Supplementary Online Content

Huang J, Liao LM, Weinstein SJ, Sinha R, Graubard BI, Albanes D. Association between plant and animal protein intake and overall and cause-specific mortality. *JAMA Intern Med*. Published online July 13, 2020. doi: 10.1001/jamainternmed.2020.2790

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

eTable 1. Baseline Characteristics of the Study Participants According to Fifths of Daily Dietary Animal Protein Intake[a]

Characteristic [b]	Fifths of animal protein intake									
	Men					Women				
	1 (N=47,407)	2 (N=47,407)	3 (N=47,408)	4 (N=47,407)	5 (N=47,407)	1 (N=35,813)	2 (N=35,814)	3 (N=35,814)	4 (N=35,814)	5 (N=35,813)
Animal protein intake (g/1000 kcal)	13.0 (3.2)	19.0 (1.2)	22.9 (1.1)	27.1 (1.4)	35.3 (5.4)	12.5 (3.3)	18.7 (1.2)	22.8 (1.2)	27.2 (1.5)	35.8 (5.8)
Age, years	62.1 (5.4)	62.0 (5.3)	61.9 (5.4)	61.6 (5.4)	61.2 (5.4)	61.7 (5.4)	61.8 (5.4)	61.7 (5.4)	61.6 (5.4)	61.4 (5.4)
Body mass index, kg/m^2	26.3 (4.0)	26.8 (4.0)	27.2 (4.1)	27.5 (4.3)	28.2 (4.7)	25.7 (5.5)	26.4 (5.8)	26.7 (5.9)	27.1 (5.9)	27.6 (6.2)
Non-Hispanic white, %	88.3	92.2	93.4	93.8	93.5	84.8	89.0	90.6	91.5	91.5
Vigorous physical activity (≥5/week), %	24.4	21.4	20.2	19.4	19.1	18.6	16.3	15.4	15.4	16.1
Education (college or postgraduate), %	43.8	45.5	46.3	46.5	46.5	29.2	29.4	30.4	31.8	32.1
Married, %	82.1	85.6	86.4	86.2	84.4	40.3	44.0	46.2	47.4	46.1
Family history of cancer, %	45.9	47.1	47.8	47.9	47.1	50.2	51.5	51.9	51.5	50.7
Diabetes mellitus, %	4.7	5.5	7.5	9.3	13.8	3.8	4.5	5.5	6.8	9.4
Current smoker, %	11.1	10.8	10.9	11.4	11.6	14.9	15.2	14.8	14.4	14.1
Alcoholic drinks (>3/day), %	21.3	12.9	9.6	7.4	4.5	5.1	3.4	2.4	1.7	1.0
Energy intake, kcal	2123 (982)	2021 (826)	2010 (804)	2015 (801)	2006 (818)	1587 (707)	1572 (652)	1575 (638)	1576 (635)	1535 (636)
Fiber intake, g/1000 kcal	23.1 (12.3)	20.9 (10.0)	20.3 (9.4)	19.7 (9.1)	18.3 (8.9)	19.7 (11.2)	18.0 (9.1)	17.7 (8.5)	17.3 (8.3)	16.2 (8.0)
Foods (servings)										
Fruit	3.7 (3.3)	3.1 (2.4)	2.9 (2.2)	2.7 (2.0)	2.4 (1.8)	3.7 (3.2)	3.1 (2.4)	2.9 (2.1)	2.7 (1.9)	2.4 (1.8)
Vegetables	4.1 (2.9)	4.0 (2.4)	4.0 (2.3)	4.0 (2.3)	3.9 (2.3)	4.1 (3.1)	3.8 (2.4)	3.8 (2.3)	3.8 (2.3)	3.7 (2.3)
Vitamin supplement use, %	52.1	52.1	51.9	52.3	52.1	58.7	60.1	61.0	61.5	62.6
Prior or current postmenopausal hormone therapy (%)	n/a	n/a	n/a	n/a	n/a	51.6	53.4	54.4	55.1	54.4
Self-reported health (poor or fair), %	6.8	6.3	6.9	7.3	8.4	9.6	9.4	9.4	9.3	10.5

[a] All exposures are associated with animal protein intake, with P<0.0001 for trend across all groups, expect for the association between use of any vitamin supplement and animal protein intake in men (P value=0.81).

