower cancer risk exclusively in males (HR = 0.687; 95% CI: 0.527–0.895) (eTable 3).

Racial stratification indicated a significant association between low dietary probiotics and reduced cancer risk in all groups except Non-Hispanic Blacks, whereas medium dietary probiotics intake showed no association with cancer risk across racial groups. High dietary probiotic intake was significantly correlated with reduced cancer mortality in Non-Hispanic White, Non-Hispanic Black, and Mexican American groups. BMI-based stratification found that low dietary probiotics were significantly associated with reduced cancer risk across all BMI groups, except those under 18.5. Conversely, high dietary probiotic intake was linked to lower cancer risk in all BMI categories except those above 30.

Furthermore, low dietary probiotic intake was significantly correlated with reduced cancer risk across varying poverty and educational levels, whereas medium dietary probiotics intake did not show this association. Increased intake of low dietary probiotics significantly correlated with lower cancer mortality risk among non-

Characteristic	Study Participants[a]						
	Low dietary probiotics group						
	Q1	Q2	Q3	Q4	Q5	P for trend	Total
Age, No. (%), years						**< 0.0001**	
20–29	1136(18.97)	1096(16.48)	1189(17.73)	1248(18.12)	1436(19.95)		6105(16.55)
30–39	893(15.39)	1070(16.80)	1182(17.54)	1349(18.79)	1644(21.94)		6138(16.64)
40–49	977(15.82)	1151(18.25)	1326(20.80)	1449(21.97)	1593(23.22)		6496(17.61)
50–59	925(15.52)	1078(17.67)	1152(18.00)	1249(19.42)	1337(20.88)		5741(15.56)
60–69	1416(13.76)	1350(14.40)	1320(14.18)	1185(13.30)	912(10.18)		6183(16.76)
70–79	1183(12.60)	990(10.73)	796(8.09)	659(6.50)	343(3.04)		3971(10.76)
≥ 80	849(7.93)	644(5.67)	413(3.66)	240(1.89)	114(0.79)		2260(6.13)
Sex, No. (%)						**< 0.0001**	
Male	2601(30.23)	3207(39.76)	3650(46.82)	4070(53.66)	5041(68.30)		18,569(50.33)
Female	4778(69.77)	4172(60.24)	3728(53.18)	3309(46.34)	2338(31.70)		18,325(49.67)
Race/Ethnicuty, No. (%)						**< 0.0001**	
Non-Hispanic White	2920(62.25)	3368(69.08)	3519(71.72)	3720(74.51)	3936(75.64)		17,463(47.33)
Non-Hispanic Black	1944(16.20)	1541(11.43)	1424(9.67)	1313(8.20)	1075(6.50)		7297(19.78)
Mexican American	1471(8.30)	1296(7.68)	1205(7.43)	1160(7.28)	1165(7.76)		6297(17.07)
Other	1044(13.26)	1174(11.81)	1230(11.19)	1186(10.01)	1203(10.10)		5837(15.82)
Marital status, No. (%)						**< 0.0001**	
Unmarried or other	3348(41.59)	2840(35.19)	2742(34.03)	2697(32.75)	2806(34.92)		14,433(39.12)
Married or living with a partner	4031(58.41)	4539(64.81)	4636(65.97)	4682(67.25)	4573(65.08)		22,461(60.88)
Educational attainment, No. (%)						**< 0.0001**	
< High school	2576(23.01)	1967(17.21)	1676(14.23)	1501(12.66)	1482(13.51)		9202(24.94)
≥ High school	4803(76.99)	5412(82.79)	5702(85.77)	5878(87.34)	5897(86.49)		27,692(75.06)
Poverty income ratio, No. (%)						**< 0.0001**	
Below poverty line (< 1.00)	1729(18.09)	1418(13.21)	1277(11.50)	1293(11.53)	1366(12.09)		7083(19.2)
At or above poverty line (≥ 1.00)	5650(81.91)	5961(86.79)	6101(88.50)	6086(88.47)	6013(87.91)		29,811(80.8)
Alcohol consumption, No. (%)						**< 0.0001**	
Never	1618(19.90)	1186(13.77)	924(10.20)	770(8.22)	519(5.14)		5017(13.6)
Former	1662(18.20)	1377(15.79)	1241(13.81)	1140(12.78)	1000(12.09)		6420(17.4)
Mild	2266(33.55)	2631(37.86)	2716(39.71)	2595(38.25)	2207(32.08)		12,415(33.65)
Moderate	933(15.16)	1073(16.53)	1135(17.23)	1252(18.90)	1240(18.37)		5633(15.27)
Heavy	900(13.19)	1112(16.04)	1362(19.06)	1622(21.85)	2413(32.33)		7409(20.08)
BMI, No. (%)						**< 0.0001**	
18.5–30.0	4680(65.12)	4703(64.76)	4606(64.51)	4391(59.97)	4386(60.33)		22,766(61.71)
< 18.5	135(2.13)	130(1.98)	104(1.41)	92(1.40)	75(1.02)		536(1.45)
≥ 30.0	2564(32.76)	2546(33.26)	2668(34.08)	2896(38.63)	2918(38.66)		13,592(36.84)
History of stroke, No. (%)						**< 0.0001**	
No	6968(95.74)	7097(96.87)	7137(97.60)	7162(97.93)	7192(98.09)		35,556(96.37)
Yes	411(4.26)	282(3.13)	241(2.40)	217(2.07)	187(1.91)		1338(3.63)
History of heart attack, No. (%)						**< 0.001**	
No	6992(95.83)	7034(96.26)	7063(96.70)	7113(97.30)	7130(97.20)		35,332(95.77)
Yes	387(4.17)	345(3.74)	315(3.30)	266(2.70)	249(2.80)		1562(4.23)
History of coronary heart disease, No. (%)						**< 0.0001**	
No	6993(95.45)	7030(96.08)	7063(96.49)	7101(96.93)	7180(97.55)		35,367(95.86)
Yes	386(4.55)	349(3.92)	315(3.51)	278(3.07)	199(2.45)		1527(4.14)
History of angina, No. (%)						**< 0.0001**	
No	7092(96.52)	7140(97.15)	7178(97.94)	7202(97.86)	7218(98.13)		35,830(97.12)
Yes	287(3.48)	239(2.85)	200(2.06)	177(2.14)	161(1.87)		1064(2.88)
History of hyperlipidemia, No. (%)						**< 0.001**	
No	1874(27.33)	1910(26.60)	2046(28.44)	2090(29.32)	2278(31.10)		10,198(27.64)
Yes	5505(72.67)	5469(73.40)	5332(71.56)	5289(70.68)	5101(68.90)		26,696(72.36)
History of congestive heart failure, No. (%)						**< 0.0001**	
No	7055(96.57)	7147(97.64)	7168(97.77)	7184(98.10)	7222(98.44)		35,776(96.97)
Yes	324(3.43)	232(2.36)	210(2.23)	195(1.90)	157(1.56)		1118(3.03)
History of hypertension, No. (%)						**< 0.0001**	
Continued							

Characteristic	Study Participants[a]						
	Low dietary probiotics group						
	Q1	Q2	Q3	Q4	Q5	P for trend	Total
No	3769(58.53)	4035(59.65)	4348(64.55)	4539(65.43)	4602(65.26)		21,293(57.71)
Yes	3610(41.47)	3344(40.35)	3030(35.45)	2840(34.57)	2777(34.74)		15,601(42.29)
History of DM, No. (%)						**0.001**	
No	5438(79.93)	5525(80.43)	5571(80.71)	5591(80.34)	5715(80.58)		27,840(75.46)
DM	1420(13.80)	1310(12.81)	1270(12.89)	1195(12.25)	1094(11.44)		6289(17.05)
IFG	337(4.35)	310(3.85)	310(3.90)	354(4.59)	357(5.11)		1668(4.52)
IGT	184(1.93)	234(2.91)	227(2.50)	239(2.82)	213(2.88)		1097(2.97)
Healthy Eating Index (2015), mean (SE), %	49.13(0.26)	50.18(0.29)	50.67(0.30)	50.80(0.26)	50.75(0.25)	< 0.0001	50.38(0.18)
HbA1c levels, mean (SE), %	5.58(0.01)	5.57(0.01)	5.56(0.01)	5.56(0.01)	5.56(0.02)	0.82	5.57(0.01)
Alt levels, mean (SE), U/L	22.69(0.21)	24.57(0.26)	25.03(0.26)	26.48(0.26)	28.84(0.45)	< 0.0001	25.78(0.14)
Ast levels, mean (SE), U/L	23.83(0.17)	24.75(0.21)	24.94(0.22)	25.51(0.22)	26.89(0.24)	< 0.0001	25.31(0.10)
Bilirubin levels, mean (SE), mg/dL	11.48(0.10)	11.74(0.10)	11.72(0.10)	11.65(0.10)	11.95(0.10)	0.01	11.73(0.07)
Alkaline phosphatase levels, mean (SE), U/L	71.09(0.53)	69.81(0.45)	68.31(0.40)	67.73(0.40)	68.18(0.35)	< 0.0001	68.88(0.27)
Albumin levels, mean (SE), g/dL	4.24(0.01)	4.27(0.01)	4.29(0.01)	4.30(0.01)	4.33(0.01)	< 0.0001	4.29(0.00)
Survival Time, mean (SE), mo	143.24(1.75)	128.35(1.54)	120.37(1.61)	110.80(1.39)	106.50(1.55)	< 0.0001	120.16(1.20)
Survival Status, No. (%)						**< 0.0001**	
Assumed alive	5472(80.10)	6026(86.54)	6358(89.78)	6640(92.54)	6803(94.14)		31,299(84.83)
Assumed deceased	1907(19.90)	1353(13.46)	1020(10.22)	739(7.46)	576(5.86)		5595(15.17)
Cause of death, No. (%)						**< 0.0001**	
AD-Specific	87(1.03)	51(0.54)	35(0.33)	18(0.13)	5(0.05)		196(0.53)
Cancer-Specific	372(3.95)	296(2.95)	249(2.65)	197(1.99)	156(1.60)		1270(3.44)
CVD-Specific	751(7.85)	506(5.00)	381(3.65)	252(2.42)	193(1.96)		2083(5.65)
DM-Specific	69(0.61)	45(0.48)	37(0.36)	23(0.28)	31(0.27)		205(0.56)
I&P-Specific	40(0.42)	32(0.29)	14(0.13)	14(0.11)	5(0.03)		105(0.28)
Other leadings	588(6.05)	423(4.20)	304(3.10)	235(2.53)	186(1.94)		1736(4.71)
Still alive	5472(80.10)	6026(86.54)	6358(89.78)	6640(92.54)	6803(94.14)		31,299(84.83)

