JAMA Internal Medicine | Original Investigation

Plant and Animal Fat Intake and Overall and Cardiovascular Disease Mortality

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IMPORTANCE The impact of dietary fat intake on long-term human health has attracted substantial research interest, and the health effects of diverse dietary fats depend on available food sources. Yet there is a paucity of data elucidating the links between dietary fats from specific food sources and health.

OBJECTIVE To study associations of dietary plant and animal fat intake with overall mortality and cardiovascular disease (CVD) mortality.

DESIGN, SETTING, AND PARTICIPANTS This large prospective cohort study took place in the US from 1995 to 2019. The analysis of men and women was conducted in the National Institutes of Health–AARP Diet and Health Study. Data were analyzed from February 2021 to May 2024.

EXPOSURES Specific food sources of dietary fats and other dietary information were collected at baseline, using a validated food frequency questionnaire.

MAIN OUTCOMES AND MEASURES Hazard ratios (HRs) and 24-year adjusted absolute risk differences (ARDs) were estimated using multivariable-adjusted Cox proportional hazards regression.

RESULTS The analysis included 407 531 men and women (231 881 [56.9%] male; the mean [SD] age of the cohort was 61.2 [5.4] years). During 8 107 711 person-years of follow-up, 185 111 deaths were ascertained, including 58 526 CVD deaths. After multivariable adjustment (including adjustment for the relevant food sources), a greater intake of plant fat (HRs, 0.91 and 0.86; adjusted ARDs, −1.10% and −0.73%; *P* for trend < .001), particularly fat from grains (HRs, 0.92 and 0.86; adjusted ARDs, −0.98% and −0.71%; *P* for trend < .001) and vegetable oils (HRs, 0.88 and 0.85; adjusted ARDs, −1.40% and −0.71%; *P* for trend < .001), was associated with a lower risk for overall and CVD mortality, respectively, comparing the highest to the lowest quintile. In contrast, a higher intake of total animal fat (HRs, 1.16 and 1.14; adjusted ARDs, 0.78% and 0.32%; *P* for trend < .001), dairy fat (HRs, 1.09 and 1.07; adjusted ARDs, 0.86% and 0.24%; *P* for trend < .001), or egg fat (HRs, 1.13 and 1.16; adjusted ARDs, 1.40% and 0.82%; *P* for trend < .001) was associated with an increased risk for mortality for overall and CVD mortality, respectively, comparing the highest to the lowest quintile. Replacement of 5% energy from animal fat with 5% energy from plant fat, particularly fat from grains or vegetable oils, was associated with a lower risk for mortality: 4% to 24% reduction in overall mortality, and 5% to 30% reduction in CVD mortality.

CONCLUSIONS AND RELEVANCE The findings from this prospective cohort study demonstrated consistent but small inverse associations between a higher intake of plant fat, particularly fat from grains and vegetable oils, and a lower risk for both overall and CVD mortality. A diet with a high intake of animal-based fat, including fat from dairy foods and eggs, was also shown to be associated with an elevated risk for both overall and CVD mortality.

JAMA Intern Med. doi:10.1001/jamainternmed.2024.3799
Published online August 12, 2024.

Supplemental content

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Dietary fats are critical macronutrients that play important roles in various biological functions including metabolic fuel, maintaining cell membrane structure, transport and absorption of fat-soluble vitamins, regulation of signal transduction, and modulation of ion channel activity.[1] Plant-derived fats are recognized for their greater composition of monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs), whereas animal-based fats are characterized by a higher proportion of saturated fatty acids (SFAs).[2]

Although earlier cross-national and experimental research suggested beneficial effects of lower total dietary fat intake, recent cohort studies, clinical trials, and meta-analyses have yielded inconsistent results.[3-9] For example, a meta-analysis showed no association between SFAs and overall mortality or cardiovascular disease (CVD); however, there was considerable heterogeneity among the studies included.[9] Similarly, although increased MUFA intake may improve lipid profiles, inflammatory status, and traditional cardiovascular risk factors, its impact on CVD risk and mortality appears to depend on the food sources (ie, animal-derived or plant-derived).[10]

To inform choices of dietary fat food sources, we evaluated the associations of plant and animal fat intake from specific foods with overall mortality and CVD mortality among more than 400 000 men and women of the National Institutes of Health (NIH)–AARP Diet and Health Study Cohort during a follow-up of up to 24 years.

Key Points

Question What are the associations between dietary fats from plant and animal food sources and mortality in the US population?

Findings In this cohort study of 407 531 participants with 24 years of follow-up and nearly 190 000 deaths, greater plant fat intake was associated with lower overall and cardiovascular disease mortality, particularly fat from grains and vegetable oils, independent of other important mortality risk factors.

Meaning These findings provide detailed information about how increased intake of dietary fat from plant sources may help improve human health and related mortality outcomes.

Methods

Study Design

The NIH-AARP Diet and Health Study enrolled 617 119 participants ages 50 to 71 years from 6 states and 2 metropolitan areas from 1995 to 1996.[11] A total of 566 398 participants completed and returned the self-administered baseline questionnaire, providing written informed consent to participate in the study. This large prospective cohort study was approved by the National Cancer Institute Special Studies Institutional Review Board. Based on the exclusion criteria (eMethods in Supplement 1), 407 531 participants remained in the final analytic cohort, including 231 881 men and 175 650 women. Data were collected from 1995 to 2019, and analysis was conducted from February 2021 to May 2024.

The baseline questionnaire collected information on demographic characteristics, anthropometric measurements, and lifestyle factors. Dietary data were obtained through the National Cancer Institute Diet History Questionnaire (DHQ) with 124 dietary items and portion sizes,[11] based on the US Department of Agriculture's 1994-1996 Continuing Survey of Food Intakes by Individuals and previously validated.[12] Total dietary fat intake included both plant sources (ie, grains, nuts, legumes, and vegetable oils) and animal sources (ie, red and white meat, dairy foods, and eggs) (eMethods in Supplement 1).

Specific causes of death were ascertained through follow-up linkage with the Social Security Administration Death Master File (eMethods in Supplement 1). A previous study showed that this mortality ascertainment had an accuracy of 95%.[13]

Statistical Analysis

Follow-up started from study entry date until date of death, or the end of follow-up (December 31, 2019), whichever came first. We conducted Cox proportional hazards regression, with person-time as the underlying time metric to compute hazard ratios (HRs) and 95% CIs for the association between dietary fat intake and risk for overall mortality. For CVD mortality, including mortality due to heart disease or stroke, we used cause-specific hazard models to take into account other causes of death as competing risks.[14,15] We also used the Fine-Gray model to assess the robustness of our findings. The proportional hazards assumption was not violated by testing cross-product interaction terms between follow-up time and the exposure, using likelihood ratio tests. In the age-adjusted and sex-adjusted model (model 1), fats from different sources were mutually adjusted for intakes of other fat sources. In model 2, we additionally adjusted for body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), race or ethnicity, smoking status, physical activity, education, marital status, diabetes, health status, vitamin supplement use, intake of total protein, carbohydrates, fiber, trans fatty acids and cholesterol, and alcohol consumption measured at baseline. Missingness of the covariate was less than 5% and was treated as a separate group. Intake of total energy was highly correlated with fat intake from various food sources (eFigure in Supplement 1); therefore adjusting for total energy intake in the models may lead to multicollinearity. Thus, we used the all-components model to provide unbiased estimates[16] and further adjusted for total energy intake in the sensitivity analyses. Finally, to separate the role of dietary fats from their related food sources, in model 3 we additionally adjusted for intake of relevant food sources for individual dietary fats. Adjusted absolute risk differences (ARDs) were calculated for each HR from the Cox model, based on the mean value of each covariate and the primary exposure variables with up to 24 years of follow-up. The 95% CI for each adjusted ARD was imputed based on 300 bootstrap samples.

