

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

## **eMethods. Assessment and Statistical Analysis**

### **Validity of protein intake assessment by food frequency questionnaire (FFQ)**

The validity of estimated nutrient intake by FFQ has been evaluated with the use of multiple dietary records in both cohorts.<sup>1-5</sup> In the NHS, after accounting for week-to-week variation, the energy-adjusted Pearson correlation coefficient between the average intake from the 1980, 1984 and 1986 questionnaires and the average intake from the six seven-day diet records in 1980 and 1986 was 0.68 for protein, 0.78 for carbohydrate, and 0.83 for total fat.<sup>5</sup> Similar findings were observed in a validation study of the HPFS.<sup>3</sup> Recently, we further validated dietary protein intake among 624 women in the NHS and NHS II cohorts, who completed two FFQs approximately one year apart and two seven-day diet records about six months apart, and provided at least one 24-hour urine sample. The Spearman correlation coefficient of intake assessed by the FFQs and dietary records was 0.56 (95% CI, 0.48-0.62) for animal protein and 0.66 (95% CI, 0.59-0.71) for plant protein, after adjusting for within-person variation and total energy intake.<sup>6</sup> Energy-adjusted protein intake estimated from FFQ was moderately correlated with urinary nitrogen measurements ( $r=0.52$ ).<sup>7</sup>

### **Assessment of covariates**

In the biennial follow-up questionnaires, we inquired and updated information on medical, lifestyle, and other health-related factors, such as body weight; cigarette smoking status; regular intake of multivitamins; history of hypertension, diabetes mellitus, myocardial infarction, and cancer; menopausal status and use of postmenopausal hormone therapy (women only). In the NHS, hours per week of moderate or vigorous activities was collected in 1980 and 1982. Detailed data on leisure-time physical activity was assessed beginning in 1986 with validated questionnaires on 10 common activities in the NHS and HPFS. Overall physical activity was calculated by summing the products of time spent on each activity with the average metabolic equivalent (MET) for that activity.

We calculated the glycemic index (GI) values for single food items on the FFQ using available databases and publications.<sup>8-10</sup> Certain foods not represented in the database were sent to the University of Sydney for GI analysis. These foods included breakfast cereals, cakes, cookies, muffin mixes, pancake mixes, and candy bars. For the remaining foods not represented in the database, we imputed their GI values from similar foods in the database. For each participant, we calculated the average dietary GI by summing the products of the carbohydrate content per serving for each food item times the average number of servings of that food per day, times its GI, and divided by the total daily carbohydrate content.<sup>11</sup>

Intakes of whole grain were estimated from all grain-containing foods (rice, bread, pasta, and breakfast cereals) according to the dry weight of the whole grain ingredients in each food.<sup>12,13</sup> Whole grain consumption from breakfast cereal was derived from more than 250 brand name cereals based on information provided by product labels and breakfast cereal manufacturers. In our study, whole grains included intact and pulverized forms that contained the expected proportion of bran, germ, and endosperm for the specific grain types. By definition, the following foods and ingredients were considered whole grains: whole wheat and whole wheat flour, whole oats and whole oat flour, whole cornmeal and whole corn flour, whole rye and whole rye flour, whole barley, bulgur, buckwheat, brown rice and brown rice flour, popcorn, amaranth, and psyllium.

### **Statistical analysis**

We used SAS 9.3 for all analyses (SAS Institute Inc., Cary, NC, USA). All statistical tests were two sided and  $P < 0.05$  was considered statistically significant.

In the Cox regression model, we stratified by calendar year of the current questionnaire cycle to account for any period effect. Proportional hazards assumption was tested by including an interaction term between time and protein intake in the model and no deviation from proportional hazards assumption

was detected. To control for confounding, we adjusted for the following covariates: total caloric intake, percent of energy from saturated fat, polyunsaturated fat, monounsaturated fat, and trans fat (continuous), multivitamin use (yes or no), smoking status (never, past smokers, current smokers 1-14, and 15+ cigarettes/day), pack-years of smoking (in women:  $\leq 15$ , 16-25, 26-45,  $>45$ ; in men:  $<10$ , 11-24, 25-44,  $\geq 45$ ), body mass index ( $<23.0$ , 23.0-24.9, 25.0-26.9, 27.0-29.9, 30.0-34.9,  $\geq 35$  kg/m<sup>2</sup>), physical activity (quintiles), alcohol consumption (in women: 0, 0.1-5.0, 5.1-15.0, and  $>15.0$  g/d; in men: 0, 0.1-10.0, 10.1-20.0, and  $>20.0$  g/d), history of hypertension diagnosis (yes or no), glycemic index (in quintiles), and intake of whole grains, total fiber, fruits, and vegetables (all in quintiles). Mutual adjustment was conducted for animal protein and plant protein analysis.