Table 1. Demographic, health behavior, and general health characteristics of participants by total and low dietary probiotics group consumed by participants. Abbreviations: AD: Alzheimer's Disease; CVD, cardiovascular disease; DM, Diabetes mellitus; I&P: Immunization and Prevention; HbA1c, Hemoglobin A1c; Alt, Alanine Transaminase; Ast, Aspartate Transaminase; mo, months; BMI, Body Mass Index (calculated as weight in kilograms divided by height in meters squared); HR, hazard ratio; CI, confidence interval [a]All proportions, means, and SEs are weighted estimates of the US population characteristics, taking into account the complex sampling design of the National Health and Nutrition Examination Survey (NHANES) * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$ Significant values are in [bold].

smokers and non-drinkers, with a clear trend (p for trend < 0.0001). High dietary probiotic intake, however, was significantly associated with reduced cancer mortality only among those without a smoking history (HR = 0.648; 95% CI: 0.457–0.919) and those with a history of alcohol consumption (HR = 0.738; 95% CI: 0.604–0.901).

Sensitivity analysis

To account for the non-linear relationship between age and mortality, the final Cox proportional hazards regression model included the square of age. A sensitivity analysis confirmed the stability of these results, which remained consistent with the main analysis (Table 4).

Discussion

Using the latest NHANES data on nutritional intake and mortality, we analyzed a representative sample of 36,894 American adults, focusing on classifying and quantifying dietary probiotic intake. Our findings reveal that dietary probiotics serve as a protective factor against cancer mortality, with the impact varying across different intake levels. Specifically, a U-shaped relationship emerges between low dietary probiotics intake and cancer mortality risk. Moderate dietary probiotics show an increasingly protective effect with higher intake, while high probiotics intake is protective at lower doses but may increase mortality risk at higher doses.

The "Old Friends Hypothesis" proposes that consuming symbiotic or benign microorganisms in food provides critical microbial stimulation that positively impacts immune health. This concept highlights the regulatory role of these microorganisms in maintaining immune balance, with recognized health benefitsprobiotics[13], defined by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) in 2012 as "dietary

Characteristic	Study Participants[a]													
	Middle dietary probiotics group							High dietary probiotics group						
	No	Total	P value	Q1	Q2	Q3	P for trend	No	Total	P value	Q1	Q2	Q3	P for trend
Age, No. (%), years			**< 0.0001**				**< 0.0001**			**0.001**				**< 0.0001**
20–29	2789(21.35)	3316(16.43)		1306(19.58)	1101(16.29)	909(13.53)		4693(18.21)	1412(18.57)		447(17.63)	537(21.04)	428(16.98)	
30–39	2596(19.31)	3542(17.78)		1320(19.80)	1146(17.01)	1076(16.61)		4703(18.38)	1435(18.32)		472(19.24)	510(19.35)	453(16.40)	
40–49	2608(20.38)	3888(20.34)		1328(20.92)	1275(19.44)	1285(20.68)		5036(20.27)	1460(20.61)		483(20.22)	481(20.79)	496(20.80)	
50–59	2274(17.37)	3467(19.24)		1041(16.38)	1164(19.32)	1262(21.93)		4506(18.55)	1235(18.47)		425(18.16)	398(18.18)	412(19.08)	
60–69	2408(11.60)	3775(13.89)		1134(12.34)	1311(14.34)	1330(14.94)		4942(12.62)	1241(14.14)		443(14.96)	368(11.80)	430(15.74)	
70–79	1499(6.73)	2472(8.40)		756(7.48)	893(8.90)	823(8.80)		3195(8.08)	776(6.88)		240(5.98)	244(6.77)	292(7.85)	
≥ 80	836(3.25)	1424(3.90)		420(3.51)	568(4.69)	436(3.50)		1829(3.89)	431(3.00)		170(3.81)	109(2.09)	152(3.15)	
Sex, No. (%)			**< 0.0001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
Male	7984(53.23)	10,585(47.04)		3596(48.14)	3522(45.56)	3467(47.45)		14,947(50.87)	3622(45.23)		1144(41.70)	1355(51.33)	1123(42.41)	
Female	7026(46.77)	11,299(52.96)		3709(51.86)	3936(54.44)	3654(52.55)		13,957(49.13)	4368(54.77)		1536(58.30)	1292(48.67)	1540(57.59)	
Race/Ethnicuty, No. (%)			**< 0.0001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
Non-Hispanic White	6482(66.78)	10,981(74.00)		3512(71.73)	3743(73.67)	3726(76.51)		12,941(68.61)	4522(78.75)		1408(76.03)	1584(80.90)	1530(79.18)	
Non-Hispanic Black	3902(13.94)	3395(7.53)		1309(9.24)	1136(7.39)	950(6.01)		6311(11.55)	986(5.49)		386(6.66)	326(5.53)	274(4.34)	
Mexican American	2168(7.01)	4129(8.06)		1433(8.56)	1401(8.07)	1295(7.57)		5150(8.33)	1147(5.75)		454(6.95)	340(5.04)	353(5.33)	
Other	2458(12.27)	3379(10.41)		1051(10.47)	1178(10.87)	1150(9.90)		4502(11.51)	1335(10.00)		432(10.37)	397(8.54)	506(11.15)	
Marital status, No. (%)			**< 0.0001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
Unmarried or other	6515(39.49)	7918(32.87)		2800(35.38)	2626(31.90)	2492(31.40)		11,554(36.44)	2879(32.41)		947(30.89)	936(31.90)	996(34.38)	
Married or living with a partner	8495(60.51)	13,966(67.13)		4505(64.62)	4832(68.10)	4629(68.60)		17,350(63.56)	5111(67.59)		1733(69.11)	1711(68.10)	1667(65.62)	
Educational attainment, No. (%)			**< 0.0001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
< High school	4273(19.62)	4929(13.25)		1833(15.65)	1688(13.35)	1408(10.83)		7905(17.88)	1297(9.39)		480(10.22)	440(9.33)	377(8.66)	
≥ High school	10,737(80.38)	16,955(86.75)		5472(84.35)	5770(86.65)	5713(89.17)		20,999(82.12)	6693(90.61)		2200(89.78)	2207(90.67)	2286(91.34)	
Poverty income ratio, No. (%)			**< 0.0001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
Below poverty line (< 1.00)	3521(16.97)	3562(10.59)		1362(12.60)	1218(10.64)	982(8.60)		5934(14.36)	1149(9.22)		394(9.07)	409(10.18)	346(8.37)	
At or above poverty line (≥ 1.00)	11,489(83.03)	18,322(89.41)		5943(87.40)	6240(89.36)	6139(91.40)		22,970(85.64)	6841(90.78)		2286(90.93)	2238(89.82)	2317(91.63)	
Alcohol consumption, No. (%)			**< 0.0001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
Never	2103(10.97)	2914(10.68)		930(10.56)	1084(11.61)	900(9.87)		4107(11.53)	910(8.70)		311(8.92)	249(7.21)	350(10.00)	
Former	2890(16.11)	3530(13.10)		1175(13.14)	1225(13.42)	1130(12.75)		5280(15.06)	1140(11.95)		386(11.82)	362(11.50)	392(12.52)	
Mild	4506(31.75)	7909(39.05)		2421(35.86)	2704(38.73)	2784(42.45)		9363(34.84)	3052(40.33)		986(39.12)	1015(39.77)	1051(42.05)	
Moderate	2211(16.67)	3422(17.85)		1159(17.51)	1127(17.69)	1136(18.35)		4253(16.62)	1380(19.63)		473(20.19)	455(19.15)	452(19.59)	
Heavy	3300(24.50)	4109(19.31)		1620(22.93)	1318(18.54)	1171(16.58)		5901(21.96)	1508(19.38)		524(19.93)	566(22.35)	418(15.84)	
BMI, No. (%)			**< 0.0001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
18.5–30.0	8872(59.30)	13,894(64.75)		4534(62.46)	4731(64.51)	4629(67.20)		17,620(61.61)	5146(65.69)		1661(63.56)	1662(63.66)	1823(69.80)	
< 18.5	247(1.68)	289(1.45)		105(1.60)	95(1.32)	89(1.43)		424(1.54)	112(1.53)		33(1.52)	37(1.39)	42(1.68)	
≥ 30.0	5891(39.02)	7701(33.80)		2666(35.94)	2632(34.17)	2403(31.38)		10,860(36.85)	2732(32.77)		986(34.91)	948(34.95)	798(28.52)	
History of stroke, No. (%)			**< 0.0001**				**0.001**			**< 0.0001**				**0.001**
No	14,359(96.87)	21,197(97.65)		7074(97.58)	7202(97.55)	6921(97.81)		27,770(97.12)	7786(98.00)		2612(98.24)	2577(97.69)	2597(98.08)	
Yes	651(3.13)	687(2.35)		231(2.42)	256(2.45)	200(2.19)		1134(2.88)	204(2.00)		68(1.76)	70(2.31)	66(1.92)	