Subgroup analyses were conducted to explore whether the associations differed by sex, age, smoking, diabetes, BMI, alcohol consumption, Healthy Eating Index 2015 (HEI-2015) score, vitamin supplement use, self-reported health status,

Table 1. Baseline Characteristics of Participants Based on Categories of Daily Dietary Plant Fat Intake[a,b]

Characteristic	Category of plant fat intake, No. (%)				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Plant fat intake, mean (SD), g	11.1 (2.9)	18.4 (1.8)	24.8 (2.0)	33.3 (3.1)	54.6 (16.2)
Age, mean (SD), y	61.3 (5.4)	61.2 (5.4)	61.2 (5.4)	61.3 (5.4)	61.0 (5.4)
Body mass index, mean (SD)[c]	26.5 (5.0)	26.7 (4.8)	26.9 (4.9)	27.2 (5.0)	27.6 (5.4)
Race and ethnicity					
Non-Hispanic Black	3327 (4.1)	2947 (3.6)	2886 (3.5)	3082 (3.8)	3918 (4.8)
Non-Hispanic White	73 145 (89.7)	74 469 (91.4)	74 888 (91.8)	74 742 (91.8)	73 788 (90.5)
Other[d]	3505 (4.3)	3014 (3.7)	2836 (3.5)	2744 (3.4)	2850 (3.5)
Unknown	1533 (1.9)	1038 (1.3)	971 (1.2)	883 (1.1)	965 (1.2)
Vigorous physical activity (≥5 times/wk)	14 844 (18.2)	14 881 (18.3)	14 992 (18.4)	15 418 (18.9)	17 012 (20.9)
Education (college or postgraduate)	31 825 (39.0)	33 036 (40.6)	33 346 (40.9)	32 178 (39.5)	29 503 (36.2)
Married	47 299 (58.0)	53 324 (65.5)	56 521 (69.3)	58 703 (72.1)	59 875 (73.4)
Family history of cancer	39 169 (48.1)	39 887 (49.0)	40 192 (49.3)	40 143 (49.3)	39 675 (48.7)
Diabetes	5258 (6.5)	5313 (6.5)	5708 (7.0)	6093 (7.5)	7252 (8.9)
Current smoking	8998 (11.0)	8767 (10.8)	9407 (11.5)	10 104 (12.4)	12 053 (14.8)
Alcoholic drinks (>3 drinks/d)	4527 (5.6)	5257 (6.5)	6118 (7.5)	6883 (8.5)	7760 (9.5)
Energy intake, mean (SD), kcal	1143 (458)	1491 (482)	1747 (529)	2055 (586)	2733 (845)
Fiber intake, mean (SD), g/1000 kcal	13.0 (6.5)	16.5 (7.3)	18.7 (8.0)	21.2 (8.8)	27.0 (11.6)
Foods, mean (SD), No. of servings					
Fruits	2.4 (1.9)	2.8 (2.2)	2.9 (2.3)	3.1 (2.5)	3.5 (2.9)
Vegetables	2.5 (1.7)	3.3 (1.9)	3.8 (2.1)	4.4 (2.3)	5.7 (3.1)
Vitamin supplement use	46 483 (57.0)	46 648 (57.3)	46 037 (56.4)	44 770 (55.0)	43 620 (53.5)
Prior or current postmenopausal hormone therapy for women	25 120 (53.9)	21 583 (55.2)	19 063 (55.0)	16 136 (53.6)	12 640 (50.2)
Poor or fair self-reported health	6172 (7.6)	6060 (7.4)	6210 (7.6)	6932 (8.5)	8211 (10.1)

[a] Dietary data are shown as daily intake.

[b] All characteristics are correlated with daily dietary plant fat intake, with all $P < .001$. P values are calculated based on analysis of variance tests for continuous variables, and χ^2 tests for categorical variables.

[c] Body mass index is calculated as weight in kilograms divided by height in meters squared.

[d] Other race and ethnicity: Hispanic, Asian, Pacific Islander, American Indian, and Alaska Native.

postmenopausal hormone therapy use, and follow-up time.[17] To minimize residual confounding from intake of other nutrients, stratified analyses were conducted by high and low (median split) intake of protein (total, plant, or animal), carbohydrates, fiber, total fruits, and total vegetables.

Sensitivity analyses were conducted. (1) To minimize reverse causality, we excluded the first 2 or 5 years of follow-up. (2) To alleviate residual confounding by intake of total energy or protein, we further adjusted for daily intake of total energy or protein from the specific foods. (3) To reduce the influence of preexisting diseases on exposure, we excluded participants with a self-reported history of diabetes at cohort entry. (4) To minimize bias from missing data, we excluded participants with missing data on any covariate. (5) To assess the soundness of the results among individuals with less extreme intakes, we compared individuals in quintile 4 of plant fat (or animal fat) intake to those in quintile 2.

The leave-1-out model was applied to evaluate the association of substituting 5% of energy from plant fat with an equal decrement in animal fat from various sources with the risk for both overall and CVD mortality. The regression coefficient for plant fat derived from this model can be interpreted as the log HR of mortality in relation to 5% increment in energy from plant fat and an equal energy decrement in animal fat, holding total energy from fat constant.

A more detailed description of this study's methods, including the study cohort, exclusion criteria, dietary data, mortality end points, and statistical analysis, is available in the eMethods and eTable 1 in Supplement 1. Based on previous studies and our a priori estimate, a 2-sided P value of .005 was used to indicate statistical significance.[18] Findings from the subgroup and sensitivity analyses were considered exploratory. All analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc), and R, version 4.2.0 (R Project for Statistical Computing).

Results

The analysis included 407 531 men and women (231 881 [56.9%] male; the mean [SD] age of the cohort was 61.2 [5.4] years). Median daily dietary fat intake from plant and animal sources was 24.7 g and 29.3 g, respectively. Participants with a greater intake of plant fat were more likely to have diabetes, higher BMI, and greater intake of total energy, fiber, alcohol, and fruit and vegetables (**Table 1**). These participants were also more likely to report their health as poor or fair, were more physically active, and were less likely to use vitamin supplements. See eTable 2 in Supplement 1 for characteristics by animal fat intake.