[b] Values are mean (standard deviation) or category percents. All dietary data are per day.

eTable 2. Risk of Overall and Cause-Specific Mortality Associated With Daily Dietary Plant Protein Intake (per 1-SD) Among 237,036 Men and 179,068 Women (Further Adjusted for Intake of Sugar-Sweetened Beverages and Carbohydrates)

Cause of death	Men		Women	
	HR (95% CI) [a]	P value	HR (95% CI) [a]	P value
Overall	0.95 (0.93, 0.96)	<0.0001	0.94 (0.92, 0.96)	<0.0001
Cancer	0.97 (0.95, 0.99)	0.02	0.96 (0.93, 0.99)	0.02
CVD	0.96 (0.93, 0.98)	0.001	0.93 (0.90, 0.97)	0.0002
Heart disease	0.97 (0.94, 1.00)	0.03	0.95 (0.91, 1.00)	0.03
Stroke	0.88 (0.82, 0.95)	0.0006	0.88 (0.81, 0.96)	0.003
Respiratory disease	0.95 (0.90, 1.01)	0.12	0.92 (0.86, 0.99)	0.02
Infection	0.98 (0.90, 1.06)	0.54	0.89 (0.81, 0.98)	0.02
Injury and accident	0.90 (0.83, 0.97)	0.007	0.95 (0.85, 1.07)	0.42
Other causes combined	0.91 (0.88, 0.94)	<0.0001	0.94 (0.90, 0.98)	0.002

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; SD, standard deviation

[a] Multivariable models were adjusted for age at entry (continuous), body mass index (<18.5, 18.5 to <25, 25 to <30, 30 to <35, ≥35 kg/m^2), alcohol consumption (none to ≤1, >1 to 3, >3 drinks per day), smoking status (never, former with ≤20 cigarettes a day, former with >20 cigarettes a day, current with ≤20 cigarettes a day, current with >20 cigarettes a day, or missing), physical activity (never/rarely, 1-3 times/month, 1-2 times/week, 3-4 times/week, ≥5 times/week, or missing), race or ethnic group (non-Hispanic white, non-Hispanic black, other race/ethnic), level of education (less than high school, high school graduate, post-high school training or some college, college graduate or higher, or missing), marital status (yes vs. no), diabetes mellitus (yes vs. no), health status (poor to fair, good, or very good to excellent or unknown), vitamin supplement use (yes vs. no), and daily dietary total energy, animal protein, saturated fat, polyunsaturated fat, monounsaturated fat, trans-fat, fiber, vegetables and fruit, and sugar-sweetened beverages and carbohydrate (all continuous). For women, the risk estimates were additionally adjusted for postmenopausal hormone replacement therapy (yes vs. no). For the endpoint of cancer mortality, the model was further adjusted for history of cancer in a first-degree relative (yes vs. no). P value achieved Bonferroni corrected threshold: 0.05/18=0.0028.

eTable 3. Risk of Overall and Cause-Specific Mortality Associated With Daily Dietary Plant Protein Intake (per 1-SD) Among 237,036 Men and 179,068 Women (Further Adjusted for Median Household Income)

Cause of death	Men		Women	
	HR (95% CI) [a]	P value	HR (95% CI) [a]	P value
Overall	0.95 (0.94, 0.97)	<0.0001	0.95 (0.93, 0.97)	<0.0001
Cancer	0.98 (0.96, 1.00)	0.10	0.97 (0.94, 1.00)	0.04
CVD	0.96 (0.93, 0.98)	0.001	0.94 (0.90, 0.97)	0.0007
Heart disease	0.97 (0.94, 1.00)	0.03	0.96 (0.92, 1.00)	0.06
Stroke	0.88 (0.82, 0.95)	0.0005	0.89 (0.82, 0.96)	0.003
Respiratory disease	0.98 (0.92, 1.04)	0.45	0.95 (0.89, 1.01)	0.12
Infection	0.98 (0.91, 1.06)	0.68	0.89 (0.81, 0.98)	0.02
Injury and accident	0.90 (0.84, 0.98)	0.01	0.95 (0.84, 1.07)	0.36
Other causes combined	0.91 (0.88, 0.95)	<0.0001	0.93 (0.90, 0.97)	0.001