Continued

Characteristic	Study Participants[a]													
	Middle dietary probiotics group							High dietary probiotics group						
	No	Total	P value	Q1	Q2	Q3	P for trend	No	Total	P value	Q1	Q2	Q3	P for trend
History of heart attack, No. (%)			**0.33**				**0.52**			**< 0.0001**				**< 0.0001**
No	14,321(96.60)	21,011(96.81)		7013(96.87)	7170(96.97)	6828(96.58)		27,583(96.41)	7749(97.65)		2588(97.61)	2576(97.83)	2585(97.51)	
Yes	689(3.40)	873(3.19)		292(3.13)	288(3.03)	293(3.42)		1321(3.59)	241(2.35)		92(2.39)	71(2.17)	78(2.49)	
History of coronary heart disease, No. (%)			**0.16**				**0.22**			**0.01**				**0.09**
No	14,414(96.80)	20,953(96.47)		7016(96.77)	7130(96.42)	6807(96.22)		27,659(96.42)	7708(97.08)		2578(96.93)	2561(97.17)	2569(97.14)	
Yes	596(3.20)	931(3.53)		289(3.23)	328(3.58)	314(3.78)		1245(3.58)	282(2.92)		102(3.07)	86(2.83)	94(2.86)	
History of angina, No. (%)			**0.06**				**0.34**			**< 0.001**				**0.005**
No	14,573(97.37)	21,257(97.73)		7114(97.73)	7217(97.69)	6926(97.76)		28,021(97.37)	7809(98.24)		2609(97.94)	2591(98.32)	2609(98.43)	
Yes	437(2.63)	627(2.27)		191(2.27)	241(2.31)	195(2.24)		883(2.63)	181(1.76)		71(2.06)	56(1.68)	54(1.57)	
History of hyperlipidemia, No. (%)			**0.78**				**0.59**			**< 0.0001**				**< 0.0001**
No	4197(28.64)	6001(28.80)		2036(29.01)	2006(28.04)	1959(29.36)		7813(27.84)	2385(31.29)		797(31.14)	797(31.39)	791(31.34)	
Yes	10,813(71.36)	15,883(71.20)		5269(70.99)	5452(71.96)	5162(70.64)		21,091(72.16)	5605(68.71)		1883(68.86)	1850(68.61)	1872(68.66)	
History of congestive heart failure, No. (%)			**0.01**				**0.09**			**< 0.001**				**0.001**
No	14,496(97.51)	21,280(97.95)		7102(97.90)	7232(97.88)	6946(98.07)		27,971(97.58)	7805(98.35)		2602(98.26)	2598(98.50)	2605(98.28)	
Yes	514(2.49)	604(2.05)		203(2.10)	226(2.12)	175(1.93)		933(2.42)	185(1.65)		78(1.74)	49(1.50)	58(1.72)	
History of hypertension, No. (%)			**0.18**				**0.23**			**< 0.0001**				**< 0.0001**
No	8520(62.49)	12,773(63.37)		4305(63.68)	4268(62.49)	4200(63.96)		16,343(61.90)	4950(66.28)		1617(65.05)	1665(65.84)	1668(67.88)	
Yes	6490(37.51)	9111(36.63)		3000(36.32)	3190(37.51)	2921(36.04)		12,561(38.10)	3040(33.72)		1063(34.95)	982(34.16)	995(32.12)	
History of DM, No. (%)			**0.68**				**0.8**			**< 0.0001**				**< 0.0001**
No	11,220(80.00)	16,620(80.68)		5587(81.10)	5631(80.08)	5402(80.87)		21,550(79.65)	6290(82.60)		2073(81.55)	2119(83.89)	2098(82.29)	
DM	2622(12.75)	3667(12.41)		1173(11.92)	1283(12.68)	1211(12.62)		5145(13.19)	1144(10.69)		415(11.19)	348(9.54)	381(11.36)	
IFG	698(4.48)	970(4.34)		338(4.41)	322(4.50)	310(4.13)		1331(4.44)	337(4.27)		118(4.53)	118(4.68)	101(3.59)	
IGT	470(2.77)	627(2.57)		207(2.57)	222(2.74)	198(2.39)		878(2.71)	219(2.45)		74(2.72)	62(1.88)	83(2.75)	
Healthy Eating Index (2015), mean (SE), %	45.64(0.16)	53.30(0.20)	< 0.0001	47.96(0.24)	52.87(0.23)	58.91(0.23)	< 0.0001	49.50(0.18)	52.89(0.24)	< 0.0001	51.69(0.33)	50.50(0.37)	56.45(0.37)	< 0.0001
HbA1c levels, mean (SE), %	5.59(0.01)	5.55(0.01)	< 0.001	5.53(0.01)	5.56(0.01)	5.55(0.01)	0.001	5.59(0.01)	5.50(0.01)	< 0.0001	5.52(0.02)	5.48(0.02)	5.50(0.02)	< 0.0001
Alt levels, mean (SE), U/L	26.14(0.21)	25.57(0.19)	0.04	25.69(0.25)	25.36(0.40)	25.65(0.28)	0.24	25.96(0.15)	25.28(0.38)	0.1	24.62(0.46)	27.16(0.97)	24.01(0.31)	< 0.0001
Ast levels, mean (SE), U/L	25.49(0.16)	25.20(0.11)	0.09	25.03(0.20)	25.08(0.19)	25.48(0.22)	0.11	25.46(0.12)	24.89(0.18)	0.01	24.56(0.25)	25.49(0.35)	24.60(0.29)	< 0.001
Continued														

Characteristic	Study Participants[a]													
	Middle dietary probiotics group							High dietary probiotics group						
	No	Total	P value	Q1	Q2	Q3	P for trend	No	Total	P value	Q1	Q2	Q3	P for trend
Bilirubin levels, mean (SE), mg/dL	11.47(0.09)	11.88(0.08)	< 0.0001	11.59(0.11)	11.78(0.10)	12.27(0.10)	< 0.0001	11.76(0.07)	11.64(0.09)	0.17	11.27(0.13)	11.81(0.15)	11.82(0.17)	0.005
Alkaline phosphatase levels, mean (SE), U/L	70.82(0.36)	67.68(0.28)	< 0.0001	69.22(0.39)	67.88(0.36)	65.99(0.34)	< 0.0001	69.73(0.30)	66.45(0.32)	< 0.0001	66.61(0.55)	67.13(0.53)	65.60(0.47)	< 0.0001
Albumin levels, mean (SE), g/dL	4.28(0.01)	4.30(0.00)	< 0.0001	4.28(0.01)	4.30(0.01)	4.32(0.01)	< 0.0001	4.29(0.00)	4.31(0.01)	< 0.001	4.29(0.01)	4.32(0.01)	4.31(0.01)	< 0.001
Survival Time, mean (SE), mo	116.72(1.48)	122.27(1.31)	< 0.0001	122.46(1.82)	122.86(1.36)	121.51(1.90)	< 0.0001	123.02(1.25)	112.00(1.59)	< 0.0001	106.22(1.91)	120.39(2.30)	109.01(2.32)	< 0.0001
Survival Status, No. (%)			**0.002**				**< 0.0001**			**< 0.0001**				**< 0.0001**
Assumed alive	12,633(88.57)	18,666(89.68)		6215(89.33)	6272(88.62)	6179(91.08)		24,197(88.18)	7102(92.31)		2372(91.90)	2362(92.65)	2368(92.37)	
Assumed deceased	2377(11.43)	3218(10.32)		1090(10.67)	1186(11.38)	942(8.92)		4707(11.82)	888(7.69)		308(8.10)	285(7.35)	295(7.63)	
Cause of death, No. (%)			**< 0.001**				**< 0.0001**			**< 0.0001**				**< 0.0001**
AD-Specific	60(0.26)	136(0.44)		44(0.44)	56(0.55)	36(0.33)		155(0.38)	41(0.35)		15(0.37)	11(0.27)	15(0.41)	
Cancer-Specific	524(2.55)	746(2.50)		239(2.28)	279(2.73)	228(2.50)		1057(2.67)	213(2.10)		73(2.06)	69(2.06)	71(2.17)	
CVD-Specific	925(4.27)	1158(3.69)		389(3.91)	432(4.19)	337(2.97)		1766(4.36)	317(2.63)		104(2.64)	110(2.65)	103(2.60)	
DM-Specific	89(0.46)	116(0.33)		37(0.32)	42(0.42)	37(0.26)		178(0.45)	27(0.20)		9(0.28)	8(0.12)	10(0.21)	
I&P-Specific	41(0.17)	64(0.18)		29(0.23)	22(0.20)	13(0.12)		84(0.19)	21(0.14)		9(0.18)	5(0.09)	7(0.15)	
Other leadings	738(3.71)	998(3.17)		352(3.49)	355(3.29)	291(2.75)		1467(3.77)	269(2.27)		98(2.58)	82(2.15)	89(2.10)	
Still alive	12,633(88.57)	18,666(89.68)		6215(89.33)	6272(88.62)	6179(91.08)		24,197(88.18)	7102(92.31)		2372(91.90)	2362(92.65)	2368(92.37)	