Table 2. Multivariable-Adjusted Hazard Ratios (HRs) of Overall Mortality and Cardiovascular Disease (CVD) Mortality With Dietary Plant Fat and Animal Fat Intake

	HR (95% CI) (N = 407 531)						
Measure	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Adjusted ARD (95% CI), %[a]	*P* for trend[b]
Plant fat, mean (SD)	11.13 (2.88)	18.36 (1.79)	24.83 (2.01)	33.30 (3.07)	54.63 (16.17)	NA	NA
Overall mortality							
No. cases per person-years	36 087 per 1 629 107	35 645 per 1 636 634	36 459 per 1 630 823	37 529 per 1 618 301	39 391 per 1 592 845	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.95 (0.94-0.97)	0.93 (0.91-0.95)	0.91 (0.90-0.93)	0.91 (0.89-0.93)	−1.10 (−1.60 to −0.64)	<.001
CVD mortality[d]							
No. cases per person-years	11 618 per 1 629 107	11 302 per 1 636 634	11 453 per 1 630 823	11 767 per 1 618 301	12 386 per 1 592 845	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.93 (0.90-0.96)	0.90 (0.87-0.93)	0.87 (0.84-0.90)	0.86 (0.82-0.89)	−0.73 (−1.10 to −0.40)	<.001
Animal fat, mean (SD)	12.19 (3.51)	21.14 (2.26)	29.38 (2.59)	40.37 (3.98)	68.07 (20.43)	NA	NA
Overall mortality							
No. cases per person-years	34 238 per 1 656 639	35 202 per 1 645 608	36 636 per 1 630 516	38 009 per 1 608 995	41 026 per 1 565 954	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.03 (1.01-1.05)	1.08 (1.05-1.10)	1.10 (1.07-1.13)	1.16 (1.12-1.19)	0.78 (0.12-1.80)	<.001
CVD mortality[d]							
No. cases per person-years	10 918 per 1 656 639	11 266 per 1 645 608	11 706 per 1 630 516	11 706 per 1 608 995	12 930 per 1 565 954	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.04 (1.01-1.08)	1.08 (1.04-1.13)	1.06 (1.02-1.12)	1.14 (1.08-1.20)	0.32 (0.05-1.10)	<.001

Abbreviations: ARD, absolute risk difference; NA, not applicable.

[a] Adjusted ARDs were calculated for each HR (the highest vs the lowest quintile of intake of dietary fat) from the Cox regression analysis based on the mean value of each covariate and the primary exposure variables with up to 24 years of follow-up. The 95% CIs were computed based on 300 bootstrap samples.

[b] Statistical significance was set at *P* < .005 to account for multiple testing.

[c] Fully adjusted model: adjusted for age at baseline, sex, body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5 to <25, 25 to <30, 30 to <35, or ≥35; calculated as weight in kilograms divided by height in meters squared), race or ethnicity (non-Hispanic Black, non-Hispanic White, or other race or ethnicity [ie, Hispanic, Asian, Pacific Islander, American Indian, and Alaska Native]), smoking status (never, former, or current), physical activity (never/rarely, 1-3 times/mo, 1-2 times/wk, 3-4 times/wk, or ≥5 times/wk), education (less than high school, high school graduate, post–high school training or some college, or college graduate or higher), married/unmarried, diabetes (yes/no), health status (poor to fair, good, or very good to excellent), vitamin supplement use (yes/no), intake of total protein (continuous variable), carbohydrates (continuous variable), fiber (quintiles), trans fatty acids (quintiles) and cholesterol (quintiles), alcohol consumption (none to ≤1, >1 to 3, or >3 drinks per day), and relevant food sources (for example, for plant fat, model was further adjusted for daily consumption of grains, nuts, beans and legumes, fruits, and vegetables. For animal fat, model was further adjusted for daily consumption of all meat, dairy, egg, and total fish). Fats from different sources were mutually adjusted for one another.

[d] HRs and their 95% CIs for CVD mortality were calculated using cause-specific hazard model.

Mortality Risk and Plant Fat Intake

During up to 24 years of observation and 8 107 711 person-years, 185 111 deaths were recorded, including 58 526 from CVD (45 634 for heart disease and 10 877 for stroke). In models 1 and 2, higher plant fat intake was associated with a reduced risk for overall and CVD mortality (eTable 3 in Supplement 1). After additional adjustment for relevant food sources (model 3), the inverse associations of plant fat intake remained statistically significant, with the HRs for overall mortality being 0.95 (95% CI, 0.94-0.97), 0.93 (95% CI, 0.91-0.95), 0.91 (95% CI, 0.90-0.93), and 0.91 (95% CI, 0.89-0.93) for quintiles 2 through 5, compared with quintile 1 (*P* for trend < .001; **Table 2**; eTable 3 in Supplement 1). Corresponding adjusted ARDs of overall mortality comparing the highest vs the lowest quintile was −1.10% (95% CI, −1.60% to −0.64%; Table 2). The HRs of CVD mortality were 0.93 (95% CI, 0.90-0.96), 0.90 (95% CI, 0.87-0.93), 0.87 (95% CI, 0.84-0.90), and 0.86 (95% CI, 0.82-0.89) for quintiles 2 through 5, compared with quintile 1 (*P* for trend < .001; Table 2; eTable 3 in Supplement 1). Corresponding adjusted ARDs of CVD mortality comparing the highest vs the lowest quintile of intake was −0.73% (95% CI, −1.10% to −0.40%; Table 2; eTable 3 in Supplement 1). Findings were generally similar and remained statistically significant for analyses using Fine-Gray models (eTable 4 in Supplement 1). In model 3, a higher intake of plant fat from grains or vegetable oils was associated with a reduced risk for overall mortality (quintile 5 vs 1: HR, 0.92 and adjusted ARD, −0.98% for fat from grains; HR, 0.88 and ARD, −1.40% for vegetable oils) and CVD mortality (HR, 0.86 and adjusted ARD, −0.71% for fat from grains; and HR, 0.85 and adjusted ARD, −0.71% for vegetable oils) (all *P* for trend < .001; **Table 3**; eTables 5 and 6 in Supplement 1). Using Fine-Gray models for CVD mortality did not significantly alter these estimates (eTable 4 in Supplement 1).