To reduce random within-person variation and to best represent long-term dietary intake, we calculated cumulative average of protein intake from our repeated FFQs.<sup>14</sup> For example, in the NHS, protein intake in 1980 was related to mortality from 1980 to 1984, the average intake from 1980 to 1984 was related to mortality from 1984 to 1986, and so forth. Participants were divided into 5 categories based on their protein intake, and the cutoffs were chosen to allow for assessment of a wide range of intake levels. Test for trend was performed using continuous intake per 10%-energy increment in an absolute amount for animal protein and per 3%-energy increment for plant protein. To reduce the influence of outliers, we employed a 99% Winsorisation technique by setting intake below the 0.5th percentile to the 0.5th percentile, and setting intake above the 99.5th percentile to the 99.5th percentile.<sup>15</sup>

In the propensity score analysis, we estimated the predicted probability (propensity score) of consuming high animal and plant protein in each participant using a logistic regression that included all the variables in our multivariable model.<sup>16,17</sup> We then adjusted for the propensity score to examine the association of protein intake with all-cause mortality.

We also assessed the HR of mortality associated with substitution for carbohydrate of 10% energy from animal protein and 3% energy from plant protein, which were approximately the difference in median intakes of extreme categories for each protein item. We tested potential nonlinear relationship between protein intake and mortality using stepwise restricted cubic spline analysis,<sup>18</sup> with a  $P = 0.05$  as the criteria for both inclusion and retention in the model. We used a likelihood ratio test to determine the significance of the non-linearity by comparing the model with only the linear term to the model with both the linear and the cubic spline terms.

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**eTable 1. Risk for All-Cause Mortality According to Percentage of Energy From Animal and Plant Protein Intake in the Nurses' Health Study and Health Professionals Follow-up Study**

	Category 1	Category 2	Category 3	Category 4	Category 5	HR (95% CI) per certain increment	<i>P</i> <sub>trend</sub>
<b>Nurses' Health Study</b>							
<b>Animal protein</b>							
Intake category	≤10 %	>10, ≤12 %	>12, ≤15 %	>15, ≤18 %	>18 %	Per 10% increment	
Median intake (% energy)	9	11	14	16	20		
No. of deaths	1,531	2,515	6,222	5,722	4,760		
Person-years	169,768	301,870	775,493	712,500	547,561		
Age-adjusted HR (95% CI)*	1 (referent)	0.90 (0.85-0.96)	0.85 (0.80-0.90)	0.81 (0.77-0.86)	0.83 (0.78-0.89)	0.93 (0.89-0.96)	<0.001
MV-adjusted HR (95% CI)†	1 (referent)	0.99 (0.93-1.06)	1.02 (0.96-1.08)	1.02 (0.96-1.08)	1.02 (0.95-1.09)	1.02 (0.98-1.07)	0.32
<b>Plant protein</b>							
Intake category	≤3 %	>3, ≤4 %	>4, ≤5 %	>5, ≤6 %	>6 %	Per 3% increment	
Median intake (% energy)	2.6	3.5	4.5	5.4	6.6		
No. of deaths	5,844	7,576	4,790	1,803	737		
Person-years	695,863	943,048	574,819	208,278	85,184		
Age-adjusted HR (95% CI)*	1 (referent)	0.91 (0.87-0.94)	0.88 (0.84-0.92)	0.83 (0.78-0.89)	0.84 (0.77-0.92)	0.85 (0.81-0.89)	<0.001
MV-adjusted HR (95% CI)†	1 (referent)	0.99 (0.95-1.03)	0.97 (0.93-1.02)	0.93 (0.87-1.00)	0.98 (0.89-1.08)	0.96 (0.91-1.02)	0.22
<b>Health Professionals Follow-up Study</b>							
<b>Animal protein</b>							
Intake category	≤10 %	>10, ≤12 %	>12, ≤15 %	>15, ≤18 %	>18 %	Per 10% increment	
Median intake (% energy)	9	11	13	16	20		
No. of deaths	2,239	3,636	5,687	2,679	1,124		
Person-years	148,083	243,052	396,422	180,547	65,495		
Age-adjusted HR (95% CI)*	1 (referent)	0.97 (0.92-1.03)	0.99 (0.94-1.05)	1.10 (1.03-1.16)	1.27 (1.18-1.37)	1.21 (1.14-1.28)	<0.001
MV-adjusted HR (95% CI)†	1 (referent)	1.01 (0.95-1.06)	1.01 (0.95-1.06)	1.01 (0.94-1.07)	1.01 (0.93-1.10)	1.00 (0.94-1.06)	0.99
<b>Plant protein</b>							
Intake category	≤3 %	>3, ≤4 %	>4, ≤5 %	>5, ≤6 %	>6 %	Per 3%	

						increment	
Median intake (% energy)	2.7	3.7	4.6	5.4	6.6		
No. of deaths	316	2,085	5,445	4,799	2,720		
Person-years	14,730	117,825	354,375	341,737	204,934		
Age-adjusted HR (95% CI)*	1 (referent)	0.82 (0.73-0.93)	0.66 (0.58-0.74)	0.55 (0.49-0.62)	0.51 (0.45-0.58)	0.64 (0.61-0.68)	<0.001
MV-adjusted HR (95% CI)†	1 (referent)	0.91 (0.80-1.03)	0.86 (0.76-0.97)	0.80 (0.70-0.92)	0.77 (0.66-0.89)	0.81 (0.75-0.87)	<0.001

Abbreviations: CI, confidence interval; HR, hazard ratio, MV, multivariable.