Table 2. Demographic, health behavior, and general health characteristics of participants by middle and high dietary probiotics group consumed by participants. Abbreviations: AD: Alzheimer's Disease; CVD, cardiovascular disease; DM, Diabetes mellitus; I&P: Immunization and Prevention; HbA1c, Hemoglobin A1c; Alt, Alanine Transaminase; Ast, Aspartate Transaminase; mo, months; BMI, Body Mass Index (calculated as weight in kilograms divided by height in meters squared); HR, hazard ratio; CI, confidence interval [a]All proportions, means, and SEs are weighted estimates of the US population characteristics, taking into account the complex sampling design of the National Health and Nutrition Examination Survey (NHANES) * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$ Significant values are in [bold].

probiotics which, when administered in adequate amounts, confer a health benefit on the host," play a significant role in immune and metabolic health[14,15]. Decadeported the link between dietary microorganisms and chronic, diet-related conditions like immune and metabolic disorders[16]. These microorganisms, once into the gut microbiome, have been shown to enhance intestinal function, bolster immunity, and reduce chronic disease susceptibility[17]. Epidemiological and intervention stconsistently linked the intake of fermented foods rich in dietary probiotics, such as yogurt and pickles, with improved metabolic and immune health[18–20]. The quantity and types of microorganisms in fmolds—depend on the food source, its processing, and its preparation method. Dietary probiotics are prevalent not only in fermented foods but also in various everyday food items. Fermented foods generally contain over 10^7 CFU (colony-forming units) per gram, while unprocessed foods like fresh fruits and vegetables contain lower levels, typically under 10^6 CFU per gram[21–23]. Refrigerated and pasteurized foods, such as milk and cooked meats, also conn reduced numbers prior to spoilage[24,25]. Sanders et al. further categorized these microbial levels, defining foods with low ($< 10^4$ CFU/g), medium (high ($> 10^7$ CFU/g) levels of dietary probiotics[26].

This study explores the relationship between varying levels of dietary probiotic intake and cancer mortality. Findings show that, below a specific threshold, increasing low dietary probiotics correlates with a reduced risk of cancer mortality. However, exceeding this threshold reverses the effect, as low dietary microorganism intake then becomes associated with elevated cancer mortality risk. For moderate probiotics, the protective impact on cancer mortality diminishes as intake levels rise, while high dietary probiotic intake displays an approximately "U"-shaped dose–response relationship with cancer mortality. Previous research suggests potential benefits of probiotics for cancer patients, particularly those who experience immune suppression and side effects, such as diarrhea, due to treatment. A systematic review of 11 studies reported that probiotics may alleviate the frequency and severity of treatment-induced diarrhea, potentially reducing the reliance on antidiarrheal medications[27]. Similarly, a meta-analysis of 34 prospective cohort studies linked high fermented dairy intake with lower cancer-specific mortality in women (RR: 0.85; 95% CI: 0.07–0.94), possibly due to the high probiotic content[28]. Contrastingly, the current study indicates that high-dose intake of high dietary probiotics may actually increase cancer mortality risk, diverging from the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort findings, which found no link between total fermented food intake and cancer mortality[29]. Intake patterns of dietary microorganisms often reflect the associated food categories. According to Marco et al., foods that undergo heat processing, such as milk, cooked meats, sauces, and cereals, contain minimal microorganism levels ($< 10^4$ CFU/g). Fresh fruits and vegetables, including juices and smoothies, provide moderate probiotic levels (10^4–10^7 CFU/g), while fermented dairy products, like yogurt, cream, and cheese, are rich in probiotics ($> 10^7$ CFU/g)[12]. Processed meats, which foster sulfur-metabolizing microorganisms, can generate H2S, a compound potentially damaging to the intestinal barrier and implicated in tumor development through changes in inflammation-related immune cells[30]. In contrast, fresh vegetables harbor fewer sulfur-metabolizing microorganisms and contain glucosinolates, sulfur-rich compounds with notable anti-inflammatory and anticancer properties[30,31]. This distinction may partially explain the protective role of moderate dietary probiotics—largely attributed to fresh fruit and vegetable intake—in cancer mortality reduction. The mechanisms underlying high dietary probiotic intake's protective effect against cancer mortality may involve specific probiotic actions. For instance, Schmid et al. suggested that probiotics modulate sex hormone levels differently across genders within the gut microbiome, enhancing IgA production, T cell activity, and macrophage functions to strengthen anticancer defenses[32]. Furthermore, certain prebiotics, such as dietary fructooligosaccharides, have demonstrated pro-inflammatory properties by increasing butyrate concentrations, suggesting that substantial probiotic intake could amplify anticancer effects[33]. Additionally, Lactobacillus reuteri (Lr) has been shown to localize within melanoma tumors, elevating interferon-γ-producing CD8 + T cells and thus bolstering antitumor immunity[34].

This study identified a protective effect of dietary probiotics on mortality risk in elderly cancer patients. However, these findings diverge from certain previous studies. For instance, Han et al. recommended that cancer patients avoid probiotics, citing potential complications such as sepsis associated with their useal. argued that tumor elimination, immune evasion, and gastrointestinal immune homeostasis are partially influenced by gut microbiota[26]. Further immunotherapy, including immune checkpoint inhibitors, exhibits varying efficacy across individuals, in part due to differences in gut microbial composition[35]. Szóstak and colleted that while gut fungal patterns are nearly identical in the 26–45 age group, participants aged 65 and above exhibit distinct microbial profiles[36]. The observed gender-specifihip between dietary probiotics and cancer mortality may relate to sex hormones' role in microbial regulation and distinct dietary patterns in males and females[36,37]. Given that dietary probiotics integrmicrobiota and modulate immune responses, these factors may partly explain the subgroup variations in the impact of dietary probiotics on cancer mortality.

To our knowledge, this study is the first to utilize a nationally representative sample and an objective classification system to assess dietary probiotic intake, aiming to delineate the dose–response relationship between broad categories of dietary probiotics and cancer mortality. Unlike prior studies that primarily describe population-level intake in cross-sectional analyses, our research employs the latest NHANES longitudinal mortality data, allowing us to assess the longer-term associations between dietary probiotic exposure and mortality outcomes. Recognizing the complex factors influencing cancer survival, we incorporated diverse demographic, medical, and lifestyle variables and applied a competing-risk model with comprehensive confounding adjustments. This approach strengthens our understanding of the relationship between various types of dietary probiotic intake and cancer mortality risk. The findings aim to inform public health policies, particularly in food and nutrition safety, with an emphasis on improving survival outcomes for cancer patients.

However, we must consider several limitations in this study. While we made efforts to include and adjust for a comprehensive set of confounding factors to enhance result accuracy, the widespread use of therapies such as radiotherapy, chemotherapy, or surgical treatments in cancer patients, which severely damage the overall