Associations similar to those of overall CVD mortality were observed between total plant fat intake, including grain sources and vegetable oils, and heart disease mortality, representing 14%, 15%, and 14% risk reductions among participants with the highest vs lowest quintiles of intake, respectively (model 3; all *P* for trend < .001; eTable 7 in Supplement 1). A higher intake

Table 3. Multivariable-Adjusted Hazard Ratios (HRs) of Overall Mortality and Mortality Due to Cardiovascular Disease (CVD) With Categories of Dietary Fat Intake

Measure	HR (95% CI)[a] (N = 407 531)					Adjusted ARD (95% CI), %[a]	*P* for trend[b]
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5		
Plant fat							
Fat from grains							
Overall mortality							
No. cases per person-years	37 265 per 1 614 069	35 714 per 1 630 915	36 523 per 1 635 180	36 724 per 1 625 398	38 885 per 1 602 150	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.94 (0.92-0.95)	0.93 (0.92-0.95)	0.91 (0.89-0.93)	0.92 (0.89-0.94)	−0.98 (−1.40 to −0.54)	<.001
CVD mortality[d]							
No. cases per person-years	11 937 per 1 614 069	11 400 per 1 630 915	11 490 per 1 635 180	11 573 per 1 625 398	12 126 per 1 602 150	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.93 (0.90-0.95)	0.90 (0.87-0.93)	0.87 (0.84-0.90)	0.86 (0.82-0.90)	−0.71 (−1.10 to −0.36)	<.001
Fat from nuts							
Overall mortality							
No. cases per person-years	37 373 per 1 619 085	35 912 per 1 629 544	35 539 per 1 613 218	37 544 per 1 642 217	38 743 per 1 603 648	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.96 (0.95-0.98)	0.95 (0.94-0.97)	0.96 (0.95-0.98)	0.97 (0.96-0.99)	−0.32 (−0.55 to −0.09)	.69
CVD mortality[d]							
No. cases per person-years	12 059 per 1 619 085	11 299 per 1 629 544	11 365 per 1 613 218	11 619 per 1 642 217	12 184 per 1 603 648	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.94 (0.92-0.97)	0.95 (0.93-0.98)	0.93 (0.90-0.95)	0.94 (0.91-0.97)	−0.32 (−0.48 to −0.14)	.03
Fat from beans and legumes							
Overall mortality							
No. cases per person-years	38 113 per 1 609 599	36 104 per 1 592 487	37 551 per 1 654 543	36 594 per 1 615 831	36 749 per 1 635 252	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.98 (0.96-0.99)	0.98 (0.97-1.00)	0.98 (0.97-1.00)	0.99 (0.97-1.01)	−0.02 (−0.30 to 0.24)	.84
CVD mortality[d]							
No. cases per person-years	12 116 per 1 609 599	11 371 per 1 592 487	11 759 per 1 654 543	11 506 per 1 615 831	11 774 per 1 635 252	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.98 (0.95-1.00)	0.98 (0.95-1.01)	0.98 (0.96-1.01)	1.00 (0.96-1.03)	0.097 (−0.12 to 0.32)	.45
Vegetable oil							
Overall mortality							
No. cases per person-years	35 789 per 1 630 742	35 829 per 1638376	36 556 per 1 626 575	37 515 per 1 619 326	39 422 per 1 592 693	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.95 (0.93-0.96)	0.92 (0.91-0.94)	0.90 (0.89-0.92)	0.88 (0.87-0.90)	−1.40 (−1.80 to −0.97)	<.001
CVD mortality[d]							
No. cases per person-years	11 527 per 1 630 742	11 396 per 1638376	11 469 per 1 626 575	11 791 per 1 619 326	12 343 per 1 592 693	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.93 (0.91-0.96)	0.90 (0.87-0.92)	0.88 (0.85-0.91)	0.85 (0.82-0.89)	−0.71 (−1.00 to −0.40)	<.001
Animal fat							
Red meat fat							
Overall mortality							
No. cases per person-years	33 790 per 1 658 757	35 348 per 1 648 959	36 985 per 1 623 485	38 368 per 1 605 368	40 620 per 1 571 144	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.02 (1.01-1.04)	1.05 (1.03-1.07)	1.05 (1.03-1.08)	1.04 (1.01-1.07)	0.43 (−0.083 to 0.92)	.13
CVD mortality[d]							
No. cases per person-years	10 846 per 1 658 757	11 179 per 1 648 959	11 692 per 1 623 485	12 031 per 1 605 368	12 778 per 1 571 144	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.01 (0.98-1.04)	1.04 (1.00-1.07)	1.03 (0.99-1.07)	1.00 (0.95-1.05)	−0.03 (−0.38 to 0.31)	.61
White meat fat							
Overall mortality							
No. cases per person-years	39 688 per 1 589 609	37 608 per 1 613 075	36 753 per 1 626 279	35 861 per 1 639 330	35 201 per 1 639 419	NA	NA

(continued)

Table 3. Multivariable-Adjusted Hazard Ratios (HRs) of Overall Mortality and Mortality Due to Cardiovascular Disease (CVD) With Categories of Dietary Fat Intake (continued)

Measure	HR (95% CI)[a] (N = 407 531) Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Adjusted ARD (95% CI), %[a]	*P* for trend[b]
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.97 (0.95-0.98)	0.96 (0.94-0.97)	0.95 (0.93-0.97)	0.95 (0.92-0.97)	−0.75 (−1.10 to −0.38)	<.001
CVD mortality[d]							
No. cases per person-years	12 560 per 1 589 609	11 622 per 1 613 075	11 545 per 1 626 279	11 321 per 1 639 330	11 478 per 1 639 419	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.96 (0.93-0.98)	0.96 (0.94-0.99)	0.96 (0.93-0.99)	0.97 (0.93-1.01)	−0.04 (−0.32 to 0.24)	.47
Dairy fat							
Overall mortality							
No. cases per person-years	35 199 per 1 647 064	35 067 per 1 641 961	36 110 per 1 639 460	37 713 per 1 611 295	41 022 per 1 567 931	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.00 (0.99-1.02)	1.02 (1.00-1.04)	1.04 (1.02-1.06)	1.09 (1.07-1.11)	0.86 (0.52-1.20)	<.001
CVD mortality[d]							
No. cases per person-years	11 290 per 1 647 064	11 247 per 1 641 961	11 482 per 1 639 460	11 745 per 1 611 295	12 762 per 1 567 931	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.01 (0.98-1.04)	1.02 (0.99-1.05)	1.02 (0.99-1.06)	1.07 (1.03-1.11)	0.24 (0.06-0.51)	<.001
Egg fat							
Overall mortality							
No. cases per person-years	33 527 per 1 651 109	35 095 per 1 658 747	35 843 per 1 630 418	38 663 per 1 610 351	41 983 per 1 557 087	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.02 (1.00-1.04)	1.03 (1.02-1.05)	1.08 (1.06-1.09)	1.13 (1.11-1.16)	1.40 (1.10-1.70)	<.001
CVD mortality[d]							
No. cases per person-years	10 649 per 1 651 109	11 088 per 1 658 747	11 162 per 1 630 418	12 306 per 1 610 351	13 321 per 1 557 087	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	1.02 (0.99-1.05)	1.03 (1.00-1.06)	1.09 (1.06-1.13)	1.16 (1.12-1.20)	0.82 (0.56-1.10)	<.001
Fish fat							
Overall mortality							
No. cases per person-years	37 964 per 1 612 994	36 114 per 1 595 438	36 673 per 1 644 796	37 354 per 1 638 756	37 006 per 1 615 727	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.97 (0.95-0.98)	0.96 (0.95-0.98)	0.98 (0.96-0.99)	0.96 (0.94-0.98)	−0.54 (−0.85 to −0.20)	.12
CVD mortality[d]							
No. cases per person-years	12 194 per 1 612 994	11 446 per 1 595 438	11 394 per 1 644 796	11 631 per 1 638 756	11 861 per 1 615 727	NA	NA
Fully adjusted (with relevant foods)[c]	1.00 [Reference]	0.95 (0.93-0.98)	0.93 (0.91-0.96)	0.94 (0.91-0.97)	0.94 (0.90-0.97)	−0.35 (−0.58 to −0.10)	.07

Abbreviations: ARD, absolute risk difference; NA, not applicable.