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; SD, standard deviation

[a] Multivariable models were adjusted for age at entry (continuous), body mass index (<18.5, 18.5 to <25, 25 to <30, 30 to <35, ≥35 kg/m^2), alcohol consumption (none to ≤1, >1 to 3, >3 drinks per day), smoking status (never, former with ≤20 cigarettes a day, former with >20 cigarettes a day, current with ≤20 cigarettes a day, current with >20 cigarettes a day, or missing), physical activity (never/rarely, 1-3 times/month, 1-2 times/week, 3-4 times/week, ≥5 times/week, or missing), race or ethnic group (non-Hispanic white, non-Hispanic black, other race/ethnic), level of education (less than high school, high school graduate, post-high school training or some college, college graduate or higher, or missing), marital status (yes vs. no), diabetes mellitus (yes vs. no), health status (poor to fair, good, or very good to excellent or unknown), vitamin supplement use (yes vs. no), median household income (quintile), and daily dietary total energy, animal protein, saturated fat, polyunsaturated fat, monounsaturated fat, trans-fat, fiber, vegetables and fruit (all continuous). For women, the risk estimates were additionally adjusted for postmenopausal hormone replacement therapy (yes vs. no). For the endpoint of cancer mortality, the model was further adjusted for history of cancer in a first-degree relative (yes vs. no). P value achieved Bonferroni corrected threshold: 0.05/18=0.0028.

eTable 4. Risk of Overall and Cause-Specific Mortality Associated With Daily Dietary Animal Protein Intake Among 237,036 Men and 179,068 Women

	Men		Women	
	1-SD Increment		1-SD Increment	
Cause of death	**HR (95% CI) [a]**	**P value**	**HR (95% CI) [a]**	**P value**
Overall	0.99 (0.98, 1.00)	0.18	0.98 (0.97, 1.00)	0.02
Cancer	0.98 (0.96, 1.00)	0.01	0.99 (0.97, 1.02)	0.61
CVD	1.02 (1.00, 1.04)	0.10	0.99 (0.97, 1.02)	0.46
Heart disease	1.02 (1.00, 1.05)	0.03	1.01 (0.98, 1.04)	0.61
Stroke	0.97 (0.92, 1.02)	0.26	0.95 (0.90, 1.01)	0.07
Respiratory disease	1.01 (0.97, 1.05)	0.69	0.96 (0.91, 1.00)	0.06
Infection	0.96 (0.91, 1.02)	0.15	0.98 (0.92, 1.05)	0.51
Injury and accident	0.99 (0.94, 1.04)	0.65	1.00 (0.92, 1.09)	0.93
Other causes combined	0.99 (0.97, 1.02)	0.52	0.97 (0.94, 1.00)	0.06

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; SD, standard deviation

[a] Multivariable models were adjusted for age at entry (continuous), body mass index (<18.5, 18.5 to <25, 25 to <30, 30 to <35, ≥35 kg/m^2), alcohol consumption (none to ≤1, >1 to 3, >3 drinks per day), smoking status (never, former with ≤20 cigarettes a day, former with >20 cigarettes a day, current with ≤20 cigarettes a day, current with >20 cigarettes a day, or missing), physical activity (never/rarely, 1-3 times/month, 1-2 times/week, 3-4 times/week, ≥5 times/week, or missing), race or ethnic group (non-Hispanic white, non-Hispanic black, other race/ethnic), level of education (less than high school, high school graduate, post-high school training or some college, college graduate or higher, or missing), marital status (yes vs. no), diabetes mellitus (yes vs. no), health status (poor to fair, good, or very good to excellent or unknown), vitamin supplement use (yes vs. no), and daily dietary total energy, plant protein, saturated fat, polyunsaturated fat, monounsaturated fat, trans-fat, fiber, vegetables and fruit (all continuous). For women, the risk estimates were additionally adjusted for postmenopausal hormone replacement therapy (yes vs. no). For the endpoint of cancer mortality, the model was further adjusted for history of cancer in a first-degree relative (yes vs. no). P value achieved Bonferroni corrected threshold: 0.05/18=0.0028.

