

The Combined Effects of Animal Products Intake and Physical Activity With Cause-specific and All-cause Mortality Among Patients With Type 2 Diabetes Mellitus in China: A Prospective Cohort Study

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Abstract

Background

To determine the associations of animal products intake and physical activity and their combined effects with cause-specific and all-cause mortality among type 2 diabetes mellitus (T2DM) patients in China.

Methods

Baseline data of 7311 type 2 diabetes mellitus (T2DM) patients recruited with a stratified random cluster sampling method were collected from December 2013 to January 2014. Participants were followed up until the date of their death or December 2019 for survivors, whichever came first. Nonlinear trends of cause-specific and all-cause mortality were assessed using restricted cubic splines with three knots placed at centiles 10, 50, and 90 of diet intake. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the combined relationship of physical activity and animal products with cause-specific and all-cause mortality.

Results

During a median follow-up of 6.1 years, 692 (9.5%) T2DM patients died. The main cause of death was cardiovascular disease (CVD) (35.8%), followed by cancer (20.6%). After multivariable adjustment, a higher level of physical activity was nonlinearly associated with lower all-cause and CVD mortality in a J-shaped pattern, with the protective effect observed >8 MET-h/d. Higher consumption of red meat, poultry, and aquatic products was associated with a lower risk of all-cause mortality (HR = 0.75, 0.64, 0.75, respectively, all $P < 0.05$). In the highest tertiles of physical activity, a higher intake of red meat, poultry, and aquatic products was associated with a lower risk for all-cause mortality than in the lowest tertiles (red meat, HR = 0.80, 0.62, 0.51, and 0.48; poultry, HR = 0.85, 0.51, 0.48, and 0.45; aquatic products, HR = 0.80, 0.57, 0.55, and 0.40, respectively). Similarly, the protective effect of moderate to high intake of poultry, aquatic products, and eggs on CVD mortality in high physical activity was found.

Conclusions

Our study highlights that in T2DM patients, better adherence to moderate to high consumption of animal products, including red meat, poultry, and aquatic products, together with engaging in moderate to high levels of physical activity exerts a beneficial effect in lowering cause-specific and all-cause mortality in China.

Background

Globally, type 2 diabetes mellitus (T2DM) has become the most widely known noncommunicable and common chronic endocrine multifactorial disease, and millions of people in developed and developing countries are affected [1]. As the social economy and way of life evolve, the prevalence of type 2 diabetes mellitus (T2DM) has been increasing in China [2, 3].

Diabetes is expected to impose a massive economic burden on individuals and countries around the world due to the high risk of mortality [4, 5]. It has been confirmed that cardiovascular diseases (CVDs) [6], kidney

failure [7], and some types of site-specific cancer [8] are the most common complications of T2DM that often arise together, which could collectively lead to a decline in life expectancy and even death [9].

Emerging evidence has demonstrated that diet and physical activity play important roles in the reduction of the mortality risk among T2DM patients [10, 11]. These factors can not only decrease the prevalence of T2DM but also improve the survival rate of patients with T2DM. Substantial studies have placed great emphasis on the potential benefits of a high-quality protein diet in health management [12]. Recommended dietary patterns in many countries are rich in a variety of protein foods, including plant-based foods and animal products [13, 14]. There is compelling evidence that eating more plant-based foods, such as fruits, nonstarchy vegetables, whole grains, nuts, seeds, and legumes, is associated with a lower risk of disease morbidity and mortality [14-16]. Humans obtain the majority of their protein from animal products, such as red meat, poultry, fish, and eggs [17]. However, in contrast to fish or beans, meat, particularly red or processed meat, is frequently regarded as unhealthy due to its high saturated fatty acid content [18, 19]. The effects of certain animal products, such as red meat, poultry, fish, and eggs, on cause-specific and all-cause mortality in T2DM patients are still being studied.

Despite consistent evidence of links between processed/red meat consumption and health outcomes, it is unclear whether these links hold across levels of physical activity [20]. It is well known that exercise therapy is important for T2DM management. However, only 40% of T2DM patients engage in exercise therapy, and only 28.2% of patients complete the recommended amount of physical activity [21]. Through improved glycemic control, moderate to vigorous intensity physical activity (MVPA) could reduce the risk of CVD and all-cause mortality in patients with T2DM [22, 23]. Adults engaging in exercise who followed the 2018 physical activity guidelines for Americans exhibited greatly reduced risk of all-cause mortality, CVD mortality, and atherosclerotic CVD, including incident coronary heart disease, ischemic stroke, and heart failure [24, 25].

Although existing epidemiological studies have clearly assessed the relationship between animal products and physical activity with mortality separately in the general population [26, 27], little is known regarding the association of animal product intake and physical activity with mortality among patients with T2DM. For T2DM patients, their diet and lifestyle may differ in a variety of ways from those of patients without T2DM. High meat intake and a high level of physical activity might influence the effectiveness of medication treatments for T2DM. Thus, the current study aimed to evaluate the joint associations of animal product intake, including red meat, poultry, aquatic products, and egg intake, and physical activity with cause-specific and all-cause mortality in patients with T2DM in China.