Variable	Assumed alive	Assumed deceased[a]	P value	HR (95% CI)[b]
Age, No. (%), years	44.69(0.20)	63.88(0.49)	< 0.0001	1.10(1.09,1.11)****
20–29	6023(20.23)	11(1.29)		1[reference]
30–39	6010(20.14)	29(3.58)		2.62(1.12, 6.11)
40–49	6172(21.81)	83(8.99)		6.00(2.72, 13.23)****
50–59	5191(19.03)	191(21.20)		18.13(8.36, 39.31)****
60–69	4930(12.01)	356(26.82)		41.37(19.98, 85.63)****
70–79	2289(5.34)	356(24.42)		90.91(42.68,193.63)****
≥ 80	684(1.43)	244(13.70)		249.80(116.12,537.40)****
BMI, No. (%)	28.82(0.07)	28.58(0.23)	0.31	1.00(0.99,1.01)
18.5–30.0	19,159(62.67)	798(62.74)		1[reference]
< 18.5	426(1.47)	31(2.25)		1.49(0.89,2.51)
≥ 30.0	11,714(35.85)	441(35.02)		1.09(0.94,1.26)
Healthy Eating Index (2015), mean (SE), %	50.23(0.19)	51.69(0.47)	0.002	1.01(1.01,1.01)****
HbA1c levels, mean (SE), %	5.52(0.01)	5.75(0.03)	< 0.0001	1.28(1.24,1.33)****
Alt levels, mean (SE), U/L	25.88(0.13)	25.61(0.89)	0.76	1.00(0.99,1.00)
Ast levels, mean (SE), U/L	25.10(0.10)	28.13(1.08)	0.01	1.00(1.00,1.00)****
Bilirubin levels, mean (SE), mg/dL	11.67(0.07)	12.31(0.19)	0.001	1.00(0.99,1.01)
Alkaline phosphatase levels, mean (SE), U/L	67.81(0.25)	77.51(1.23)	< 0.0001	1.01(1.01,1.01)****
Albumin levels, mean (SE), g/dL	4.31(0.00)	4.21(0.01)	< 0.0001	0.31(0.25,0.39)****
History of DM, No. (%)			< 0.0001	
No	24,515(82.53)	831(69.68)		1[reference]
DM	4532(10.68)	311(20.14)		2.85(2.38,3.40)****
IFG	1336(4.21)	92(7.24)		2.60(1.99,3.40)****
IGT	916(2.58)	36(2.94)		1.67(1.09,2.57)
History of hypertension, No. (%)			< 0.0001	
No	19,664(66.76)	457(40.50)		1[reference]
Yes	11,635(33.24)	813(59.50)		3.19(2.76,3.69)****
History of hyperlipidemia, No. (%)			< 0.0001	
No	9118(30.02)	266(18.60)		1[reference]
Yes	22,181(69.98)	1004(81.40)		1.79(1.50,2.15)****
History of congestive heart failure, No. (%)			< 0.0001	
No	30,776(98.74)	1176(93.09)		1[reference]
Yes	523(1.26)	94(6.91)		6.57(4.98,8.67)****
History of coronary heart disease, No. (%)			< 0.0001	
No	30,470(97.68)	1157(91.56)		1[reference]
Yes	829(2.32)	113(8.44)		4.36(3.43,5.54)****
History of angina, No. (%)			< 0.0001	
No	30,712(98.37)	1193(93.88)		1[reference]
Yes	587(1.63)	77(6.12)		3.99(3.01,5.28)****
History of heart attack, No. (%)			< 0.0001	
No	30,455(97.79)	1141(90.02)		1[reference]
Yes	844(2.21)	129(9.98)		5.34(4.18,6.83)****
History of stroke, No. (%)			< 0.0001	
No	30,553(98.21)	1178(93.48)		1[reference]
Yes	746(1.79)	92(6.52)		4.52(3.47,5.90)****
Sex, No. (%)			< 0.001	
Male	15,390(49.08)	763(56.13)		1[reference]
Female	15,909(50.92)	507(43.87)		0.76(0.65,0.88)***
Race/Ethnicuty, No. (%)			< 0.0001	
Non-Hispanic White	13,973(70.15)	754(80.28)		1[reference]
Non-Hispanic Black	6259(9.98)	263(11.05)		1.00(0.85,1.17)
Mexican American	5615(8.16)	163(3.49)		0.40(0.32,0.49)****
Other	5452(11.71)	90(5.18)		0.44(0.34,0.57)****
Marital status, No. (%)			0.04	
Unmarried or other	11,850(34.43)	532(37.71)		1[reference]
Married or living with a partner	19,449(65.57)	738(62.29)		0.84(0.74,0.96)
Continued				

Variable	Assumed alive	Assumed deceased[a]	P value	HR (95% CI)[b]
Educational attainment, No. (%)			< 0.0001	
< High school	7074(13.99)	447(27.59)		1[reference]
≥ High school	24,225(86.01)	823(72.41)		0.48(0.41,0.56)****
Poverty income ratio, No. (%)			0.79	
Below poverty line (< 1.00)	5998(12.78)	243(13.05)		1[reference]
At or above poverty line (≥ 1.00)	25,301(87.22)	1027(86.95)		0.96(0.80,1.14)
Alcohol consumption, No. (%)			< 0.0001	
Never	4109(10.28)	160(10.11)		1[reference]
Former	4517(12.15)	416(30.20)		2.28(1.76,2.96)****
Mild	10,676(36.74)	404(33.17)		0.98(0.75,1.28)
Moderate	5158(18.33)	142(13.05)		0.77(0.57,1.05)
Heavy	6839(22.51)	148(13.47)		0.62(0.44,0.88)
Smoke history, No. (%)			< 0.0001	
Never	17,498(55.29)	422(31.78)		1[reference]
Former	7138(23.66)	525(39.73)		2.86(2.40,3.40)****
Current	6663(21.05)	323(28.49)		2.08(1.75,2.48)****

Table 3. Due to cancer-causes mortality by demographic, health-related behaviors and general health characteristics. Abbreviations: AD: Alzheimer's Disease; CVD, cardiovascular disease; DM, Diabetes mellitus; I&P: Immunization and Prevention; HbA1c, Hemoglobin A1c; Alt, Alanine Transaminase; Ast, Aspartate Transaminase; mo, months; BMI, Body Mass Index (calculated as weight in kilograms divided by height in meters squared); HR, hazard ratio; CI, confidence interval [a]All-cause mortality was assessed through December 31, 2020. All proportions, means, and SEs are weighted estimates of the US population characteristics, taking into account the complex sampling design of the National Health and Nutrition Examination Survey (NHANES) [b]Adjusted for age and sex *p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001

immune system, can influence the impact of dietary intake of dietary probiotics on patient survival. Additionally, the effects of medication on gastrointestinal barrier function and gut microbiota, crucial confounding factors, were not incorporated in this study. The investigators responsible for conducting the survey and follow-up were all Americans, and the complexity of the population, along with no significant differences observed in ethnic subgroup results, makes it challenging to generalize the research findings to other countries. Cancer mortality rates encompass a range of highly heterogeneous diseases. While we analyzed overall mortality rates, we did not categorize or discuss them based on pathological subtypes or distinctive tissue characteristics. Particularly noteworthy is the potential oversight of the prognostic impact of dietary probiotics on patients, especially for prevalent diseases with higher mortality rates in recent years, such as lung cancer and colorectal cancer. The types and quantities of dietary probiotics (including microorganisms, yeast, and molds) in food vary based on the degree of food processing, the duration of storage before consumption, and storage conditions. For instance, in the case of foods subjected to pasteurization, ready-to-eat meats, and pre-packaged vegetables, new microbial growth (including both lactic acid microorganisms and non-lactic acid microorganisms) may occur during storage. Consequently, products classified as "low" ($< 10^4$ CFU/g) may approach levels close to $> 10^7$ CFU/g when consumed. Moreover, microorganisms may die during storage, implying that even foods considered to have a high content of dietary probiotics could drop below 10^7 CFU/g over time. This variability could significantly impact the assessment of the number of dietary probiotics encountered through dietary intake, classification, and health analysis results. The specific microbial species present in different types of foods vary. Most microorganisms in fermented dairy products belong to the lactic acid microorganisms family, while those on the surfaces of fruits and vegetables are more diverse, typically including microorganisms from the Pseudomonadaceae family. The positive contributions of these microorganisms to human health remain insufficiently studied, and more experimental evidence is needed for a comprehensive evaluation. Due to inherent limitations in the data, we were unable to subgroup intake of dietary probiotics by species, making it challenging to distinguish whether the substantial intake of controversial foods such as yogurt and pickles is beneficial for cancer patients.

Methods

Sample and study population

This study utilized data from ten cycles (1999–2018) of the National Health and Nutrition Examination Survey (NHANES), a large-scale database administered by the Centers for Disease Control and Prevention (CDC). NHANES, which employs a stratified multistage sampling design, provides comprehensive information on the health and nutritional status of US ambulatory populations. To obtain a representative sample, participants underwent a series of questionnaires, physical exams, and lab tests either at home or in a mobile examination center (MEC). Detailed methods of sampling and testing have been previously described. For this analysis, individuals under 18 years of age and those missing key confounding variables were excluded. All participants provided written informed consent following the Helsinki Declaration guidelines. The NHANES program