eTable 5. Risk of Overall and Cause-Specific Mortality Associated With Substitution of 3% Energy From Different Sources of Plant Protein for Egg Protein Among 237,036 Men And 179,068 Women[a]

	Men		Women	
	3% Energy Substitution		3% Energy Substitution	
	HR (95% CI) [b]	P value	HR (95% CI) [b]	P value
Protein from bread, cereal and pasta				
Overall	0.70 (0.67, 0.74)	<0.0001*	0.75 (0.70, 0.81)	<0.0001*
Cancer	0.82 (0.75, 0.91)	<0.0001*	0.80 (0.71, 0.91)	0.0007*
CVD	0.67 (0.61, 0.74)	<0.0001*	0.69 (0.60, 0.80)	<0.0001*
Heart disease	0.68 (0.61, 0.76)	<0.0001*	0.69 (0.59, 0.81)	<0.0001*
Stroke	0.63 (0.48, 0.82)	0.0008*	0.73 (0.53, 1.02)	0.06
Respiratory disease	0.55 (0.45, 0.68)	<0.0001*	0.61 (0.48, 0.78)	<0.0001*
Infection	0.83 (0.62, 1.11)	0.20	0.80 (0.54, 1.17)	0.24
Injury and accident	0.65 (0.48, 0.87)	0.004	0.56 (0.35, 0.89)	0.01
Other causes combined	0.64 (0.56, 0.72)	<0.0001*	0.86 (0.73, 1.01)	0.07
Protein from nuts				
Overall mortality	0.90 (0.83, 0.97)	0.009	0.96 (0.86, 1.08)	0.50
Cancer mortality	0.88 (0.77, 1.01)	0.06	0.96 (0.79, 1.16)	0.65
CVD mortality	0.92 (0.80, 1.06)	0.25	0.83 (0.66, 1.04)	0.11
Heart disease	0.96 (0.83, 1.12)	0.62	0.88 (0.68, 1.14)	0.33
Stroke	0.78 (0.54, 1.14)	0.20	0.68 (0.41, 1.15)	0.15
Respiratory disease	0.79 (0.59, 1.07)	0.12	0.93 (0.64, 1.36)	0.71
Infection	1.28 (0.86, 1.90)	0.23	1.13 (0.63, 2.03)	0.69
Injury and accident	0.91 (0.61, 1.36)	0.64	1.40 (0.73, 2.70)	0.31
Other causes combined	0.91 (0.77, 1.08)	0.29	1.12 (0.87, 1.45)	0.38
Protein from beans and legumes				
Overall mortality	0.89 (0.82, 0.97)	0.006	0.88 (0.79, 0.98)	0.020
Cancer mortality	0.96 (0.84, 1.10)	0.57	0.76 (0.63, 0.91)	0.0026*
CVD mortality	0.93 (0.80, 1.07)	0.31	1.01 (0.83, 1.23)	0.94
Heart disease	0.96 (0.82, 1.13)	0.61	1.00 (0.79, 1.25)	0.97
Stroke	0.75 (0.50, 1.12)	0.16	1.15 (0.74, 1.78)	0.55
Respiratory disease	0.70 (0.51, 0.98)	0.04	0.92 (0.64, 1.31)	0.64
Infection	0.90 (0.58, 1.40)	0.63	0.97 (0.55, 1.68)	0.90
Injury and accident	0.74 (0.48, 1.14)	0.17	0.76 (0.41, 1.42)	0.39
Other causes combined	0.84 (0.70, 1.01)	0.06	0.98 (0.77, 1.24)	0.85
Protein from other sources				
Overall	0.92 (0.85, 0.99)	0.02	0.85 (0.78, 0.93)	0.0004*

	Men		Women	
	3% Energy Substitution		3% Energy Substitution	
	HR (95% CI) [b]	P value	HR (95% CI) [b]	P value
Cancer	0.98 (0.87, 1.11)	0.76	0.91 (0.78, 1.06)	0.21
CVD	0.92 (0.81, 1.05)	0.24	0.75 (0.63, 0.89)	0.0009*
Heart disease	0.96 (0.83, 1.11)	0.56	0.76 (0.63, 0.93)	0.006
Stroke	0.81 (0.57, 1.15)	0.25	0.73 (0.49, 1.08)	0.12
Respiratory disease	0.69 (0.52, 0.91)	0.01	0.73 (0.55, 0.98)	0.04
Infection	1.29 (0.89, 1.87)	0.18	0.71 (0.44, 1.13)	0.15
Injury and accident	0.76 (0.52, 1.12)	0.16	0.66 (0.38, 1.15)	0.14
Other causes combined	0.87 (0.74, 1.02)	0.08	1.02 (0.84, 1.24)	0.85