Methods

Participants and procedure

The prospective cohort study "Comprehensive intervention and application of diabetes in the community" was carried out from December 2013 to January 2014 in Jiangsu Province to collect baseline diet data of T2DM patients. We used a stratified cluster random sampling method to obtain a representative sample including 30 towns/streets randomly selected from all towns/streets. According to resident health records in the essential public health service management system, a total of 9759 patients aged 18 years or older with diabetes residing in the selected towns or streets were enrolled in the study.

After excluding participants with missing values of questionnaires, 7311 people were successfully included in the final analysis, yielding an excellent response rate of 74.9%. Participants were followed up until December 31, 2019.

Data collection

Standard questionnaires were administered by well-trained staff to collect information concerning demographic characteristics (age, sex, educational level, marital status, household income, duration of diabetes, and HbA1c), health-related behaviors (frequency of smoking, frequency of drinking, physical activity, and sleep duration), and related complications (overweight or obesity, hypertension, dyslipidemia, stroke, coronary heart disease, and kidney disease).

Covariates assessment

T2DM was defined as FPG \geq 7.0 mmol/L on at least two separate occasions by previous physician diagnosis or use of medication according to the 2010 diagnostic standard of the American Diabetes Association [28]. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters and divided into four levels: BMI<18.5 (underweight), 18.5 \leq BMI<24.0 (normal weight), 24.0 \leq BMI<28.0 (overweight), and BMI \geq 28.0 (obesity). For this study, the current definitions were used: never smoker, was not smoking at the time of the interview and answered “NO” to the question “Have you smoked at least 100 cigarettes in your life?”. Based on answers to “Do you now smoke cigarettes (yes, no)?”, respondents were categorized into former or current smokers. Never alcohol drinker involved not drinking at the time of the interview and a “NO” answer to the question “Have you ever drunk in your life?”. Current alcohol drinker involved drinking in the past 30 days. Former alcohol drinker referred to drinking in the past 12 months but no drinking in the past 30 days.

Dietary intake assessment

Dietary intake was evaluated through a validated food frequency questionnaire (FFQ) by trained investigators. Data on the average intake and frequency of various foods consumed in the last year were collected using a paper questionnaire. Information on the average daily intake of each kind of food, which included poultry meat, red meat, aquatic products, and eggs, was calculated (g/day).

Physical activity assessment

Physical activity information was obtained through the global physical questionnaire [29]. The level of physical activity was calculated using the met value of various physical activities and the duration and frequency of various activities. For each physical activity group, participants who reported no physical activity were first classified as zero physical activity, with the remainder divided into tertiles of level of physical activity: low level (first tertile), moderate level (second tertile), and high level (third tertile).

Outcome assessment

The primary outcomes were cause-specific and all-cause mortality. We followed up on the participants' vital status from the baseline survey to December 31, 2019. The mortality data were obtained through their linkage

with the Chinese cause-of-death surveillance system, which records the date of death and the underlying cause of death with the International Classification of Diseases, Tenth Revision. The endpoint of our study was cause-specific mortality, including E10-E14 [30].

Statistical analysis

Baseline characteristics are presented as medians and interquartile ranges (nonnormally distributed continuous variables) and frequencies and percentages (categorical variables). For each participant, follow-up time was defined as the time from December 2013 until the date of death or December 2019 for survivors, whichever came first.

Combinations of the categories of intake of various foods and physical activity were used to jointly classify study participants into nine strata. Patients at the lowest level of physical activity and in the lowest category of intake of four kinds of foods were used as the reference category in these analyses.

We performed a nonlinear dose response analysis to explore the association between red meat, poultry, aquatic products, and egg intake, physical activity, and dietary factors with cause-specific and all-cause mortality using restricted cubic splines with three knots placed at the 10th, 50th, and 90th percentiles, with intake of red meat, poultry, aquatic products, and egg and physical activity as continuous variables [31].

Multivariable-adjusted Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between red meat, poultry, aquatic products, and egg intake, physical activity, and dietary factors with cause-specific and all-cause mortality, respectively. All statistical analyses were performed using R version 4.0.2 software. The 2-tailed test was used, and $P < 0.05$ was considered statistically significant.

Results

Characteristics of the study sample

Overall, the mean age of the cohort patients was 66.2 years (SD = 10.0; range 21-92), and 38.3% of them were men. During a median follow-up of 6.1 years, 692 (9.5%) T2DM patients died. The main cause of death was CVD (35.8%), followed by cancer (20.6%). Among deceased participants, their mean age at death was 68.7 years (SD = 8.8). In terms of health-related behaviors, current smokers and drinkers accounted for 23.0% and 18.0% of the sample, respectively. There were significant differences on all variables, except for frequency of drinking and kidney diseases ($P > 0.05$) (**Table 1**).

Association between red meat, poultry, aquatic product, and egg intake and physical activity with mortality

After multivariable adjustment, a higher level of physical activity was associated with a lower all-cause (HR = 0.64 95% CI 0.53-0.78) and CVD mortality (HR = 0.56 95% CI 0.40-0.79). For the consumption of red meat and poultry, a statistically significant inverse trend across quartiles was found (P for trend < 0.001 ; P for trend = 0.009). Higher consumption of red meat, poultry, and aquatic products was associated with a lower risk of all-cause mortality (HR = 0.75 95% CI 0.59-0.95; HR = 0.64 95% CI 0.51-0.81; HR = 0.75 95% CI 0.59-0.95) (**Tables 2 and 3**).