[a] Adjusted ARDs were calculated for each HR (the highest vs the lowest quintile of intake of dietary fat) from the Cox regression analysis based on the mean value of each covariate and the primary exposure variables with up to 24 years of follow-up. The 95% CIs were computed based on 300 bootstrap samples.

[b] Statistical significance was set at $P < .005$ to account for multiple testing.

[c] Fully adjusted model: adjusted for age at baseline, sex, body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5 to <25, 25 to <30, 30 to <35, or ≥35), race or ethnicity (non-Hispanic Black, non-Hispanic White, or other race or ethnicity [ie, Hispanic, Asian, Pacific Islander, American Indian, and Alaska Native]), smoking status (never, former, or current), physical activity (never/rarely, 1-3 times/mo, 1-2 times/wk, 3-4 times/wk, or ≥5 times/wk), education (less than high school, high school graduate, post–high school training or some college, or college graduate or higher), married/unmarried, diabetes (yes/no), health status (poor to fair, good, or very good to excellent), vitamin supplement use (yes/no), intake of total protein (continuous variable), carbohydrates (continuous variable), fiber (quintiles), trans fatty acids (quintiles) and cholesterol (quintiles), alcohol consumption (none to ≤1, >1 to 3, or >3 drinks per day), and relevant food sources (for example, for fat from grains, model was further adjusted for daily consumption of bread, cereals and pasta. For fat from nuts, model was further adjusted for daily consumption of nuts. For fat from beans and legumes, model was further adjusted for daily consumption of beans and legumes. For red meat fat, model was further adjusted for daily consumption of red meat. For white meat fat, model was further adjusted for daily consumption of white meat. For dairy fat, model was further adjusted for daily consumption of total dairy products. For egg fat, model was further adjusted for daily consumption of eggs. For fish fat, model was further adjusted for daily consumption of fish). Fats from different sources were mutually adjusted for one another. Fat from grains is calculated based on foods containing grains, including bread, cereals, and pasta.

[d] HRs and 95% CIs for CVD mortality were calculated using cause-specific hazard model.

of total plant fat or fat from grains or vegetable oils was also associated with a decreased risk for stroke mortality, although the inverse associations were attenuated after adjusting for relevant food sources (model 3, eTable 8 in Supplement 1). A higher intake of fat from beans and legumes was not associated with any of the mortality outcomes (Table 3; eTables 5-8 in Supplement 1) except for inverse associations between nut fat intake and risk for overall and CVD mortality that disappeared after adjustment for nut consumption (model 3; Table 3; eTables 5 and 6 in Supplement 1).

Mortality Risk and Animal Fat Intake

Higher intake of animal fat was associated with elevated risks for overall, CVD, and heart disease mortality (quintile 5 vs 1: fully adjusted HR, 1.16 [95% CI, 1.12-1.19], 1.14 [95% CI, 1.08-1.20], and 1.14 [95% CI, 1.07-1.21], respectively; all *P* for trend < .001; Table 2; eTables 3 and 7 in Supplement 1). Corresponding adjusted ARDs comparing the highest vs the lowest quintile of animal fat intake was 0.78% for overall mortality and 0.32% for CVD mortality (Table 2; eTable 3 in Supplement 1). Using the Fine-Gray model attenuated the association for CVD mortality (eTable 4 in Supplement 1).

In model 3, higher intakes of fat from dairy products and eggs were associated with increased risks of overall mortality (quintile 5 vs 1: HR, 1.09 and adjusted ARD, 0.86% for dairy fat; and HR, 1.13 and adjusted ARD, 1.40% for egg fat, respectively; *P* for trend < .001; Table 3; eTable 5 in Supplement 1), CVD mortality (quintile 5 vs 1: HR, 1.07 and adjusted ARD, 0.24% for dairy fat; HR, 1.16 and adjusted ARD, 0.82% for egg fat, respectively; *P* for trend < .001; Table 3; eTable 6 in Supplement 1), and heart disease mortality (quintile 5 vs 1: HRs, 1.09 and 1.14 for dairy and egg fat, respectively; *P* for trend < .001; eTable 7 in Supplement 1). Greater intake of fat from white meat was associated with a lower risk for overall mortality (quintile 5 vs 1: HR, 0.95 and adjusted ARD, −0.75%; *P* for trend < .001; Table 3; eTable 5 in Supplement 1), but not CVD (HR, 0.97 and adjusted ARD −0.04%; *P* for trend = .47; Table 3; eTable 6 in Supplement 1), heart disease (HR, 0.96; *P* for trend = .26; eTable 7 in Supplement 1), or stroke mortality (HR, 1.06; *P* for trend = .21; eTable 8 in Supplement 1).

In model 2, we found that a higher intake of red meat fat was associated with an increased risk for overall mortality, CVD mortality, and heart disease mortality (quintile 5 vs 1: HRs, 1.11 [95% CI, 1.09-1.14], 1.09 [95% CI, 1.05-1.14] and 1.11 [95% CI, 1.06-1.17], respectively; all *P* for trend < .001; eTables 5-7 in Supplement 1). However, the associations were attenuated after additionally adjusting for red meat consumption (model 3, quintile 5 vs 1: HRs, 1.04, 1.00, and 1.01, and *P* for trend = .13, .61, and .94, respectively; Table 3; eTables 5-7 in Supplement 1). We also found that, after additionally adjusting for fish consumption (model 3), a higher fat intake from fish was not significantly associated with risk for overall, CVD, heart disease, or stroke mortality (Table 3; eTables 5-8 in Supplement 1). A higher intake of egg fat was associated with an elevated risk for stroke mortality (quintile 5 vs 1: HR, 1.22; *P* for trend < .001), but no association was noted for intake of fat from red meat, white meat, or dairy (eTable 8 in Supplement 1).

Subgroup Analyses

The inverse association of plant fat intake with overall mortality was significant among younger participants (<60 years at baseline) and those who consumed 1 to 3 alcoholic drinks per day. In contrast, the positive animal fat–mortality association was greater for men, those aged 60 to 65 years, or with lower BMI (<25), or consuming 1 to 3 alcoholic drinks per day, and during the first 5 years of follow-up, for which all interactions were statistically significant (**Figure**). The association of animal fat intake with CVD mortality was stronger among younger participants and during the 5 to 10 years of follow-up (eFigure 2 in Supplement 1). None of the associations changed materially in the analyses stratified by low or high intake of protein, carbohydrates, fiber, or total fruits, although the associations between plant fat intake and overall mortality or CVD mortality were stronger among individuals with a high vegetable consumption (eTables 9-12 in Supplement 1).