\* Cox proportional hazards model with age as the time scale was stratified by sex and calendar time, and adjusted for total caloric intake, and percent of energy from saturated fat, polyunsaturated fat, monounsaturated fat, and trans fat (continuous).

† Multivariable model was further adjusted for multivitamin use (yes or no), smoking status (never, past smokers, current smokers 1-14, and 15+ cigarettes/day), pack-years of smoking (in women: ≤15, 16-25, 26-45, >45; in men: <10, 11-24, 25-44, ≥45), body mass index (<23.0, 23.0-24.9, 25.0-26.9, 27.0-29.9, 30.0-34.9, ≥35 kg/m<sup>2</sup>), physical activity (quintiles), alcohol consumption (in women: 0, 0.1-5.0, 5.1-15.0, and >15.0 g/d; in men: 0, 0.1-10.0, 10.1-20.0, and >20.0 g/d), postmenopausal status and hormone use (women only: never, past and current use), history of hypertension diagnosis (yes or no), glycemic index (in quintiles), and intake of whole grains, total fiber, fruits, and vegetables (all in quintiles). Mutual adjustment was conducted for animal protein and plant protein analysis.



**eTable 2. Hazard Ratio (95% CI) for All-Cause Mortality According to Percentage of Energy From Animal and Plant Protein Intake by Duration of Follow-up**

Duration of follow-up	Category 1	Category 2	Category 3	Category 4	Category 5	HR (95% CI) per certain increment	<i>P</i> <sub>trend</sub>	<i>P</i> <sub>interaction</sub> <sup>†</sup>
<b>Animal protein</b>	≤10 %	>10, ≤12 %	>12, ≤15 %	>15, ≤18 %	>18 %	Per 10% increment		0.09
≤16 years								
No. of deaths	800	1134	2301	1800	1279			
HR (95% CI)*	1 (referent)	0.92 (0.84-1.01)	0.89 (0.82-0.97)	0.89 (0.81-0.98)	0.89 (0.80-0.99)	0.94 (0.87-1.01)	0.08	
>16, ≤20 years								
No. of deaths	465	797	1588	1061	791			
HR (95% CI)*	1 (referent)	1.06 (0.94-1.19)	1.09 (0.97-1.21)	1.04 (0.92-1.18)	1.14 (0.99-1.31)	1.05 (0.95-1.16)	0.32	
>20, ≤28 years								
No. of deaths	1461	2501	4836	3307	2294			
HR (95% CI)*	1 (referent)	1.02 (0.96-1.09)	1.04 (0.98-1.11)	1.04 (0.97-1.12)	1.06 (0.98-1.15)	1.05 (0.99-1.11)	0.11	
>28 years								
No. of deaths	1044	1719	3184	2233	1520			
HR (95% CI)*	1 (referent)	1.00 (0.92-1.08)	1.00 (0.93-1.08)	1.04 (0.95-1.13)	1.00 (0.90-1.10)	1.01 (0.94-1.08)	0.76	
<b>Plant protein</b>	≤3 %	>3, ≤4 %	>4, ≤5 %	>5, ≤6 %	>6 %	Per 3% increment		0.28
≤16 years								
No. of deaths	1397	2159	2071	1119	568			
HR (95% CI)*	1 (referent)	0.98 (0.91-1.05)	0.96 (0.87-1.05)	0.89 (0.80-1.00)	0.89 (0.76-1.02)	0.91 (0.82-1.01)	0.07	
>16, ≤20 years								
No. of deaths	817	1217	1308	878	482			
HR (95% CI)*	1 (referent)	0.89 (0.80-0.98)	0.85 (0.75-0.95)	0.90 (0.78-1.04)	0.98 (0.81-1.17)	1.00 (0.88-1.13)	0.99	
>20, ≤28 years								
No. of deaths	2369	3752	4165	2737	1376			
HR (95% CI)*	1 (referent)	0.97 (0.92-1.03)	0.96 (0.90-1.03)	0.92 (0.85-1.00)	0.86 (0.78-0.96)	0.89 (0.83-0.96)	0.003	
>28 years								
No. of deaths	1577	2533	2691	1868	1031			
HR (95% CI)*	1 (referent)	1.01 (0.94-1.08)	0.98 (0.90-1.07)	0.89 (0.81-0.99)	0.93 (0.81-1.06)	0.91 (0.83-1.00)	0.04	

Abbreviations: CI, confidence interval; HR, hazard ratio.