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; SD, standard deviation

[a] Plant, animal and total protein were modeled as percentages of energy, using energy from the specific protein divided by total energy intake, and the leave-one-out model was used as the substitution approach: to evaluate the substitution of 3% energy from the specific plant protein for egg protein, energy from each specific plant protein, total protein, and other three components of animal protein were simultaneously included in the model. The hazard ratios represent the relative risk of overall mortality with 3% energy substitution to the specific plant protein from egg protein.

[b] Multivariable models were included various sources of plant protein and all animal protein components considered, and adjusted for age at entry (continuous), body mass index (<18.5, 18.5 to <25, 25 to <30, 30 to <35, ≥35 kg/m^2), alcohol consumption (none to ≤1, >1 to 3, >3 drinks per day), smoking status (never, former with ≤20 cigarettes a day, former with >20 cigarettes a day, current with ≤20 cigarettes a day, current with >20 cigarettes a day, or missing), physical activity (never/rarely, 1-3 times/month, 1-2 times/week, 3-4 times/week, ≥5 times/week, or missing), race or ethnic group (non-Hispanic white, non-Hispanic black, other race/ethnic), level of education (less than high school, high school graduate, post-high school training or some college, college graduate or higher, or missing), marital status (yes vs. no), diabetes mellitus (yes vs. no), health status (poor to fair, good, or very good to excellent or unknown), vitamin supplement use (yes vs. no), and daily dietary total energy, animal protein, saturated fat, polyunsaturated fat, monounsaturated fat, trans-fat, fiber, vegetables and fruit (all continuous). For women, the risk estimates were additionally adjusted for postmenopausal hormone replacement therapy (yes vs. no). For the endpoint of cancer mortality, the model was further adjusted for history of cancer in a first-degree relative (yes vs. no). * P value achieved Bonferroni corrected threshold: 0.05/18=0.0028.

eTable 6. Risk of Overall and Cause-Specific Mortality Associated With Substitution of 3% Energy From Different Sources of Plant Protein for Red Meat Protein Among 237,036 Men and 179,068 Women[a]

	Men		Women	
	3% Energy Substitution		3% Energy Substitution	
Cause of death	**HR (95% CI)** [b]	**P value**	**HR (95% CI)** [b]	**P value**
Protein from bread, cereal and pasta				
Overall	0.79 (0.76, 0.82)	<0.0001*	0.80 (0.76, 0.83)	<0.0001*
Cancer	0.88 (0.83, 0.94)	<0.0001*	0.87 (0.80, 0.93)	0.0001*
CVD	0.76 (0.72, 0.81)	<0.0001*	0.76 (0.70, 0.83)	<0.0001*
Heart disease	0.77 (0.72, 0.82)	<0.0001*	0.78 (0.71, 0.86)	<0.0001*
Stroke	0.71 (0.60, 0.84)	<0.0001*	0.72 (0.59, 0.87)	0.0007*
Respiratory disease	0.74 (0.65, 0.86)	<0.0001*	0.72 (0.62, 0.84)	<0.0001*
Infection	0.83 (0.69, 0.99)	0.04	0.73 (0.58, 0.92)	0.008
Injury and accident	0.72 (0.60, 0.86)	0.0004*	0.72 (0.55, 0.96)	0.03
Other causes combined	0.70 (0.65, 0.76)	<0.0001*	0.78 (0.71, 0.86)	<0.0001*
Protein from nuts				
Overall	1.01 (0.95, 1.07)	0.82	1.01 (0.92, 1.12)	0.78
Cancer	0.94 (0.85, 1.05)	0.29	1.03 (0.88, 1.21)	0.73
CVD	1.05 (0.93, 1.17)	0.43	0.92 (0.76, 1.11)	0.37
Heart disease	1.08 (0.95, 1.22)	0.24	1.00 (0.80, 1.24)	0.99
Stroke	0.89 (0.65, 1.20)	0.43	0.67 (0.43, 1.03)	0.07
Respiratory disease	1.07 (0.84, 1.36)	0.59	1.09 (0.79, 1.51)	0.60
Infection	1.28 (0.93, 1.76)	0.13	1.04 (0.63, 1.70)	0.88
Injury and accident	1.01 (0.73, 1.38)	0.98	1.80 (1.07, 3.05)	0.03
Other causes combined	1.00 (0.87, 1.15)	0.97	1.02 (0.82, 1.26)	0.86
Protein from beans and legumes				
Overall	1.01 (0.95, 1.08)	0.67	0.94 (0.86, 1.02)	0.15
Cancer	1.04 (0.94, 1.16)	0.45	0.82 (0.71, 0.95)	0.007
CVD	1.08 (0.96, 1.20)	0.21	1.13 (0.97, 1.32)	0.13
Heart disease	1.10 (0.97, 1.24)	0.15	1.15 (0.96, 1.37)	0.13
Stroke	0.87 (0.64, 1.18)	0.38	1.11 (0.80, 1.55)	0.53
Respiratory disease	0.99 (0.76, 1.31)	0.96	1.10 (0.82, 1.48)	0.52
Infection	0.90 (0.64, 1.28)	0.55	0.88 (0.57, 1.37)	0.58
Injury and accident	0.84 (0.60, 1.16)	0.28	1.02 (0.63, 1.64)	0.94
Other causes combined	0.94 (0.82, 1.08)	0.39	0.89 (0.74, 1.06)	0.19
Protein from other sources				
Overall	1.03 (0.97, 1.09)	0.31	0.90 (0.84, 0.96)	0.0024*