Sensitivity Analyses

The results did not change substantially when excluding the first 2 or 5 years of follow-up, further adjusting for daily total energy intake or intake of protein from specific foods, excluding participants who reported a history of diabetes or had missing covariate data, or comparing quintile 4 to quintile 2 levels of intake (eTables 13-25 in Supplement 1).

Substitution Analyses

Replacing 5% energy from total animal fat, red meat fat, dairy fat, or egg fat with an equivalent amount of total plant fat, fat from grains, or vegetable oils was associated with a 4% to 24% lower risk for overall mortality and a 5% to 30% lower risk for CVD mortality (*P* < .001). In contrast, replacing 5% energy from fish fat (or white meat fat) with the same amount of total plant fat or fat from vegetable oil was not associated with a reduced risk for overall mortality (**Table 4**). A more detailed description of the subgroup, sensitivity, and substitution analyses is available in the eResults in Supplement 1.

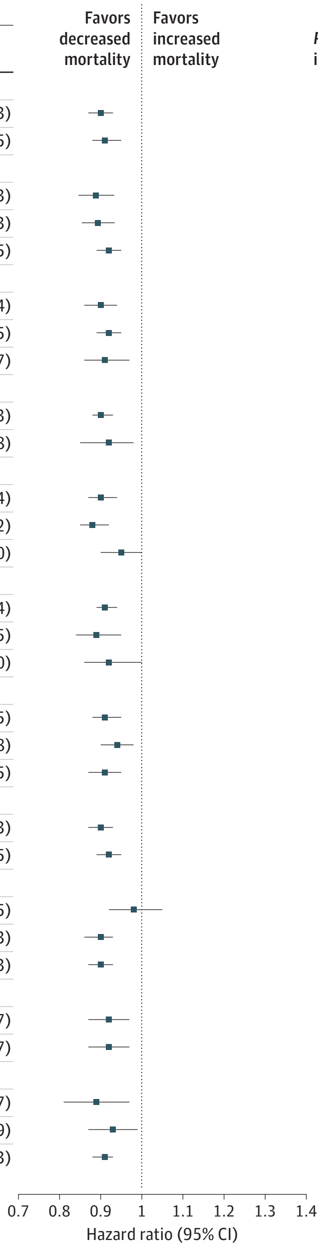
Discussion

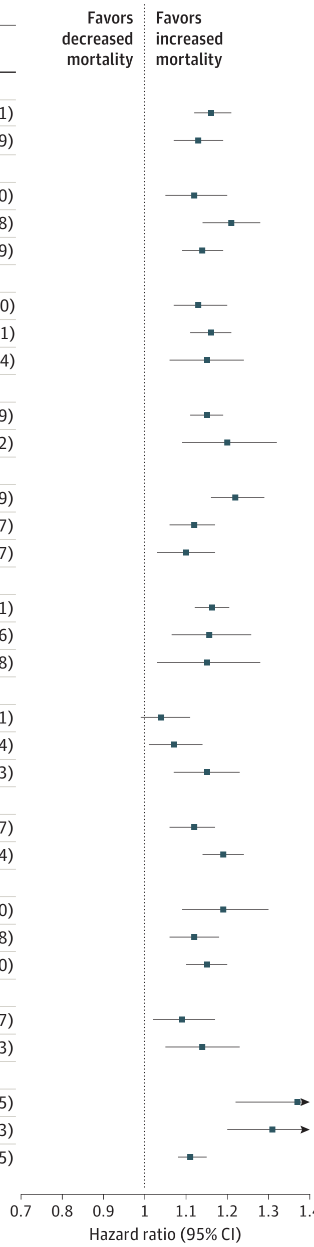
In this large prospective cohort study of men and women with 24 years of follow-up, a higher intake of plant fat, particularly fat from grains and vegetable oils, was associated with a lower risk for both overall and CVD mortality. We also found that a greater intake of fat from animal, dairy, and egg sources was associated with increased risks of overall mortality and CVD mortality. These associations were independent of important mortality risk factors and were generally noted among various subgroups of the cohort. Some of these associations were attenuated slightly after adjustment for the relevant food sources of the specific dietary fats, although most did not. Replacement of 5% energy from animal fat, red meat fat, dairy fat, or egg fat with an equivalent amount of plant fat, grain fat, or vegetable oil fat was associated with a lower risk for mortality. Effect sizes of the observed risk estimates were small.

Relatively few prospective studies have evaluated the associations of dietary fat sources with mortality. We observed consistent associations of a higher intake of plant fat, particularly fat from grains and vegetable oils, with reduced risks of overall mortality and CVD mortality. Consistent with these findings, in a meta-analysis of 877 897 participants, greater consumption of whole grains was associated with a lower risk for CVD and overall mortality.[19] Additionally, a pooled analysis of 44 prospective cohort studies demonstrated that greater dietary intake of linoleic acids, particularly those found in grains and cereals,[20-22] was associated with decreased risks of both overall and CVD mortality.[23] Evidence from a randomized clini-

Figure. Risk for Overall Mortality With Plant Fat and Animal Fat Intake According to Subgroups

Subgroup	Plant fat Hazard ratio (95% CI)	P value for interaction	Animal fat Hazard ratio (95% CI)	P value for interaction
Sex				
Men	0.90 (0.87-0.93)	.15	1.16 (1.12-1.21)	.003
Women	0.91 (0.88-0.95)		1.13 (1.07-1.19)	
Age at baseline, y				
<60	0.89 (0.85-0.93)	.004	1.12 (1.05-1.20)	<.001
60-65	0.89 (0.85-0.93)		1.21 (1.14-1.28)	
≥65	0.92 (0.89-0.95)		1.14 (1.09-1.19)	
Smoking status				
Never	0.90 (0.86-0.94)	.77	1.13 (1.07, 1.20)	.17
Former	0.92 (0.89-0.95)		1.16 (1.11, 1.21)	
Current	0.91 (0.86-0.97)		1.15 (1.06, 1.24)	
Diabetes				
No	0.90 (0.88-0.93)	.07	1.15 (1.11-1.19)	.63
Yes	0.92 (0.85-0.98)		1.20 (1.09-1.32)	
BMI				
<25	0.90 (0.87-0.94)	.01	1.22 (1.16-1.29)	<.001
25 to <30	0.88 (0.85-0.92)		1.12 (1.06-1.17)	
≥30	0.95 (0.90-1.00)		1.10 (1.03-1.17)	
Alcoholic drinks per d				
0-1	0.91 (0.89-0.94)	<.001	1.16 (1.12-1.21)	<.001
>1 to 3	0.89 (0.84-0.95)		1.16 (1.07-1.26)	
>3	0.92 (0.86-1.00)		1.15 (1.03-1.28)	
HEI-2015				
Low	0.91 (0.88-0.95)	.81	1.04 (0.99-1.11)	.01
Intermediate	0.94 (0.90-0.98)		1.07 (1.01-1.14)	
High	0.91 (0.87-0.95)		1.15 (1.07-1.23)	
Supplemental vitamin use				
No	0.90 (0.87-0.93)	.68	1.12 (1.06-1.17)	.06
Yes	0.92 (0.89-0.95)		1.19 (1.14-1.24)	
Health status				
Poor to fair	0.98 (0.92-1.05)	.01	1.19 (1.09-1.30)	.05
Good	0.90 (0.86-0.93)		1.12 (1.06-1.18)	
Very good to excellent	0.90 (0.87-0.93)		1.15 (1.10-1.20)	
Postmenopausal hormone therapy				
No	0.92 (0.87-0.97)	.81	1.09 (1.02-1.17)	.15
Yes	0.92 (0.87-0.97)		1.14 (1.05-1.23)	
Follow-up, y				
0 to <5	0.89 (0.81-0.97)	.29	1.37 (1.22-1.55)	<.001
5 to <10	0.93 (0.87-0.99)		1.31 (1.20-1.43)	
≥10	0.91 (0.88-0.93)		1.11 (1.08-1.15)	