\* Cox proportional hazards model with age as the time scale was stratified by sex and calendar time, and adjusted for total caloric intake, percent of energy from saturated fat, polyunsaturated fat, monounsaturated fat and *trans* fat (all continuous), multivitamin use (yes or no), smoking status (never, past smokers, current smokers 1-14, and 15+ cigarettes/day), pack-years of smoking (in women:  $\leq 15$ , 16-25, 26-45,  $>45$ ; in men:  $<10$ , 11-24, 25-44,  $\geq 45$ ), body mass index ( $<23.0$ , 23.0-24.9, 25.0-26.9, 27.0-29.9, 30.0-34.9,  $\geq 35$  kg/m<sup>2</sup>), physical activity (quintiles), alcohol consumption (in women: 0, 0.1-5.0, 5.1-15.0, and  $>15.0$  g/d; in men: 0, 0.1-10.0, 10.1-20.0, and  $>20.0$  g/d), history of hypertension diagnosis (yes or no), glycemic index (in quintiles), and intake of whole grains, total fiber, fruits, and vegetables (all in quintiles). Mutual adjustment was conducted for animal protein and plant protein analysis.

† Likelihood ratio test was used to calculate the *P* for interaction, by comparing the model with the product terms between protein intake (continuous) and duration of follow-up (in four categories) to the model without these terms.

**eTable 3. Risk for All-Cause Mortality According to Percentage of Energy From Animal and Plant Protein Intake With Adjustment for Propensity Score \***

	Category 1	Category 2	Category 3	Category 4	Category 5	HR (95% CI) per certain increment	$P_{\text{trend}}$
<b>Animal protein</b>							
Intake category	≤10 %	>10, ≤12 %	>12, ≤15 %	>15, ≤18 %	>18 %	Per 10% increment	
Propensity score-adjusted HR (95% CI)†	1 (referent)	1.00 (0.96- 1.05)	1.02 (0.98- 1.06)	1.02 (0.98- 1.07)	1.03 (0.98- 1.08)	1.02 (0.99- 1.06)	0.25
<b>Plant protein</b>							
Intake category	≤3 %	>3, ≤4 %	>4, ≤5 %	>5, ≤6 %	>6 %	Per 3% increment	
Propensity score-adjusted HR (95% CI)†	1 (referent)	0.98 (0.94- 1.01)	0.95 (0.91- 1.00)	0.91 (0.86- 0.96)	0.89 (0.84- 0.96)	0.90 (0.86- 0.95)	<0.00 1

Abbreviations: CI, confidence interval; HR, hazard ratio.

\* Cox proportional hazards model with age as the time scale was stratified by sex and calendar time, and adjusted for propensity score of high animal/plant protein intake as well as other covariates, including total caloric intake, percent of energy from saturated fat, polyunsaturated fat, monounsaturated fat and *trans* fat (all continuous), multivitamin use (yes or no), smoking status (never, past smokers, current smokers 1-14, and 15+ cigarettes/day), pack-years of smoking (in women: ≤15, 16-25, 26-45, >45; in men: <10, 11-24, 25-44, ≥45), body mass index (<23.0, 23.0-24.9, 25.0-26.9, 27.0-29.9, 30.0-34.9, ≥35 kg/m<sup>2</sup>), physical activity (quintiles), alcohol consumption (in women: 0, 0.1-5.0, 5.1-15.0, and >15.0 g/d; in men: 0, 0.1-10.0, 10.1-20.0, and >20.0 g/d), history of hypertension diagnosis (yes or no), glycemic index (in quintiles), and intake of whole grains, total fiber, fruits, and vegetables (all in quintiles). Mutual adjustment was conducted for animal protein and plant protein analysis.

**eTable 4. Association of Animal and Plant Protein Intake With All-Cause Mortality According to History of Diabetes**

	History of diabetes	No history of diabetes	<i>P</i> for interaction
Animal protein (per 10% increment)	1.07 (1.00-1.15)	1.00 (0.96-1.03)	0.06
Plant protein (per 3% increment)	0.84 (0.77-0.90)	0.91 (0.87-0.96)	0.02

Note: All HRs were multivariable-adjusted. *P* for interaction is estimated from likelihood ratio test.