Cancer-Specific mortality		Crude model HR (95% CI)	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)	Model 3[c] HR (95% CI)
Low dietary probiotics group	Q1	1[reference]	1[reference]	1[reference]	1[reference]
	Q2	0.82(0.68,0.97)*	0.78(0.65,0.93)*	0.82(0.68,0.98)*	0.82(0.68,0.99)*
	Q3	0.77(0.63,0.95)*	0.80(0.65,0.99)*	0.83(0.67,1.04)	0.83(0.67,1.04)
	Q4	0.63(0.51,0.77)****	0.77(0.62,0.97)*	0.81(0.64,1.01)	0.81(0.65,1.01)
	Q5	0.52(0.39,0.70)****	0.84(0.63,1.13)	0.87(0.65,1.16)	0.87(0.65,1.17)
	P for trend (integer)	< 0.0001	0.19	0.26	0.27
	P for trend (Median value)	< 0.0001	0.34	0.4	0.42
Middle dietary probiotics group	No	1[reference]	1[reference]	1[reference]	1[reference]
	Total	0.92(0.79,1.07)	0.74(0.64,0.86)****	0.81(0.69,0.95)*	0.81(0.69,0.95)*
	P for trend	0.29	< 0.0001	0.01	0.01
	Q1	0.84(0.69,1.02)	0.81(0.67,0.99)*	0.86(0.70,1.05)	0.86(0.70,1.05)
	Q2	1.01(0.83,1.23)	0.76(0.63,0.91)**	0.83(0.69,1.01)	0.83(0.69,1.01)
	Q3	0.91(0.75,1.11)	0.67(0.55,0.82)****	0.75(0.61,0.92)*	0.75(0.61,0.92)*
	P for trend (integer)	0.61	< 0.0001	0.01	0.01
	P for trend (Median value)	0.64	0.09	0.26	0.26
High dietary probiotics group	No	1[reference]	1[reference]	1[reference]	1[reference]
	Total	0.85(0.71,1.03)	0.92(0.76,1.12)	1.00(0.82,1.21)	1.00(0.82,1.21)
	P for trend	0.1	0.4	0.96	0.96
	Q1	0.90(0.66,1.22)	0.94(0.69,1.28)	1.02(0.75,1.40)	1.02(0.75,1.40)
	Q2	0.77(0.59,1.02)	0.90(0.68,1.19)	0.99(0.74,1.32)	0.99(0.74,1.32)
	Q3	0.91(0.66,1.25)	0.92(0.67,1.28)	0.97(0.70,1.35)	0.98(0.70,1.35)
	P for trend (integer)	0.16	0.44	0.89	0.9
	P for trend (Median value)	0.69	0.95	0.88	0.86

Table 4. Hazard ratios (HR) of Cancer-Specific mortality according to all of the dietary probiotics group components consumed by participants. Abbreviations: HR, hazard ratio; CI, confidence interval [a]Adjusted for age, sex [b]Adjusted for age, sex, race/ethnicity, marital status, educational attainment, poverty income ratio, alcohol consumption, BMI, as well as various medical history variables such as history of stroke, heart attack, coronary heart disease, angina, hyperlipidemia, congestive heart failure, hypertension, and diabetes mellitus (DM), were adjusted. Additionally, laboratory measurements including Healthy Eating Index (2015), HbA1c levels, Alt levels, Ast levels, Bilirubin levels, Alkaline phosphatase levels, and Albumin levels [c]Adjusted for age, squared age, sex, race/ethnicity, marital status, educational attainment, poverty income ratio, alcohol consumption, BMI, as well as various medical history variables such as history of stroke, heart attack, coronary heart disease, angina, hyperlipidemia, congestive heart failure, hypertension, and diabetes mellitus (DM), were adjusted. Additionally, laboratory measurements including Healthy Eating Index (2015), HbA1c levels, Alt levels, Ast levels, Bilirubin levels, Alkaline phosphatase levels, and Albumin levels $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$; $^{****}P < 0.0001$

(1999–2018) received approval from the National Center for Health Statistics and the Research Ethics Review Board, and the dataset is openly accessible without additional ethical or administrative clearances.

Dietary intake and categories of dietary probiotics

To assess participants' dietary intake, the National Center for Health Statistics linked 24-h food and beverage consumption data to the USDA Food Survey Nutritional Database, allowing for estimations of daily energy and nutrient intake. Using the classification system proposed by Mary E. Sanders and colleagues in 2022, the NHANES database estimated viable microorganism counts (CFU per gram) for 9,388 food items across 48 subcategories. Based on these counts, foods were classified into three categories of viable microorganisms: low ($< 10^4$ CFU/g), moderate (10^4–10 CFU/g), and high ($> 10^7$ CFU/g). This classification was determined through extensive literature reviews, expert guidelines, and considerations of food processing effects (e.g., pasteurization) on microbial viability. Any assessment discrepancies were resolved collaboratively within the team and through consultation with Fred Breidt, a microbiologist at the USDA Agricultural Research Service.

Mortality data

In this study, participant mortality data were obtained through a probabilistic matching algorithm that used the publicly available 2019 Linked Mortality File and the National Death Index (NDI) file. Participants aged 20 and older from NHANES were linked to individual identifiers (such as name, gender, and date of birth) in the NDI database. Those without a match in the death records were considered alive. Cancer-specific mortality was classified according to the International Classification of Diseases, Tenth Revision (ICD-10), with codes C00-C97 indicating cancer-related deaths. Follow-up time was calculated as the duration from the baseline

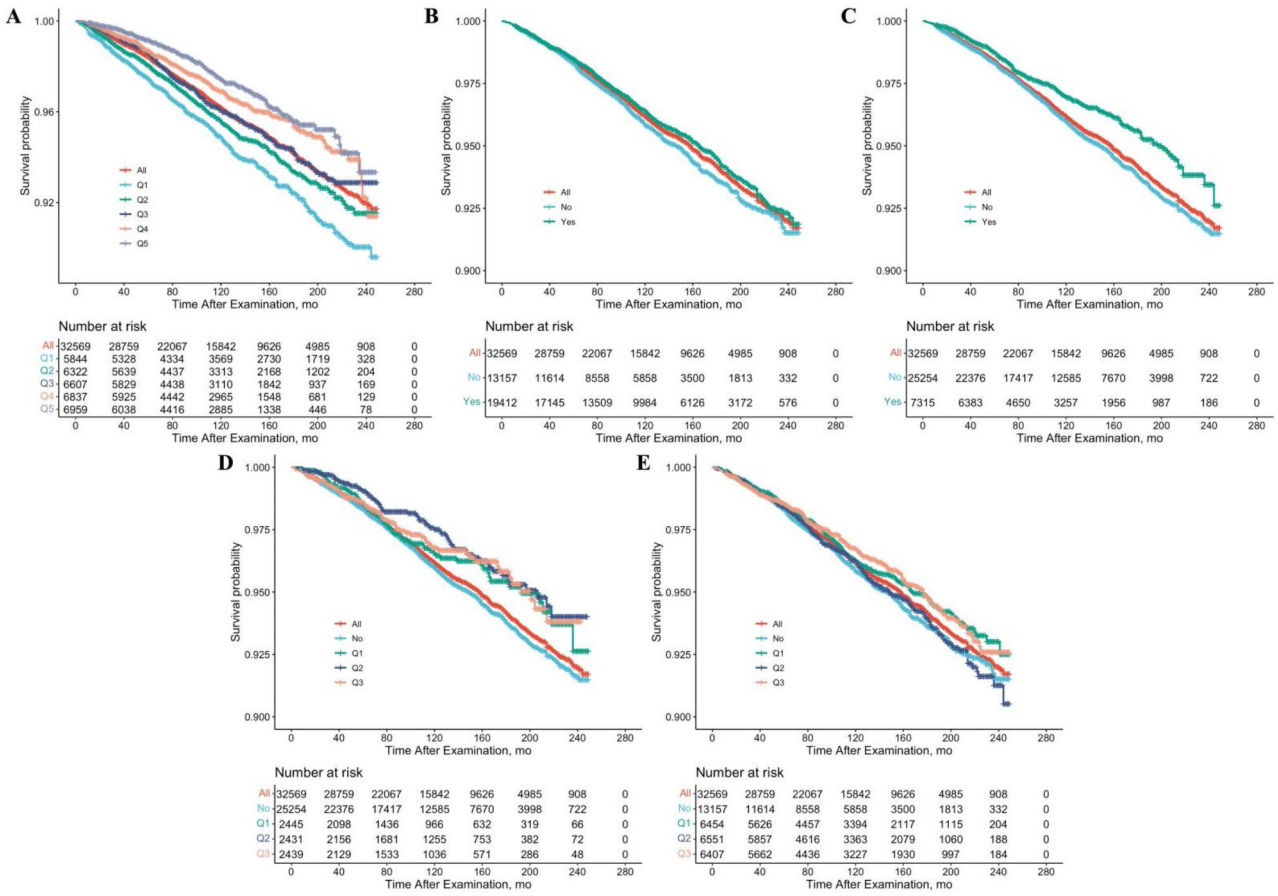

Fig. 1. Adjusted Kaplan–Meier curve for cancer-specific mortality by dietary probiotics groups. Study results were stratified according to dietary probiotics groups (**A**) Low dietary probiotics Group, (**B**) Middle dietary probiotics Group and (**C**) High dietary probiotics Group (Binary classification, intake or not), (**D**) Middle dietary probiotics Group and (**E**) High dietary probiotics Group (Ternary classification, intake level), using 1999–2018 National Health and Nutrition Examination Survey data.

interview date to either the date of death or the study's review end date (December 31, 2019), whichever came first.