Hazard ratios and 95% CIs for overall mortality were calculated by comparing the highest vs the lowest quintile of intake of plant fat and animal fat. The analyses were adjusted for age at baseline, sex, body mass index (BMI; <18.5, 18.5 to <25, 25 to <30, 30 to <35, or ≥35; calculated as weight in kilograms divided by height in meters squared), race or ethnicity (non-Hispanic Black, non-Hispanic White, or other race or ethnicity [ie, Hispanic, Asian, Pacific Islander, American Indian, and Alaska Native]), smoking status (never, former, or current), physical activity (never/rarely, 1-3 times/mo, 1-2 times/wk, 3-4 times/wk, or ≥5 times/wk), education (less than high school, high school graduate, post–high school training or some college, or college graduate or higher), married/unmarried, diabetes (yes/no), health status (poor to fair, good, or very good to excellent), vitamin supplement use (yes/no), intake of total protein (continuous variable), carbohydrates (continuous variable), fiber (quintiles), trans fatty acids (quintiles) and cholesterol (quintiles), and alcohol consumption (none to ≤1, >1 to 3, or >3 drinks per day). Fats from different sources were mutually adjusted for one another (eg, for plant fat, models were further adjusted for red meat fat, white meat fat, dairy fat, egg fat, and fish fat; for animal fat, models were further adjusted for fat from grains, fat from nuts, fat from beans and legumes, and vegetable oils). All analyses were additionally adjusted for relevant food sources. For example, for plant fat, model was further adjusted for daily consumption of bread, cereals and pasta, nuts, beans and legumes, fruits, and vegetables. For animal fat, model was further adjusted for daily consumption of all meat, dairy, egg, and total fish. HEI-2015 indicates Healthy Eating Index 2015.

cal trial has also shown that dietary linoleic acid may contribute to reduced circulating low-density lipoprotein cholesterol, triglycerides, and apolipoprotein B, enhanced insulin sensitivity, and decreased liver fat.[24] Regarding vegetable oils, a meta-analysis of 24 prospective cohort studies showed associations between greater consumption of olive, canola, and

Table 4. Risk for Overall Mortality and Cardiovascular Disease (CVD) Mortality With Substitution of 5% Plant Fat Energy Intake for Various Animal Fat Sources[a,b]

Plant fat sources	Overall mortality, HR (95% CI)	*P* value[c]	CVD mortality, HR (95% CI)[d]	*P* value[c]
Total plant fat				
Total animal fat	0.96 (0.95-0.96)	<.001	0.95 (0.94-0.97)	<.001
Red meat fat	0.91 (0.90-0.92)	<.001	0.90 (0.88-0.91)	<.001
White meat fat	0.98 (0.96-0.99)	.01	0.93 (0.90-0.96)	<.001
Dairy fat	0.92 (0.91-0.93)	<.001	0.92 (0.90-0.94)	<.001
Egg fat	0.84 (0.82-0.85)	<.001	0.79 (0.76-0.82)	<.001
Fish fat	0.98 (0.94-1.02)	.29	1.00 (0.94-1.07)	.97
Fat from grains				
Total animal fat	0.84 (0.83-0.86)	<.001	0.80 (0.78-0.83)	<.001
Red meat fat	0.83 (0.82-0.85)	<.001	0.79 (0.76-0.81)	<.001
White meat fat	0.90 (0.88-0.92)	<.001	0.83 (0.80-0.86)	<.001
Dairy fat	0.84 (0.82-0.85)	<.001	0.81 (0.79-0.84)	<.001
Egg fat	0.76 (0.74-0.78)	<.001	0.70 (0.67-0.73)	<.001
Fish fat	0.89 (0.86-0.93)	<.001	0.88 (0.82-0.95)	<.001
Fat from vegetable oil				
Total animal fat	0.95 (0.95-0.96)	<.001	0.95 (0.94-0.96)	<.001
Red meat fat	0.92 (0.91-0.93)	<.001	0.90 (0.88-0.92)	<.001
White meat fat	0.98 (0.96-1.00)	.01	0.93 (0.90-0.96)	<.001
Dairy fat	0.92 (0.91-0.93)	<.001	0.92 (0.90-0.93)	<.001
Egg fat	0.84 (0.82-0.86)	<.001	0.80 (0.77-0.83)	<.001
Fish fat	1.01 (0.97-1.05)	.62	1.05 (0.98-1.13)	.18

Abbreviation: HR, hazard ratio.

[a] The leave-1-out model was used as substitution approach: to evaluate the effect of substituting 5% dietary energy intake from different animal fat sources (ie, red meat fat, white meat fat, dairy fat, egg fat, or fish fat with the same amount of plant fat) on mortality.

[b] Models were adjusted for age at baseline, sex, body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5 to <25, 25 to <30, 30 to <35, or ≥35; calculated as weight in kilograms divided by height in meters squared), race or ethnicity (non-Hispanic Black, non-Hispanic White, or other race or ethnicity [ie, Hispanic, Asian, Pacific Islander, American Indian, and Alaska Native]), smoking status (never, former, or current), physical activity (never/rarely, 1-3 times/mo, 1-2 times/wk, 3-4 times/wk, or ≥5 times/wk), education (less than high school, high school graduate, post–high school training or some college, or college graduate or higher), married/unmarried, diabetes (yes/no), health status (poor to fair, good, or very good to excellent), vitamin supplement use (yes/no), intake of total protein (continuous variable), carbohydrates (continuous variable), fiber (quintiles), trans fatty acids (quintiles) and cholesterol (quintiles), and alcohol consumption (none to ≤1, >1 to 3, or >3 drinks per day). Fats from different sources were mutually adjusted for one another (eg, for plant fat, models were further adjusted for red meat fat, white meat fat, dairy fat, egg fat, and fish fat; for animal fat, models were further adjusted for fat from grains, fat from nuts, fat from beans and legumes, and vegetable oils; for fat from grains, fat from nuts, fat from beans and legumes, vegetable oils, red meat fat, white meat fat, dairy fat, egg fat, or fish fat, they were mutually adjusted for one another). Fat from grains is calculated based on foods containing grains, including bread, cereals, and pasta.