**eTable 5. Median Protein Intake (% of Energy) of Various Food Origins and Their Correlations**

Protein source	Median (interquartile range)	Spearman correlation coefficient among protein intake from various sources						
		Plant	Processed red meat	Unprocessed red meat	Poultry	Fish	Egg	Dairy
Plant	4.01 (3.18, 4.95)	1	-0.18	-0.48	0.09	0.13	-0.05	-0.05
Processed red meat	0.28 (0.13, 0.50)	-	1	0.18	-0.15	-0.17	0.17	-0.14
Unprocessed red meat	4.89 (3.00, 7.73)	-	-	1	-0.16	-0.21	0.004	-0.28
Poultry	2.72 (1.75, 4.54)	-	-	-	1	0.34	0.02	-0.03
Fish	1.38 (0.84, 2.30)	-	-	-	-	1	0.03	0.05
Egg	0.49 (0.20, 0.79)	-	-	-	-	-	1	0.03
Dairy	3.19 (2.10, 4.73)	-	-	-	-	-	-	1

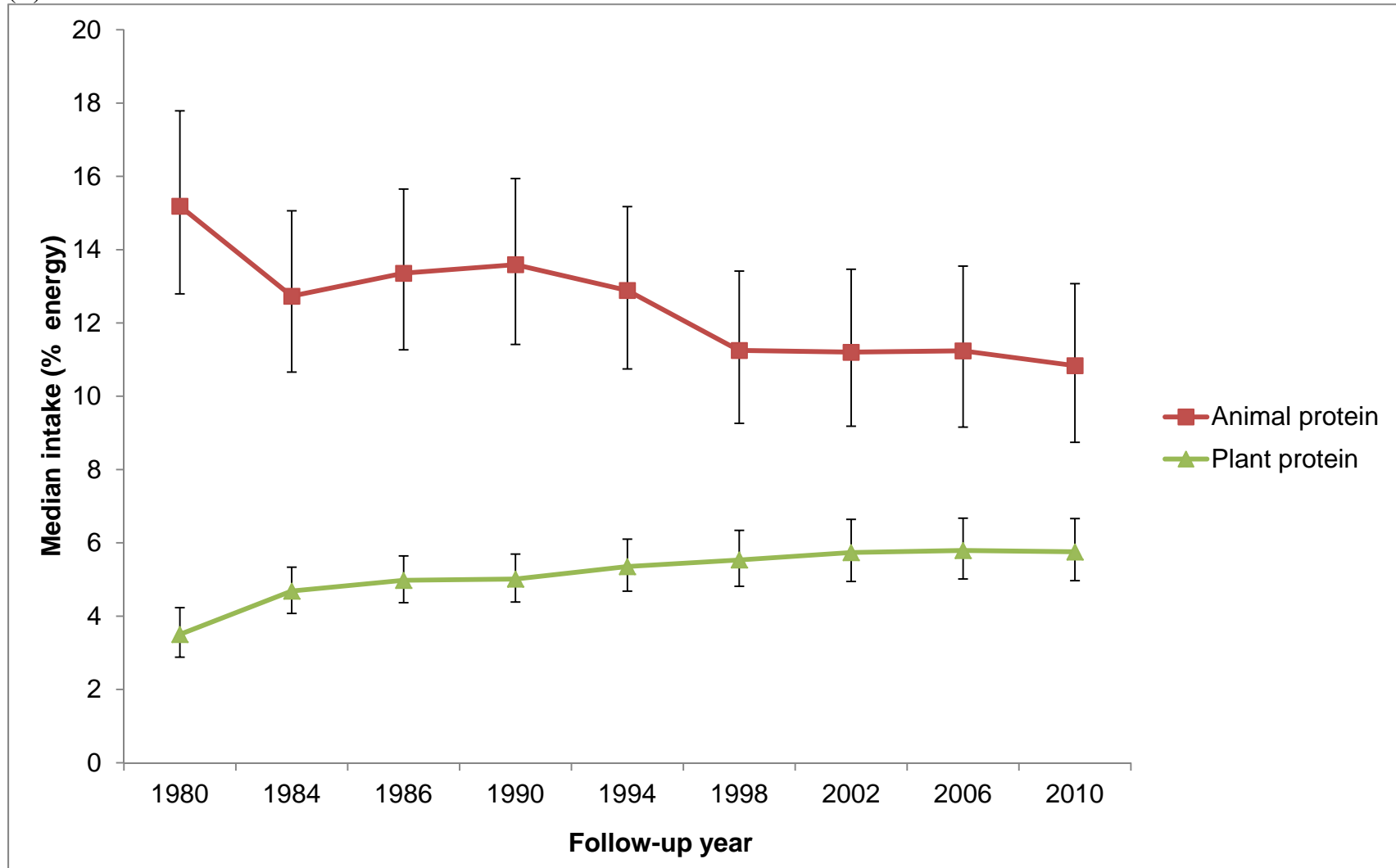
**eTable 6. Hazard Ratio (95% CI) of All-Cause and Cause-Specific Mortality According to Percentage of Energy Intake From Protein of Various Animal Foods With Mutual Adjustment for Each Other\***