As shown in Tables 3 and 4, a high intake of poultry and aquatic products had a protective effect on the risk of CVD mortality ($P=0.05$). Such associations between egg consumption and all-cause mortality, CVD mortality, and cancer mortality were not observed.

Dose–response relationships between red meat, poultry, aquatic product, and egg consumption and mortality

Likewise, we observed nonlinear associations between red meat, poultry, and aquatic product consumption and all-cause mortality (P for nonlinear = 0.032; P for nonlinear < 0.001; P for nonlinear < 0.001). The consumption of 42-194 g/day of red meat was significantly negatively associated with all-cause mortality. When the intake of poultry and aquatic products was 15-59 g/day and 23-41 g/day, respectively, the protective effects on all-cause mortality were significant. The lowest risk values were observed for the following kinds of foods: poultry (at 34 g/day, HR = 0.71, 95% CI 0.53-0.96) and aquatic products (at 59 g/day, HR=0.78, 95% CI 0.59-1.04). However, no significant association between eggs and all-cause mortality was observed (**Fig. 1**).

Nonlinear relationships for poultry and aquatic products with CVD mortality were observed (P for nonlinear = 0.046; P for nonlinear=0.016). Moderate intake of red meat, poultry meat, aquatic products, and eggs was positively correlated with the risk of CVD mortality, but there were no significant differences (**Fig. 1**).

In addition, we also observed nonlinear associations between physical activity and poultry consumption and cancer mortality (P for nonlinear = 0.019; P for nonlinear=0.004). High intake of red meat, poultry, and aquatic products was positively related to the risk of cancer mortality, but there were no significant differences (**Fig. 1**).

Hazard ratios of the combined effect of quartiles of red meat, poultry, aquatic product, and egg consumption and physical activity

We cross-classified participants according to their joint exposures to diet (assessed with the quartile of average daily intake of each kind of food) and physical activity (three categories). The group of participants with the lowest intake of foods and lowest physical activity was used as the reference category.

Participants who engaged in high physical activity within each of the four categories of consumption of red meat exhibited a significantly reduced risk of mortality, with a downward trend from the lowest to the highest quartile (HR = 0.80 95% CI 0.58-1.11; HR = 0.62 95% CI 0.44-0.88; HR = 0.51; 95% CI 0.33-0.80; HR = 0.48 95% CI 0.31-0.74, respectively). There were similar trends in the intake of poultry and aquatic products (**Fig. 2 and Supplementary Table1**).

Likewise, a reduced mortality risk was found among participants who consumed high amounts of red meat and any adherence to physical activity, particularly with a similar declining trend across quartiles of physical activity level (HR = 0.93 95% CI 0.66-1.31; HR = 0.56 95% CI 0.37-0.84; HR = 0.48 95% CI 0.31-0.74, respectively). There were similar trends in the intake of poultry and aquatic products.

In the highest tertiles of physical activity, a higher intake of red meat, poultry, and aquatic products was associated with a lower risk for all-cause mortality than in the lowest tertiles (red meat, HR = 0.80, 0.62, 0.51, and 0.48; poultry, HR = 0.85, 0.51, 0.48, and 0.45; aquatic products, HR = 0.80, 0.57, 0.55, and 0.40, respectively). Similarly, there is a protective effect of moderate to high intake of poultry, aquatic products, and eggs on CVD mortality in high physical activity (red meat, HR = 0.80, 0.62, 0.53, and 0.39; poultry, HR = 0.71,

0.54, 0.34, and 0.42; aquatic products, HR = 0.62, 0.60, 0.38, and 0.29; eggs, HR = 0.65, 0.45, 0.52, and 0.61, respectively). However, no associations were observed for all kinds of food, except for poultry and red meat, with cancer mortality (red meat, HR = 1.12, 0.91, 0.31, and 0.81; poultry, HR = 1.18, 0.43, 0.59, and 0.80, respectively). (Fig. 2 and Supplementary Table1).

Discussion

To the best of our knowledge, this is the first study to investigate the relationships between animal products, such as red meat, poultry, aquatic products, eggs, and physical activity as well as their combined effects on cause-specific and all-cause mortality in T2DM patients in China. In this cohort study, moderate to vigorous physical activity and a high consumption of red meat, poultry, and aquatic products were associated with a lower risk of mortality. When their combined effect was investigated, we discovered a significant relative decrease in all-cause mortality and CVD mortality.

Concerning previous studies in patients with T2DM, several studies have demonstrated that when adjusting for confounding factors [32-34], a high level of physical activity helped reduce the risk of CVD mortality and mortality caused by other reasons, with the highest level of physical activity being connected to a 36% and 44% decreased risk of CVD mortality and mortality, respectively, caused by other reasons. However, physical activity may have a different effect on mortality in different studies. This may be partly explained by the different methods of physical activity measurement. In addition, the definition and classification criteria of physical activity were also different.