Participant characteristics and confounders

To assess the association between dietary probiotics and cancer-related mortality, we considered a wide range of variables based on both existing literature and clinical insights. Demographic and health-related information was obtained from NHANES interviews and physical exams, including age, gender (male or female), and ethnicity (categorized as non-Hispanic White, non-Hispanic Black, Mexican American, and others). Education level was grouped by whether participants had a high school diploma, and marital status was categorized as married or cohabiting, unmarried, or other. Economic status was determined by the poverty income ratio (PIR), classified as below the poverty line (<1.00) or at/above the poverty line (≥ 1.00). Alcohol consumption was classified into five categories: never drinkers, former drinkers, current heavy drinkers (≥ 3 drinks per day for women or ≥ 4 for men, or binge drinking at least 5 days per month), current moderate drinkers (≥ 2 drinks per day for women or ≥ 3 for men, or binge drinking at least 2 days per month), and current light drinkers. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2), with categories of normal/overweight (18.5–30.0), underweight (<18.5), and obese (≥ 30.0). Diabetes was defined based on a self-reported diabetes diagnosis, HbA1c $>6.5\%$, fasting blood glucose ≥ 7.0 mmol/L, random blood glucose ≥ 11.1 mmol/L, two-hour OGTT blood glucose ≥ 11.1 mmol/L, or the use of diabetes medications. Hypertension was defined by self-reported history, antihypertensive use, or measured blood pressure $\geq 140/90$ mm Hg. Hyperlipidemia was identified by triglycerides ≥ 150 mg/dL, total cholesterol ≥ 200 mg/dL, LDL cholesterol ≥ 130 mg/dL, HDL cholesterol <40 mg/dL for men or <50 mg/dL for women (values converted to mmol/L using a factor of 0.0259), or lipid-lowering medication use. Renal function was assessed with the estimated glomerular filtration rate (eGFR), calculated using the CKD-EPI Scr 2009 formula. The Healthy Eating Index-2015 (HEI-2015) scores, as described by Reedy et al., quantified healthy dietary habits among participantscal markers—including HbA1c, ALT, AST, bilirubin, alkaline phosphatase, and albumin—were obtained from blood samples[38]. History of

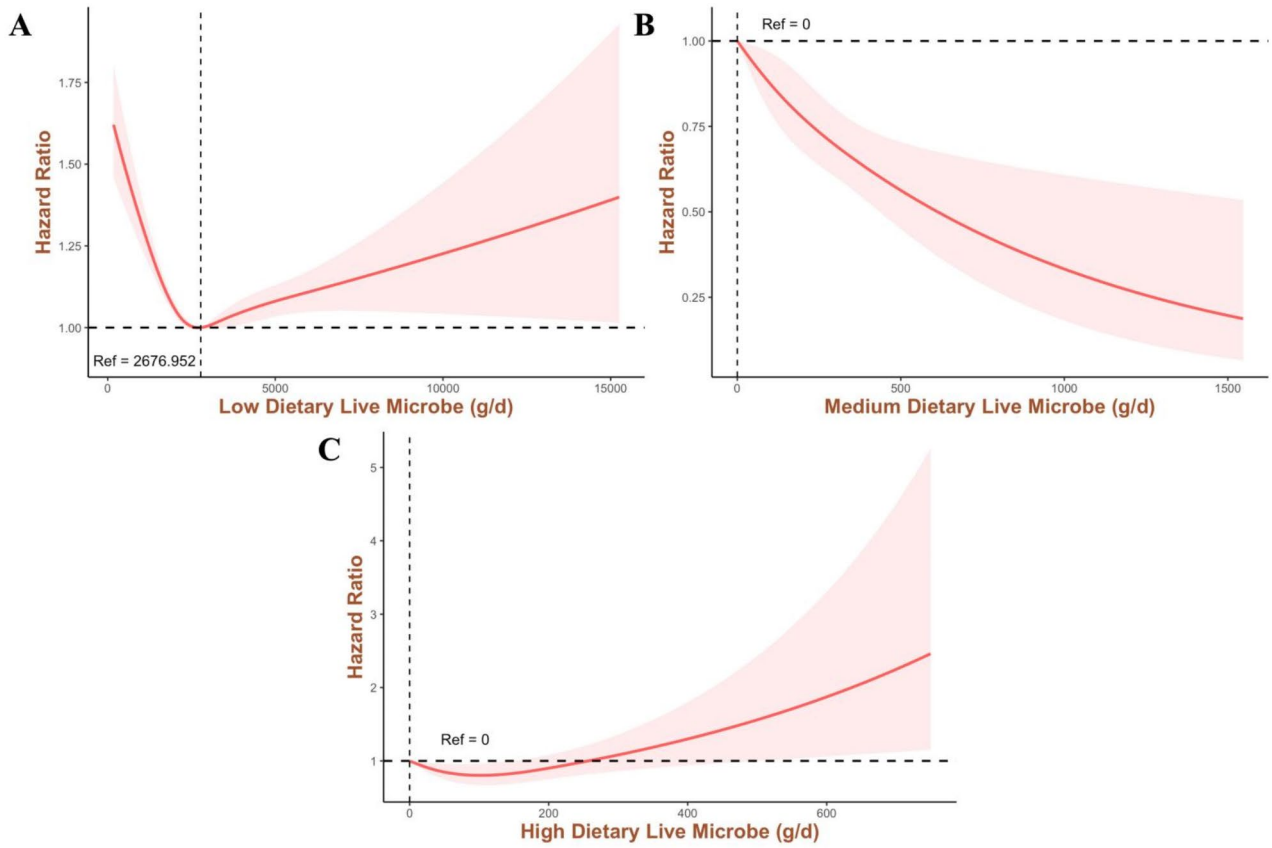

Fig. 2. Dose–Response Curves for Cancer-Specific Mortality across Three dietary probiotics groups: (**A**) Low dietary probiotics Group, (**B**) Middle dietary probiotics Group, and (**C**) High dietary probiotics Group. Analysis based on 1999–2018 National Health and Nutrition Examination Survey Data.

systemic complications was derived from self-reported diagnoses of congestive heart failure, coronary heart disease, angina, myocardial infarction, and stroke.

Statistical analysis

We combined data from ten NHANES cycles (1999–2018), conducting all analyses in accordance with the NHANES Analytics and Reporting Guide, which outlines the complex stratified design and sample weights. Baseline characteristics of participants were described as means ± standard deviation (SD) for continuous variables and counts with weighted percentages for categorical variables. To compare the distribution of continuous and categorical variables and assess mortality features, we applied design-adjusted unpaired t-tests and Rao-Scott Pearson χ^2 tests, respectively. Probiotic exposure was categorized based on food code assignments into three groups: low dietary probiotics (five categories), moderate dietary probiotics (no intake and three intake levels), and high dietary probiotics (no intake and three intake levels). Kaplan–Meier methods were used to generate survival curves across these groups. Cox proportional hazards regression models provided hazard ratios (HR) and 95% confidence intervals (CI) for survival, linking baseline characteristics to the survival endpoint while adjusting for confounding factors significantly associated with both mortality and probiotic intake. Three models were tested: Model 1 (unadjusted), Model 2 (adjusted for age and gender), and Model 3 (adjusted for additional demographic factors and all covariates based on Model 1). Subgroup analyses considered age, gender, race, education level, poverty status, smoking and drinking habits, and underlying conditions such as hypertension and hyperlipidemia. Interaction tests showed no statistically significant interactions between confounding factors ($P > 0.05$). The proportional hazards assumption for each confounding factor was confirmed by evaluating interactions with follow-up time ($P > 0.05$).

In sensitivity analyses, we examined the non-linear relationship between age and mortality by adjusting for age and age squared in the final model. Variance inflation factor (VIF) testing indicated minimal collinearity among confounding factors, with all VIFs below 1.22 (mean [standard error], 1.10 [0.04]). A two-sided P-value of less than 0.05 was considered statistically significant. Data analyses were performed in R software (version 4.2.1) using packages including “nhanesR”, “reshape2”, “survey”, “do” and "dplyr."

Conclusion

Our study revealed significant associations between dietary intake of probiotics and cancer-specific mortality risk, utilizing the comprehensive and updated NHANES records. This analysis, conducted on a large, nationally

representative sample of U.S. non-hospitalized individuals, is the first to demonstrate that medium and moderately low dietary probiotic intake correlates with a reduced risk of cancer-specific mortality. Additionally, dose–response curves clarified the associations between varying levels of probiotic intake and cancer mortality risk, supporting the potential role of dietary probiotics as a beneficial lifestyle factor in cancer survival and contributing valuable insights for healthcare interventions and drug development.