Animal protein sources	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	HR (95% CI) per 3% increment	<i>P</i> <sub>trend</sub>
<b>All-cause mortality</b>							
Processed red meat	1 (referent)	1.00 (0.97-1.03)	1.02 (0.99-1.06)	1.03 (0.99-1.07)	1.09 (1.05-1.14)	1.42 (1.26-1.59)	<0.001
Unprocessed red meat	1 (referent)	1.04 (1.00-1.07)	1.09 (1.05-1.13)	1.09 (1.04-1.14)	1.15 (1.08-1.22)	1.07 (1.04-1.09)	<0.001
Poultry	1 (referent)	1.00 (0.97-1.04)	1.00 (0.97-1.04)	1.00 (0.96-1.03)	0.98 (0.94-1.01)	1.00 (0.98-1.01)	0.49
Fish	1 (referent)	0.98 (0.94-1.01)	0.99 (0.95-1.02)	1.00 (0.97-1.04)	0.99 (0.95-1.02)	1.00 (0.98-1.02)	0.93
Egg	1 (referent)	1.02 (0.99-1.06)	1.03 (1.00-1.07)	1.04 (1.01-1.08)	1.08 (1.04-1.12)	1.16 (1.08-1.23)	<0.001
Dairy	1 (referent)	0.99 (0.95-1.02)	1.02 (0.98-1.05)	1.03 (1.00-1.07)	1.04 (0.99-1.08)	1.02 (1.00-1.04)	0.02
<b>Cardiovascular mortality</b>							
Processed red meat	1 (referent)	1.02 (0.98-1.06)	1.01 (0.97-1.06)	1.00 (0.86-1.17)	1.31 (0.99-1.74)	1.46 (1.15-1.85)	0.002
Unprocessed red meat	1 (referent)	1.02 (0.98-1.06)	1.01 (0.89-1.16)	1.01 (0.87-1.18)	1.31 (0.99-1.73)	1.08 (1.03-1.13)	<0.001
Poultry	1 (referent)	1.20 (1.09-1.33)	0.99 (0.96-1.02)	1.14 (1.01-1.28)	0.84 (0.67-1.05)	0.99 (0.96-1.02)	0.44
Fish	1 (referent)	1.19 (1.08-1.31)	0.99 (0.95-1.02)	1.13 (1.01-1.27)	0.81 (0.66-1.00)	1.02 (0.98-1.06)	0.31
Egg	1 (referent)	1.20 (1.08-1.32)	0.99 (0.96-1.02)	1.13 (1.00-1.27)	0.85 (0.69-1.06)	1.02 (0.89-1.16)	0.82
Dairy	1 (referent)	1.20 (1.09-1.33)	0.99 (0.96-1.02)	1.15 (1.02-1.29)	0.84 (0.68-1.05)	1.01 (0.97-1.06)	0.53
<b>Cancer mortality</b>							
Processed red meat	1 (referent)	0.94 (0.89-1.00)	0.92 (0.87-0.98)	0.92 (0.85-0.99)	1.64 (1.37-1.97)	1.16 (0.96-1.40)	0.13
Unprocessed red meat	1 (referent)	1.11 (1.05-1.17)	1.13 (1.07-1.20)	0.92 (0.85-0.99)	1.63 (1.35-1.96)	1.04 (1.00-1.08)	0.06
Poultry	1 (referent)	1.08 (1.02-1.14)	1.12 (1.05-1.19)	0.91 (0.85-0.99)	1.64 (1.37-1.97)	1.01 (0.98-1.03)	0.70
Fish	1 (referent)	0.95 (0.86-1.05)	1.01 (0.90-1.13)	0.95 (0.83-1.09)	0.96 (0.90-1.03)	1.01 (0.98-1.04)	0.51
Egg	1 (referent)	1.03 (0.90-1.17)	0.96 (0.80-1.15)	0.98 (0.86-1.12)	1.12 (0.77-1.65)	1.20 (1.08-1.33)	<0.001
Dairy	1 (referent)	0.99 (0.90-1.09)	0.97 (0.87-1.08)	0.98 (0.85-1.12)	1.15 (0.78-1.68)	0.99 (0.96-1.02)	0.47
<b>Other mortality</b>							
Processed red meat	1 (referent)	1.04 (0.97-1.13)	1.01 (0.87-1.16)	0.80 (0.73-0.88)	1.24 (0.95-1.63)	1.66 (1.38-1.99)	<0.001
Unprocessed red meat	1 (referent)	1.06 (0.98-1.14)	1.11 (0.96-1.28)	0.72 (0.65-0.81)	1.26 (0.96-1.65)	1.09 (1.05-1.13)	<0.001
Poultry	1 (referent)	1.06 (0.98-1.15)	1.10 (0.95-1.27)	0.72 (0.64-0.80)	1.31 (1.00-1.72)	0.99 (0.97-1.01)	0.38
Fish	1 (referent)	1.06 (0.98-1.15)	1.10 (0.95-1.27)	0.73 (0.65-0.81)	1.27 (0.96-1.66)	0.98 (0.95-1.01)	0.15
Egg	1 (referent)	1.07 (0.99-1.16)	1.09 (0.94-1.26)	0.72 (0.64-0.80)	1.31 (1.00-1.72)	1.21 (1.09-1.33)	<0.001
Dairy	1 (referent)	1.03 (0.97-1.09)	1.03 (0.98-1.09)	1.08 (1.02-1.14)	1.12 (1.05-1.19)	1.06 (1.03-1.10)	<0.001