Cause of death	Men		Women	
	3% Energy Substitution		3% Energy Substitution	
	HR (95% CI) [b]	P value	HR (95% CI) [b]	P value
Cancer	1.06 (0.96, 1.16)	0.25	0.98 (0.88, 1.10)	0.74
CVD	1.06 (0.96, 1.17)	0.28	0.83 (0.73, 0.94)	0.004
Heart disease	1.08 (0.97, 1.21)	0.17	0.87 (0.75, 1.01)	0.06
Stroke	0.93 (0.71, 1.22)	0.59	0.71 (0.53, 0.95)	0.02
Respiratory disease	0.94 (0.75,1.18)	0.60	0.87 (0.69, 1.09)	0.23
Infection	1.29 (0.97, 1.71)	0.08	0.65 (0.46, 0.93)	0.02
Injury and accident	0.85 (0.63, 1.14)	0.28	0.87 (0.58, 1.31)	0.51
Other causes combined	0.96 (0.85, 1.08)	0.48	0.93 (0.81, 1.07)	0.32

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; SD, standard deviation

[a] Plant, animal and total protein were modeled as percentages of energy, using energy from the specific protein divided by total energy intake, and the leave-one-out model was used as the substitution approach: to evaluate the substitution of 3% energy from the specific plant protein for red meat protein, energy from each specific plant protein, total protein, and other three components of animal protein were simultaneously included in the model. The hazard ratios represent the relative risk of overall mortality with 3% energy substitution to the specific plant protein from red meat protein.

[b] Multivariable models were included various sources of plant protein and all animal protein components considered, and adjusted for age at entry (continuous), body mass index (<18.5, 18.5 to <25, 25 to <30, 30 to <35, ≥35 kg/m^2), alcohol consumption (none to ≤1, >1 to 3, >3 drinks per day), smoking status (never, former with ≤20 cigarettes a day, former with >20 cigarettes a day, current with ≤20 cigarettes a day, current with >20 cigarettes a day, or missing), physical activity (never/rarely, 1-3 times/month, 1-2 times/week, 3-4 times/week, ≥5 times/week, or missing), race or ethnic group (non-Hispanic white, non-Hispanic black, other race/ethnic), level of education (less than high school, high school graduate, post-high school training or some college, college graduate or higher, or missing), marital status (yes vs. no), diabetes mellitus (yes vs. no), health status (poor to fair, good, or very good to excellent or unknown), vitamin supplement use (yes vs. no), and daily dietary total energy, animal protein, saturated fat, polyunsaturated fat, monounsaturated fat, trans-fat, fiber, vegetables and fruit (all continuous). For women, the risk estimates were additionally adjusted for postmenopausal hormone replacement therapy (yes vs. no). For the endpoint of cancer mortality, the model was further adjusted for history of cancer in a first-degree relative (yes vs. no). * P value achieved Bonferroni corrected threshold: 0.05/18=0.0028.