Previous studies have revealed significant regional variations in the meat-mortality relationship. The majority of the positive connections found between meat consumption and mortality were found in studies conducted in North America and Europe [35-38], whereas results from Asian studies revealed a clear negative association [17, 39]. In T2DM patients, there was a negative correlation between red meat consumption and the risk of all causes of death, which was consistent with the results in Asia. However, such associations between red meat and CVD and cancer mortality were not found in our study. Over the last few years, many chronic disease risk factors in Asian countries, such as obesity, hypertension, and smoking, have become stronger predictors of disease than meat consumption [39, 40]. On the other hand, the food preparation technique, which is not taken into account in observational prospective cohort studies, might play a role. In addition, confounders such as socioeconomic condition in relation to people's access to meat may be significant, as both people's accessibility to and the availability of food are concerned with their income in the Asia-Pacific region [41], implying that at this stage in the epidemiologic transition, a higher meat intake is likely to be an indicator of other protective elements, such as adequate energy intake and access to medical care.

Several studies demonstrated that higher quantities of consumption of poultry and aquatic products were connected to a decrease in all-cause and CVD mortality risk in our study. This is in agreement with the results of our study. Because subjects who consume more white meat and aquatic products also consume less red meat, it is hard to examine the health effect of white meat consumption. However, people who eat less red meat intend to consume other proteins, including those found in vegetables, which may prevent CVD. However, in contrast to vegetable products, white meat and aquatic products are both quality protein sources. They consist of less fat and a better fatty acid profile (i.e., mostly unsaturated fatty acids) [42, 43] than lamb, pork,

or beef as well as a lower concentration of heme iron, which are good for cardiometabolic health and may aid in cancer prevention and treatment [44, 45]. Furthermore, instead of red meat, people may choose poultry and fish as lower-fat alternatives because they are not preserved with nitrite-based salts. Substituting these alternatives for packed and red meat may reduce the risk of getting sick and, therefore, prevent premature death caused by CVD or cancer.

Finally, in the highest tertiles of physical activity, more consumption of aquatic products, poultry, and red meat was linked to a lower risk of all-cause and CVD mortality, respectively, compared to the lowest tertiles. Physical activity is linked to all-cause and CVD mortality, and it is crucial in assessing functional status and cardiovascular health [46, 47]. The level of physical activity is strongly related to objectively assessed cardiorespiratory fitness [46]. As a result, participants who engage in more physical activity may have improved cardiorespiratory endurance and fitness, which may be protective. If one has a fitter body, in particular, he or she is more likely to be metabolically flexible in dealing with physiological stressors caused by packed meat and red meat consumption than people with poorer health [20]. This is in line with other epidemiological and experimental studies that have found that physical activity and cardiorespiratory health help mitigate the effect of risk elements, including alcohol, BMI, and sedentary time, and thus reduce mortality [48-50]. Therefore, we should not only focus on the positive effects of moderate to high meat consumption but also manage behaviors that are beneficial to physical health in a comprehensive manner to effectively reduce mortality.

The study has some limitations. First, because the data of this research only represented Jiangsu Province, the generalizability of the results may be limited. Second, our conclusions apply only to individuals with T2DM and cannot be generalized to other populations. Finally, although some covariates were adjusted, the retrospective method of the food frequency survey and self-reporting history of diseases impeded the avoidance of the possibility of recall bias and other unknown confounding factors, which may have affected the results of the analysis.

Conclusions

In T2DM patients, adherence to moderate to high consumption of red meat, poultry, and aquatic products was related to lower mortality. Physical activity was also not linearly associated with mortality, with a protective effect observed $>8\text{MET-h/d}$. Finally, our study highlights that better adherence to moderate to high consumption of red meat, poultry, and aquatic products together with engaging in moderate to high levels of physical activity exerts a beneficial effect in lowering cause-specific and all-cause mortality among T2DM in China.

Abbreviations

BMI Body mass index

CIs Confidence intervals

CVDs Cardiovascular diseases

FFQ Food frequency questionnaire

HRs Hazard Ratios

T2DM Type 2 diabetes mellitus

Declarations

Authors' contributions Conceptualization, Methodology: Wei Wang, Xunbao Zhang; Data curation, Writing-Original draft preparation: Chenlu He, Hao Hou, Yifei Pei; Supervision, Validation: Peian Lou, Zhongming Sun and Enchun Pan; Writing- Reviewing and Editing: Qian Chen, Ying Zhang, Jingjing Wang, Jie Tang, Na Yan, Wei Wang.

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Availability of data and materials Data supporting the results presented in the paper are available upon reasonable requests.

Competing interests The authors declare no conflict competing interests.

Ethical approval and consent to participate Approval was obtained from the ethics committee of the Huai'an Center for Disease Control and Prevention and Xuzhou Medical University. The procedures used in this study adhere to the tenets of the Declaration of Helsinki. All participants gave their written informed consent before their inclusion in the study.

Consent for publication Not applicable.