\* Cox proportional hazards model with age as the time scale was stratified by sex and calendar time, and adjusted for plant protein intake (continuous), total caloric intake, percent of energy from saturated fat, polyunsaturated fat, monounsaturated fat and *trans* fat (all continuous), multivitamin use (yes or no), smoking status (never, past smokers, current smokers 1-14, and 15+ cigarettes/day), pack-years of smoking (in women: ≤15, 16-25, 26-45, >45; in men: <10, 11-24, 25-44, ≥45), body mass index (<23.0, 23.0-24.9, 25.0-26.9, 27.0-29.9, 30.0-34.9, ≥35 kg/m<sup>2</sup>), physical activity (quintiles), alcohol consumption (in women: 0, 0.1-5.0, 5.1-15.0, and >15.0 g/d; in men: 0, 0.1-10.0, 10.1-20.0, and >20.0 g/d), history of hypertension diagnosis (yes or no), glycemic index (in quintiles), and intake of whole grains, total fiber, fruits, and vegetables (all in quintiles). Mutual adjustment was conducted for protein intake from various animal sources.

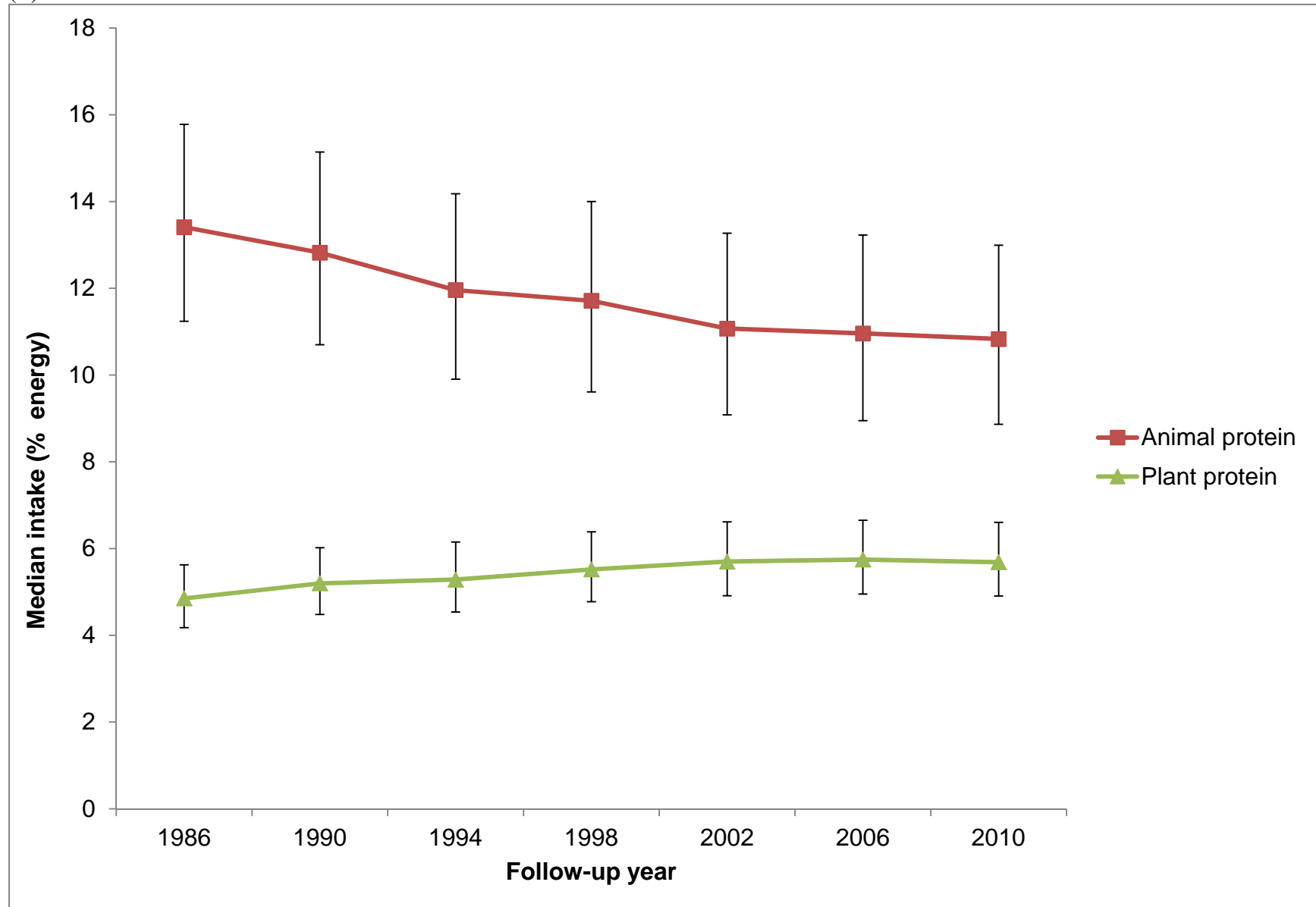
**eFigure 1. Median Intake and Interquartile Range of Animal and Plant Protein in Women (A) and Men (B) During Follow-up**