eAppendix 1. Methods: Mortality Assessment and Statistical Analysis

Mortality assessment

Codes from the International Classification of Diseases, Ninth Revision (ICD-9), and International Classification of Diseases, 10th Revision (ICD-10) were applied to define the underlying causes of death: cancer (ICD-9, 140-239; ICD-10, C00-C97 and D00-D48), CVD (ICD-9, 390–459; ICD-10, I00-I99), heart disease (ICD-9, 390-398, 401-404, 410-429 and 440-448; ICD-10, I00-I13, I20-I51, and I70-I78), stroke (ICD-9, 430-438; ICD-10, I60-I69), respiratory disease (ICD-9, 480-487 and 490-496; ICD-10, J10-J18 and J40-J47), infection (ICD-9, 001-139; ICD-10, A00-B99), injury and accident (ICD-9, 800-978; ICD-10, V01-X59, Y85-Y86, U03, X60-X84, Y87.0, U01-U02, X85-Y09, Y35, Y87.1, and Y89.0), and all other causes combined.

Statistical analysis

The final multivariable-adjusted model included: age at entry (continuous); body mass index (BMI) (<18.5, 18.5 to <25, 25 to <30, 30 to <35, ≥35 kg/m^2); smoking status (never smoker, former smokers who smoked ≤20 cigarettes/day, former smokers who smoked >20 cigarettes/day, current smokers who smoked ≤20 cigarettes/day, current smokers who smoked >20 cigarettes/day); physical activity (never/rarely, 1-3 times/month, 1-2 times/week, 3-4 times/week, ≥5 times/week); race or ethnic group (non-Hispanic white, non-Hispanic black, other race/ethnic); education (less than high school, high school graduate, post-high school training or some college, college graduate or higher); marital status (yes, no); diabetes (yes, no); health status (poor to fair, good, very good to excellent); daily dietary total energy, animal protein, saturated fat, polyunsaturated fat, monounsaturated fat, trans-fat, and total fiber; consumption of total vegetables, fruit, and alcohol (none -≤1, >1-3, >3 drinks per day); and vitamin supplement use (yes, no). Models for cancer mortality are additionally adjusted for history of cancer in a first-degree relative (yes, no), and for women, mortality risk estimates were adjusted for postmenopausal hormone replacement therapy use (yes, no).

In secondary analyses, we generated propensity scores for each quintile of plant protein intake (quintile 1 to quintile 5) using the above-mentioned covariates included in the multivariable adjusted model, and the Cox regression models were adjusted for the generated propensity scores to address the possibility of residual confounding. Using similar final multivariable-adjusted model, we also estimated the associations between animal protein (per 1-SD increment) and risk of overall and cause-specific mortality.

We constructed models to examine mortality associations of substituting 3% of energy from specific plant protein (bread, cereal and pasta; nuts; beans and legumes; other sources) with an equivalent decrement in egg protein or red meat protein. Plant, animal and total protein were modeled as percentages of energy, using energy from the specific protein divided by total energy intake. To evaluate the substitution of 3% energy from the specific plant protein for egg or red meat protein, energy from each specific plant protein, total protein, and other three components of animal protein were simultaneously included in the model. The hazard ratios represent the relative risk of overall mortality with 3% energy from the specific plant protein substituted for egg or red meat protein energy.

eAppendix 2. Results: Animal Protein Intake and Dietary and Lifestyle Factors

Animal Protein Intake and Dietary and Lifestyle Factors

eTable 1 provides data on baseline cohort characteristics according to categories of animal protein intake, with median cohort intake for men and women being 42.4 and 32.8 grams/day (22.9 and 22.8 gram/1000 kcal per day). Participants with higher animal protein intake tended to be younger, non-Hispanic white, physically inactive, have higher education and BMI, lower intake of fiber, fruit and vegetables, and more likely to have diabetes or report poor or fair health