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Tables

Table 1. Baseline characteristics of T2DM patients according to survival status

Variables	Overall	Survivors	All-cause deaths	c ² /Z	P
Age(years)	62.1(55.7,74.3)	61.5(55.1,67.6)	69.7(63.7,72.1)	-19.903	<0.001
Duration of diabetes (years)	3.0(1.0,7.0)	3.0(1.0,7.0)	4.0(1.0,10.0)	-3.627	<0.001
HbA1c (%)	7.2(6.3,8.7)	7.2(6.2,8.7)	7.7(6.5,9.3)	-6.309	<0.001
Gender				26.703	<0.001
Male	2801(38.3)	2473(37.4)	328(47.4)		
Female	4510(61.7)	4146(62.6)	364(52.6)		
Level of education				30.030	<0.001
Primary school or less	4958(67.8)	4431(66.9)	527(76.2)		
Secondary school	1494(20.4)	1373(20.7)	121(17.5)		
High school	592(8.1)	561(8.5)	31(4.5)		
College or above	267(3.7)	254(3.8)	13(1.9)		
Marital status				79.012	<0.001
Never married	73(1.0)	63(1.0)	10(1.4)		
Married/Cohabiting	6370(87.1)	5841(88.2)	529(76.4)		
Divorced/Widowed/Separated	868(11.9)	715(10.8)	153(22.1)		
Household income (yuan)				20.737	<0.001
≤30000	4411(60.3)	3943(59.6)	468(67.6)		
30000-110000	2606(35.6)	2396(36.2)	210(30.3)		
110000-160000	236(3.2)	226(3.4)	10(1.4)		
≥160000	58(0.8)	54(0.8)	4(0.6)		
Frequency of smoking				29.579	<0.001
Current smokers	1682(23.0)	1492(22.5)	190(27.5)		
Former smokers	387(5.3)	327(4.9)	60(8.7)		
Never smokers	5242(71.7)	4800(72.5)	442(63.9)		
Frequency of drinking				2.401	0.301
Current drinkers	1319(18.0)	1202(18.2)	117(59.1)		
Former drinkers	392(5.4)	347(5.2)	45(15.6)		
Never drinkers	5600(76.6)	5070(76.6)	530(25.3)		
Sleep duration				15.539	<0.001

6-8h/day	4776(65.3)	4367(66.0)	409(59.1)		
<6 h/day	1070(14.6)	962(14.5)	108(15.6)		
>8 h/day	1465(20.0)	1290(19.5)	175(25.3)		
Hypertension				8.433	0.004
Yes	3578(48.9)	3203(48.4)	375(54.2)		
No	3733(51.1)	3416(51.6)	317(45.8)		
Dyslipidemia				16.258	<0.001
Yes	1521(20.8)	1418(21.4)	103(14.9)		
No	5790(79.2)	5201(78.6)	589(85.1)		
Coronary heart disease				7.628	0.006
Yes	741(10.1)	650(9.8)	91(13.2)		
No	6570(89.9)	5969(90.2)	601(86.8)		
Stroke				44.718	<0.001
Yes	882(12.1)	744(11.2)	138(19.9)		
No	6429(87.9)	5875(88.8)	554(80.1)		
Kidney diseases				0.285	0.593
Yes	239(3.3)	214(3.2)	25(3.6)		
No	7072(96.7)	6405(96.8)	667(96.4)		
Overweight or obesity				30.600	<0.001
Yes	5157(70.5)	4732(71.5)	425(61.4)		
No	2154(29.5)	1887(28.5)	267(38.6)		

Data are expressed median (interquartile range), or n (%) where appropriate.

Table 2 Hazard ratios for all-cause mortality according quartiles of red meat, poultry, aquatic products, eggs and tertiles of physical activity.

Physical activity	Low	Medium	High		P for trend
N	2444	2430	2437		
Death	321	218	153		
Person-years	13901	14112	14325		
Crude	1	0.67(0.56-0.79) **	0.46(0.38-0.56) **		<0.001
Multivariable adjusted ^a	1	0.76(0.64-0.90) *	0.63(0.51-0.76) **		<0.001
Multivariable adjusted ^b	1	0.77(0.65-0.92) *	0.64(0.53-0.78) **		<0.001
Red meat	Q1	Q2	Q3	Q4	P for trend
N	1896	2343	1485	1587	
Death	220	218	145	109	
Person-years	10868	13608	8578	9285	
Crude	1	0.79(0.66-0.95) *	0.83(0.68-1.03)	0.58(0.46-0.73) **	<0.001
Multivariable adjusted ^a	1	0.79(0.66-0.96) *	1.01(0.81-1.24)	0.72(0.57-0.91) *	0.005
Multivariable adjusted ^b	1	0.82(0.68-0.99) *	1.05(0.85-1.30)	0.75(0.59-0.95) *	0.009
Poultry	Q1	Q2	Q3	Q4	P for trend
N	1841	2161	1729	1580	
Death	242	203	134	113	
Person-years	10487	12553	10055	9243	
Crude	1	0.70(0.58-0.84) **	0.58(0.47-0.71) **	0.53(0.42-0.66) **	<0.001
Multivariable adjusted ^a	1	0.75(0.62-0.91) *	0.65(0.53-0.81) **	0.62(0.49-0.78) **	<0.001
Multivariable adjusted ^b	1	0.78(0.64-0.94) *	0.69(0.56-0.86) *	0.64(0.51-0.81) **	<0.001
Aquatic products	Q1	Q2	Q3	Q4	P for trend
N	2144	1515	2293	1359	

Death	251	147	195	99	
Person-years	12336	8749	13305	7948	
Crude	1	0.83(0.67-1.01)	0.72(0.60-0.87) *	0.61(0.48-0.77) **	<0.001
Multivariable adjusted ^a	1	0.83(0.67-1.01)	0.82(0.68-0.99) *	0.72(0.57-0.91) *	0.026
Multivariable adjusted ^b	1	0.85(0.69-1.04)	0.86(0.71-1.04)	0.75(0.59-0.95) *	0.086
Eggs	Q1	Q2	Q3	Q4	P for trend
N	1868	2520	2451	472	
Death	198	236	212	46	
Person-years	10823	14556	14228	2731	
Crude	1	0.89(0.73-1.07)	0.81(0.67-0.99) *	0.92(0.67-1.27)	0.223
Multivariable adjusted ^a	1	0.95(0.79-1.15)	0.90(0.74-1.10)	0.90(0.65-1.25)	0.773
Multivariable adjusted ^b	1	0.96(0.80-1.16)	0.91(0.75-1.12)	0.91(0.66-1.26)	0.822

Multivariable adjusted^a: Adjusted for age, duration of diabetes, gender, marital status, level of education, household income and HbA1c.