**(A) Women**





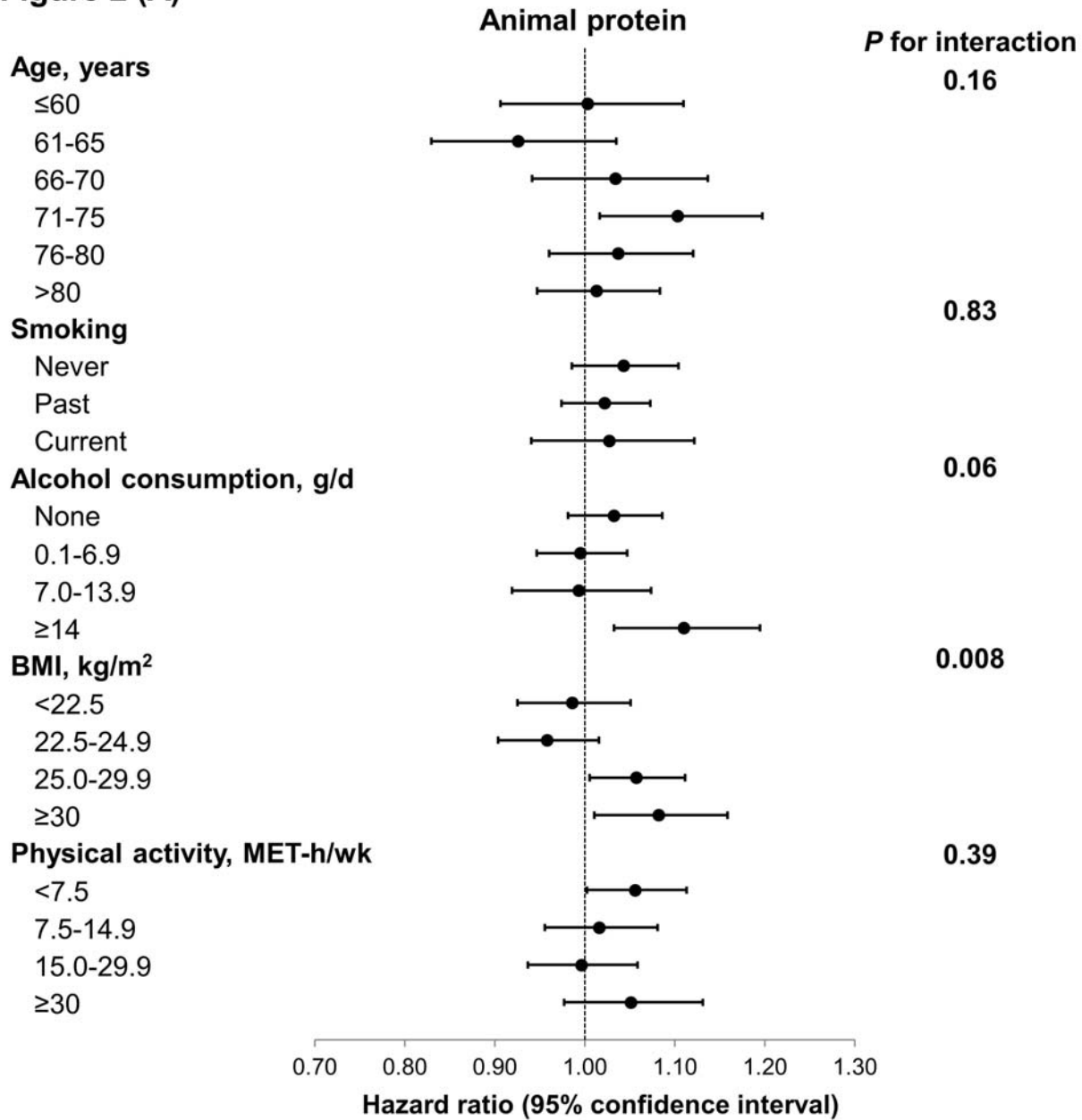
**(B) Men**



**eFigure 2. Association of Animal and Plant Protein Intake With All-Cause Mortality According to Age and Lifestyle Factors**

Hazard ratio represents the change in mortality per substitution for carbohydrate of 10% energy from animal protein (A) and 3% from plant protein (B). Multivariable model was adjusted for the same set of covariates as in Table 2. Likelihood ratio test was used to calculate the *P* for interaction.

**eFigure 2 (A)**



**eFigure 2 (B)**