Data availability

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Received: 7 June 2024; Accepted: 17 December 2024
Published online: 06 January 2025

References

1. Singh, R. K. et al. Influence of diet on the gut microbiome and implications for human health. *J. Transl. Med.* **15**, 73. https://doi.org/10.1186/s12967-017-1175-y (2017).
2. Cani, P. D. et al. Changes in gut microbiota control metabolic endotoxemia-induced inflammation in high-fat diet-induced obesity and diabetes in mice. *Diabetes* **57**, 1470–1481. https://doi.org/10.2337/db07-1403 (2008).
3. Roselli, M. et al. Colonization ability and impact on human gut microbiota of foodborne microbes from traditional or probiotic-added fermented foods: A systematic review. *Front Nutr* **8**, 689084. https://doi.org/10.3389/fnut.2021.689084 (2021).
4. Zmora, N., Suez, J. & Elinav, E. You are what you eat: Diet, health and the gut microbiota. *Nat. Rev. Gastroenterol. Hepatol.* **16**, 35–56. https://doi.org/10.1038/s41575-018-0061-2 (2019).
5. Belkaid, Y. & Harrison, O. J. Homeostatic immunity and the microbiota. *Immunity* **46**, 562–576. https://doi.org/10.1016/j.immuni.2017.04.008 (2017).
6. Soerjomataram, I. & Bray, F. Planning for tomorrow: Global cancer incidence and the role of prevention 2020–2070. *Nat. Rev. Clin. Oncol.* **18**, 663–672. https://doi.org/10.1038/s41571-021-00514-z (2021).
7. Andreas, S., Rittmeyer, A., Hinterthaner, M. & Huber, R. M. Smoking cessation in lung cancer-achievable and effective. *Dtsch Arztebl Int.* **110**, 719–724. https://doi.org/10.3238/arztebl.2013.0719 (2013).
8. Hojman, P., Gehl, J., Christensen, J. F. & Pedersen, B. K. Molecular mechanisms linking exercise to cancer prevention and treatment. *Cell Metab.* **27**, 10–21. https://doi.org/10.1016/j.cmet.2017.09.015 (2018).
9. McTiernan, A. Weight, physical activity and breast cancer survival. *Proc. Nutr. Soc.* **77**, 403–411. https://doi.org/10.1017/s0029665118000010 (2018).
10. Vitale, S. et al. One-year nutrition counselling in the context of a Mediterranean diet reduced the dietary inflammatory index in women with breast cancer: a role for the dietary glycemic index. *Food Funct.* **14**, 1560–1572. https://doi.org/10.1039/d2fo02198f (2023).
11. Mima, K. et al. The microbiome and hepatobiliary-pancreatic cancers. *Cancer Lett.* **402**, 9–15. https://doi.org/10.1016/j.canlet.2017.05.001 (2017).
12. Marco, M. L. et al. A classification system for defining and estimating dietary intake of live microbes in US adults and children. *J. Nutr.* **152**, 1729–1736. https://doi.org/10.1093/jn/nxac074 (2022).
13. Rook, G. A. 99th Dahlem conference on infection, inflammation and chronic inflammatory disorders: darwinian medicine and the "hygiene" or "old friends" hypothesis. *Clin. Exp. Immunol.* **160**, 70–79. https://doi.org/10.1111/j.1365-2249.2010.04133.x (2010).
14. Hill, C. *et al.* Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat. Rev. Gastroenterol. Hepatol.* **11**, 506–514 (2014). https://doi.org/10.1038/nrgastro.2014.66
15. Ambrose, J. A. & Barua, R. S. The pathophysiology of cigarette smoking and cardiovascular disease: An update. *J. Am. Coll. Cardiol.* **43**, 1731–1737. https://doi.org/10.1016/j.jacc.2003.12.047 (2004).
16. Merenstein, D. J., Sanders, M. E. & Tancredi, D. J. Probiotics as a Tx resource in primary care. *J. Fam. Pract.* **69**, E1-e10 (2020).
17. Marco, M. L. et al. Should there be a recommended daily intake of microbes?. *J. Nutr.* **150**, 3061–3067. https://doi.org/10.1093/jn/nxaa323 (2020).
18. Dimidi, E., Cox, S. R., Rossi, M. & Whelan, K. Fermented foods: Definitions and characteristics, impact on the gut microbiota and effects on gastrointestinal health and disease. *Nutrients* **11** (2019). https://doi.org/10.3390/nu11081806
19. Savaiano, D. A. & Hutkins, R. W. Yogurt, cultured fermented milk, and health: A systematic review. *Nutr. Rev.* **79**, 599–614. https://doi.org/10.1093/nutrit/nuaa013 (2021).
20. Wastyk, H. C. et al. Gut-microbiota-targeted diets modulate human immune status. *Cell* **184**, 4137-4153.e4114. https://doi.org/10.1016/j.cell.2021.06.019 (2021).
21. Rezac, S., Kok, C. R., Heermann, M. & Hutkins, R. Fermented foods as a dietary source of live organisms. *Front. Microbiol.* **9**, 1785. https://doi.org/10.3389/fmicb.2018.01785 (2018).
22. Jeddi, M. Z. et al. Microbial evaluation of fresh, minimally-processed vegetables and bagged sprouts from chain supermarkets. *J. Health Popul. Nutr.* **32**, 391–399 (2014).
23. Valentin-Bon, I., Jacobson, A., Monday, S. R. & Feng, P. C. Microbiological quality of bagged cut spinach and lettuce mixes. *Appl. Environ. Microbiol.* **74**, 1240–1242. https://doi.org/10.1128/aem.02258-07 (2008).
24. Ziyaina, M., Govindan, B. N., Rasco, B., Coffey, T. & Sablani, S. S. Monitoring shelf life of pasteurized whole milk under refrigerated storage conditions: Predictive models for quality loss. *J. Food Sci.* **83**, 409–418. https://doi.org/10.1111/1750-3841.13981 (2018).
25. Montville, R. & Schaffner, D. W. Statistical distributions describing microbial quality of surfaces and foods in food service operations. *J. Food. Prot.* **67**, 162–167. https://doi.org/10.4315/0362-028x-67.1.162 (2004).
26. Han, L. & Wang, Q. Association of dietary live microbe intake with cardiovascular disease in US adults: A cross-sectional study of NHANES 2007–2018. *Nutrients* **14** (2022). https://doi.org/10.3390/nu14224908
27. Redman, M. G., Ward, E. J. & Phillips, R. S. The efficacy and safety of probiotics in people with cancer: A systematic review. *Ann. Oncol.* **25**, 1919–1929. https://doi.org/10.1093/annonc/mdu106 (2014).
28. Jin, S. & Je, Y. Dairy consumption and total cancer and cancer-specific mortality: A meta-analysis of prospective cohort studies. *Adv. Nutr.* **13**, 1063–1082. https://doi.org/10.1093/advances/nmab135 (2022).
29. Praagman, J. et al. The relationship between fermented food intake and mortality risk in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *Br. J. Nutr.* **113**, 498–506. https://doi.org/10.1017/s0007114514003766 (2015).
30. Nguyen, L. H. et al. Association between sulfur-metabolizing bacterial communities in stool and risk of distal colorectal cancer in men. *Gastroenterology* **158**, 1313–1325. https://doi.org/10.1053/j.gastro.2019.12.029 (2020).
31. Ananthakrishnan, A. N. et al. A prospective study of long-term intake of dietary fiber and risk of Crohn's disease and ulcerative colitis. *Gastroenterology* **145**, 970–977. https://doi.org/10.1053/j.gastro.2013.07.050 (2013).
32. Schmid, D. et al. Yogurt consumption in relation to mortality from cardiovascular disease, cancer, and all causes: A prospective investigation in 2 cohorts of US women and men. *Am. J. Clin. Nutr.* **111**, 689–697. https://doi.org/10.1093/ajcn/nqz345 (2020).

33. Rhodes, J. M. Nutrition and gut health: The impact of specific dietary components—It's not just five-a-day. *Proc. Nutr. Soc.* **80**, 9–18. https://doi.org/10.1017/s0029665120000026 (2021).
34. Bender, M. J. et al. Dietary tryptophan metabolite released by intratumoral Lactobacillus reuteri facilitates immune checkpoint inhibitor treatment. *Cell* **186**, 1846-1862.e1826. https://doi.org/10.1016/j.cell.2023.03.011 (2023).
35. Zhou, C. B., Zhou, Y. L. & Fang, J. Y. Gut microbiota in cancer immune response and immunotherapy. *Trends Cancer* **7**, 647–660. https://doi.org/10.1016/j.trecan.2021.01.010 (2021).
36. Szóstak, N. *et al.* Host factors associated with gut mycobiome structure. *mSystems* **8**, e0098622 (2023). https://doi.org/10.1128/msystems.00986-22
37. Markle, J. G. et al. Sex differences in the gut microbiome drive hormone-dependent regulation of autoimmunity. *Science* **339**, 1084–1088. https://doi.org/10.1126/science.1233521 (2013).
38. Reedy, J. et al. Evaluation of the healthy eating index-2015. *J. Acad. Nutr. Diet* **118**, 1622–1633. https://doi.org/10.1016/j.jand.2018.05.019 (2018).

Acknowledgements

We thank the Department of Oncology of the First Affiliated Hospital of Anhui Medical University for their collaborative and logistical work. And also thanks to Zhang Jing (Shanghai Tongren Hospital) for his work on the NHANES database. His outstanding work, nhanesR package and webpage, makes it easier for us to explore NHANES database.

Author contributions

Conceptualization, Y.Y and J.Q.H; methodology, X.X; software, Y.Y; validation, J.J.L; formal analysis, Y.Y; writing—original draft preparation, M.S.P, X.X.Y and J.Q.H; writing, review and editing, Y.Y and Q.J; visualization, Y.Y; supervision, X.X; project administration, J.Q.H; funding acquisition, J.Q.H. All authors have read and agreed to the published version of the manuscript.

Funding

This study was supported by the Research Fund Project of Anhui Institute of Translational Medicine with the fund number (2023zhyx-C79).

Declarations

Competing interests

The authors declare no competing interests.

Ethics statement

These studies involving humans have been approved by the Ethics Review Board of the National Center for Health Statistics. The studies were conducted in accordance with local legislation and institutional requirements. According to national legislation and institutional requirements, participants or their legal guardians/next of kin do not require written informed consent.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-83722-8.

Correspondence and requests for materials should be addressed to J.H.