Multivariable adjusted^b: Adjusted for age, duration of diabetes, gender, marital status, level of education, household income, HbA1c, frequency of smoking, frequency of drinking, hypertension, dyslipidemia, coronary heart disease, kidney diseases, overweight or obesity and sleep duration.

* $P < 0.05$; ** $P < 0.001$

Table 3. Hazard ratios for CVD mortality according quartiles of red meat, poultry, aquatic products, eggs and tertiles of physical activity.

Physical activity	Low	Medium	High		P for trend
N	2444	2430	2437		
Death	126	76	48		
Person-years	13901	14112	14325		
Crude	1	0.59(0.45-0.79) **	0.37(0.26-0.51) **		<0.001
Multivariable adjusted ^a	1	0.67(0.51-0.90) *	0.53(0.37-0.74) **		<0.001
Multivariable adjusted ^b	1	0.71(0.53-0.95) *	0.56(0.40-0.79) *		0.002
Red meat	Q1	Q2	Q3	Q4	P for trend
N	1896	2343	1485	1587	
Death	77	83	48	42	
Person-years	10868	13608	8578	9285	
Crude	1	0.86(0.63-1.17)	0.79(0.55-1.13)	0.64(0.44-0.93) *	0.123
Multivariable adjusted ^a	1	0.86(0.63-1.17)	0.98(0.68-1.41)	0.81(0.56-1.19)	0.630
Multivariable adjusted ^b	1	0.89(0.65-1.21)	1.06(0.74-1.53)	0.88(0.60-1.30)	0.704
Poultry	Q1	Q2	Q3	Q4	P for trend
N	1841	2161	1729	1580	
Death	83	79	45	43	
Person-years	10487	12553	10055	9243	
Crude	1	0.79(0.58-1.08)	0.57(0.39-0.81) *	0.58(0.40-0.84) *	0.004
Multivariable adjusted ^a	1	0.85(0.62-1.16)	0.66(0.46-0.95) *	0.69(0.48-1.01)	0.095
Multivariable adjusted ^b	1	0.89(0.65-1.22)	0.68(0.47-0.99) *	0.72(0.49-1.05)	0.140
Aquatic products	Q1	Q2	Q3	Q4	P for trend
N	2144	1515	2293	1359	
Death	95	53	71	31	
Person-years	12336	8749	13305	7948	

Crude	1	0.79(0.56-1.10)	0.69(0.51-0.94) *	0.50(0.34-0.76) *	0.005
Multivariable adjusted ^a	1	0.78(0.56-1.10)	0.80(0.59-1.09)	0.59(0.39-0.88) *	0.069
Multivariable adjusted ^b	1	0.81(0.58-1.14)	0.84(0.61-1.15)	0.62(0.41-0.93) *	0.136
Eggs	Q1	Q2	Q3	Q4	P for trend
N	1868	2520	2451	472	
Death	76	81	75	18	
Person-years	10823	14556	14228	2731	
Crude	1	0.80(0.58-1.09)	0.75(0.55-1.03)	0.94(0.56-1.57)	0.299
Multivariable adjusted ^a	1	0.85(0.62-1.17)	0.86(0.62-1.19)	0.90(0.53-1.51)	0.752
Multivariable adjusted ^b	1	0.86(0.63-1.18)	0.85(0.61-1.18)	0.91(0.54-1.54)	0.739

Multivariable adjusted^a: Adjusted for age, duration of diabetes, gender, marital status, level of education, household income and HbA1c.

Multivariable adjusted^b: Adjusted for age, duration of diabetes, gender, marital status, level of education, household income, HbA1c, frequency of smoking, frequency of drinking, hypertension, dyslipidemia, coronary heart disease, kidney diseases, overweight or obesity and sleep duration.

* $P < 0.05$; ** $P < 0.001$

Table 4. Hazard ratios for cancer mortality according quartiles of red meat, poultry, aquatic products, eggs and tertiles of physical activity.

Physical activity	Low	Medium	High		P for trend
N	2444	2430	2437		
Death	83	61	57		
Person-years	13901	14112	14325		
Crude	1	0.72(0.52-1.01)	0.67(0.47-0.93) *		0.035
Multivariable adjusted ^a	1	0.82(0.59-1.14)	0.87(0.62-1.23)		0.461
Multivariable adjusted ^b	1	0.82(0.59-1.15)	0.88(0.62-1.24)		0.502
Red meat	Q1	Q2	Q3	Q4	P for trend
N	1896	2343	1485	1587	
Death	62	59	41	39	
Person-years	10868	13608	8578	9285	
Crude	1	0.76(0.53-1.08)	0.84(0.56-1.24)	0.74(0.49-1.10)	0.365
Multivariable adjusted ^a	1	0.77(0.64-1.10)	0.96(0.65-1.43)	0.82(0.55-1.24)	0.453
Multivariable adjusted ^b	1	0.79(0.55-1.13)	0.98(0.66-1.47)	0.82(0.54-1.23)	0.502
Poultry	Q1	Q2	Q3	Q4	P for trend
N	1841	2161	1729	1580	
Death	71	47	44	39	
Person-years	10487	12553	10055	9243	
Crude	1	0.55(0.38-0.80) *	0.65(0.44-0.94) *	0.62(0.42-0.92) *	0.006
Multivariable adjusted ^a	1	0.57(0.40-0.83) *	0.68(0.46-0.99) *	0.65(0.44-0.98) *	0.018
Multivariable adjusted ^b	1	0.58(0.40-0.84) *	0.70(0.47-1.03)	0.65(0.43-0.97) *	0.022
Aquatic products	Q1	Q2	Q3	Q4	P for trend
N	2144	1515	2293	1359	
Death	62	59	41	39	
Person-years	12336	8749	13305	7948	
Crude	1	1.05(0.71-1.53)	0.87(0.61-1.24)	0.88(0.58-1.32)	0.728
Multivariable adjusted ^a	1	1.04(0.71-1.52)	0.94(0.65-1.35)	0.95(0.62-1.44)	0.956
Multivariable adjusted ^b	1	1.06(0.72-1.55)	0.96(0.66-1.38)	0.96(0.63-1.47)	0.963
Eggs	Q1	Q2	Q3	Q4	P for trend

N	1868	2520	2451	472	
Death	57	71	62	11	
Person-years	10823	14556	14228	2731	
Crude	1	0.93(0.65-1.31)	0.83(0.58-1.19)	0.77(0.40-1.46)	0.703
Multivariable adjusted ^a	1	0.96(0.67-1.36)	0.86(0.59-1.24)	0.73(0.38-1.40)	0.711
Multivariable adjusted ^b	1	0.95(0.67-1.35)	0.85(0.58-1.23)	0.72(0.37-1.38)	0.680

Multivariable adjusted^a: Adjusted for age, duration of diabetes, gender, marital status, level of education, household income and HbA1c.

Multivariable adjusted^b: Adjusted for age, duration of diabetes, gender, marital status, level of education, household income, HbA1c, frequency of smoking, frequency of drinking, hypertension, dyslipidemia, coronary heart disease, kidney diseases, overweight or obesity and sleep duration.

* $P < 0.05$; ** $P < 0.001$

Figures

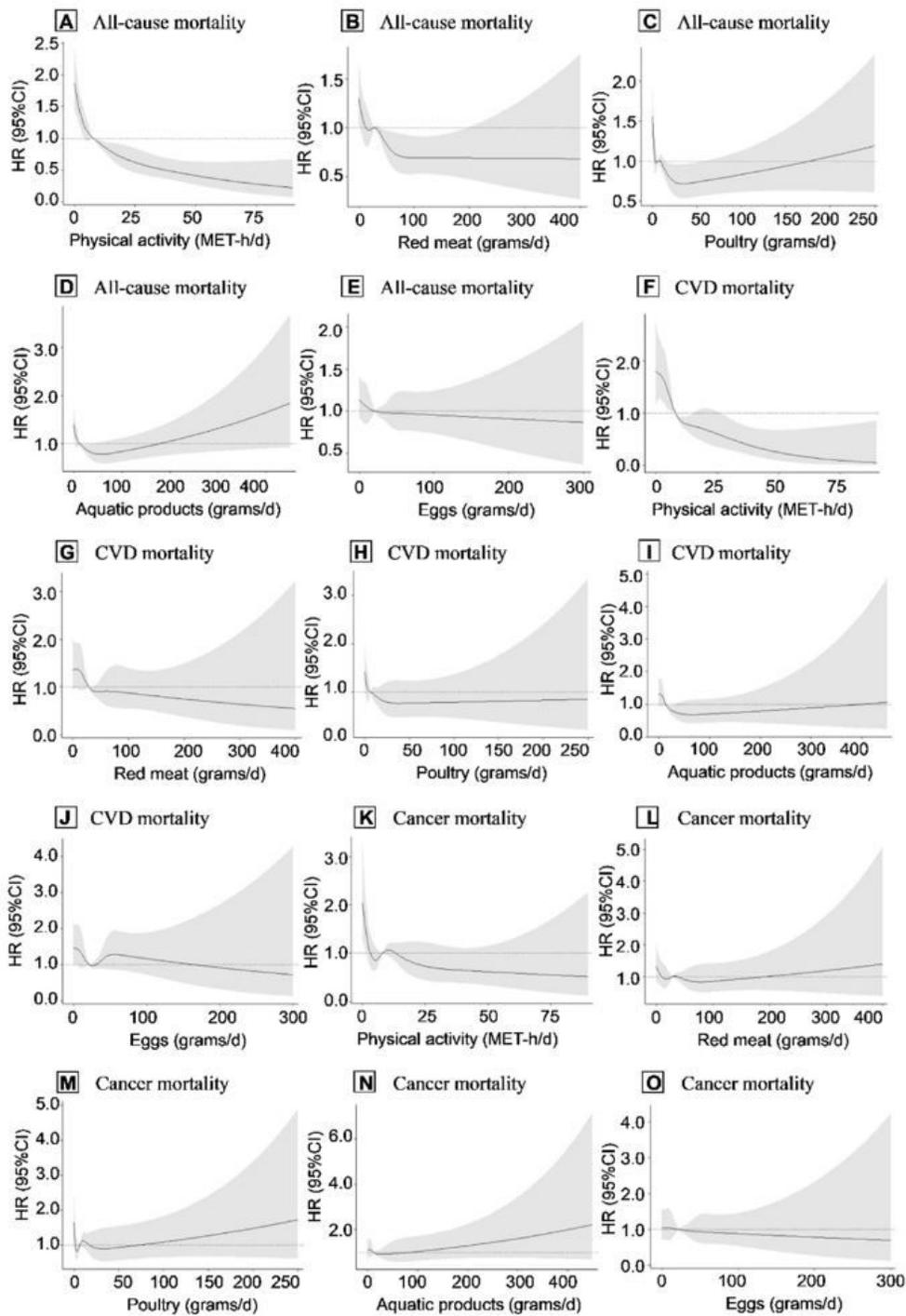


Figure 1

Dose-response relationships between red meat, poultry, aquatic product, egg consumption and all-cause and cause-specific mortality

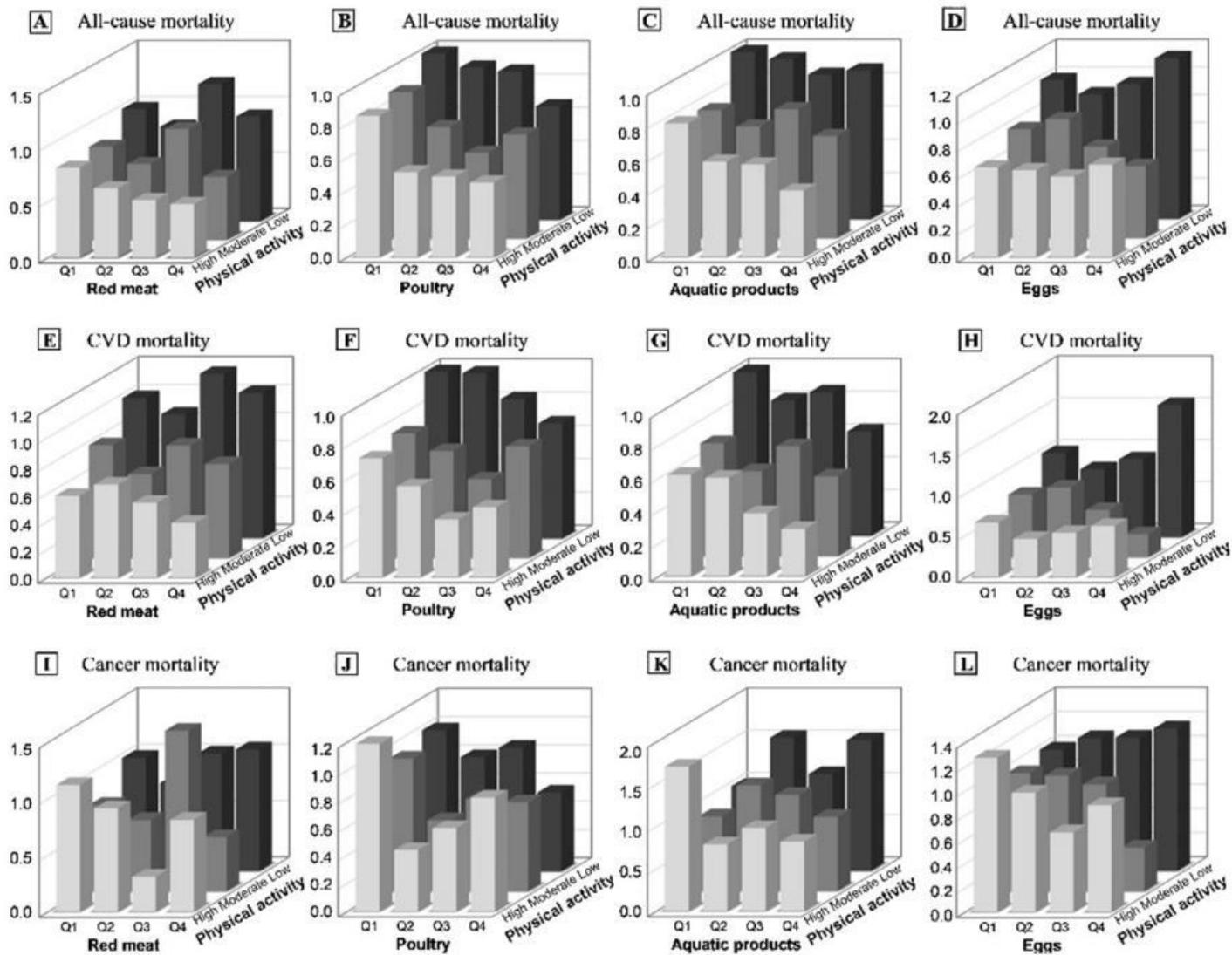


Figure 2

Hazard ratios of the combined effect of quartiles of red meat, poultry, aquatic product, egg consumption and physical activity

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