[c] Statistical significance was set at $P < .005$ to account for multiple testing.

[d] HRs and their 95% CIs for CVD mortality were calculated using cause-specific hazard model.

corn oils and reduced CVD risk.[25-28] The beneficial effects of vegetable oils, which are enriched with MUFA, PUFA, and phytosterols, may be partially attributed to a reduction in lipogenesis, an increase in β-oxidation, a decrease in intestinal cholesterol uptake, and enhancement of endothelial function.[29,30]

Prospective cohort studies have demonstrated that a greater consumption of nuts is associated with reduced risks of CVD and overall mortality.[31,32] In contrast, we found no such associations, particularly when adjusting for nut consumption, suggesting that the beneficial role of nuts in health may be attributable to other constituents present in nuts, such as minerals (eg, potassium and magnesium), vitamins (eg, vitamins E and B6), and phenolic compounds, rather than the fats.[33,34] A recent meta-analysis of 27 cohorts with 989 209 participants and 93 373 deaths revealed an inverse association between legume consumption and overall mortality risk, although not in cohorts in the US and Europe.[35] The meta-analysis showed no association between legumes and CVD mortality[35]; however, the results from this study remained consistent with our findings.

The positive associations between a greater intake of animal fats, particularly from dairy foods and eggs, and overall mortality and CVD mortality risk align with previous studies,[36-39] which demonstrate, for example, that consumption of whole milk rather than skim or low-fat milk is associated with an increased risk for CVD mortality.[38] Although a paucity of data regarding egg fat intake and mortality exists, several large cohort studies and a meta-analysis demonstrate that greater egg consumption is associated with elevated overall and CVD mortality, especially in the US.[37,40,41] By contrast, another meta-analysis showed weak but statistically significant inverse associations for unprocessed white meat consumption,[42] in line with the present findings, and we found that after adjusting for total red meat consumption, the positive mortality associations of red meat fat intake were no longer significant, suggesting that components of red meat other than fat may be the primary mediators of the association. For example, the presence of pro-oxidants, such as heme iron and nitrates/nitrites, in red meat products can increase oxidative stress and inflammation, potentially underlying the red meat-mortality associations.[43,44] Increased fish consumption, particularly fatty fish, has also been related to reduced mortality, including CVD mortality,[45-47] and a meta-analysis of 19 studies showed that consumption of fatty (but not lean) fish was inversely associated with risk for coronary heart disease, CVD mortality, and overall mortality.[46] Fish fat has a high content of long-chain n-3 PUFAs, which may explain the beneficial role of fish fat in different health outcomes, particularly CVD.[48,49] The inverse association we observed for fat intake from fish and overall and CVD mortality was, however, attenuated after adjustment for fish consumption. Variation in the amount and types of fish consumed across study populations may contribute to the discrepant data.

Our findings revealed that substituting animal fat intake with plant fat, such as fat from grains or vegetable oils, may result in lower overall and CVD mortality risk. In line with these findings, large prospective studies such as the Nurses' Health Study and Health Professionals Follow-Up Study have shown lower risk for CVD when SFAs and trans fats were isocalorically substituted with plant-based, but not animal-based, MUFA,[50] supporting the beneficial role of increased plant fat intake in cardiovascular health.

Strengths and Limitations

Strengths of our study encompass its large sample of men and women, a substantial number of mortality outcomes, and a long follow-up period which result in substantial statistical power for identifying associations of moderate magnitude and enabling subgroup analyses (eg, by age, sex, and BMI). Additionally, we used an all-components model for unbiased risk estimates,[16] and the leave-1-out model as the substitution approach.

Study limitations included the observational design. We could not rule out the possibility of residual confounding, although the dietary fat–mortality associations were stable to adjustment for a wide range of potential confounding factors, including diabetes and BMI. The food frequency questionnaire we used to estimate dietary fat intake could be subject to measurement error (eg, underreporting or overreporting of dietary intakes[51]), which given the prospective design of the study might have led to random errors and underestimated associations biased toward the null. However, a previous validation study of the NIH-AARP DHQ with 24-hour dietary recall data yielded favorable correlations for total fat intake of 0.72 and 0.62 in men and women, respectively, indicating a considerably high level of reliability.[12] Dietary fat intake was calculated based on baseline data and may not reflect possible dietary modifications during follow-up. As most cohort participants were of non-Hispanic White ethnicity, our findings may not generalize to other racial and ethnic populations.

Conclusions

In this large prospective cohort study, we demonstrated that a greater intake of plant fat, particularly fat from grains or vegetable oils, is associated with a decreased risk for overall mortality and CVD mortality. The study also provides evidence that diets high in animal-based fats, including dairy and eggs, are associated with elevated risks of overall and CVD mortality. Replacement of animal fat with an equivalent amount of plant fat, particularly fat from grains or vegetable oils, was associated with a lower risk of mortality in our study. Therefore, these findings offer detailed insights relevant to dietary guidelines that could be useful for improving human health and related outcomes.

ARTICLE INFORMATION

Accepted for Publication: June 15, 2024.

Published Online: August 12, 2024. doi:10.1001/jamainternmed.2024.3799

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Author Contributions: Drs Albanes and Huang had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr Zhao and Ms Gan contributed equally to this work as co–first authors. Drs Chen, Albanes, and Huang contributed equally to this work.
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Drafting of the manuscript: Zhao, Gan, Graubard, Huang.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: Zhao, Gan, Graubard, Huang.
Obtained funding: Huang.
Administrative, technical, or material support: Liao, Sinha, Huang.
Supervision: Fang, Chen, Albanes, Huang.

Conflict of Interest Disclosures: Dr Männistö reported grants from the Research Council of Finland paid to the institution outside the submitted work. No other disclosures were reported.

Funding/Support: This research was supported in part by the Intramural Research Program of the National Institutes of Health (NIH), National Cancer Institute. Cancer incidence data from the Atlanta metropolitan area were collected by the Georgia Center for Cancer Statistics, Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta. Cancer incidence data from California were collected by the California Cancer Registry, California Department of Public Health's Cancer Surveillance and Research Branch, Sacramento. Cancer incidence data from the Detroit metropolitan area were collected by the Michigan Cancer Surveillance Program, Community Health Administration, Lansing. The Florida cancer incidence data used in this report were collected by the Florida Cancer Data System (Miami) under contract with the Florida Department of Health, Tallahassee. Cancer incidence data from Louisiana were collected by the Louisiana Tumor Registry, Louisiana State University Health Sciences Center School of Public Health, New Orleans. Cancer incidence data from New Jersey were collected by the New Jersey State Cancer Registry, The Rutgers Cancer Institute of New Jersey, New Brunswick. Cancer incidence data from North Carolina were collected by the North Carolina Central Cancer Registry, Raleigh. Cancer incidence data from Pennsylvania were supplied by the Division of Health Statistics and Research, Pennsylvania Department of Health, Harrisburg. Cancer incidence data from Arizona were collected by the Arizona Cancer Registry, Division of Public Health Services, Arizona Department of Health Services, Phoenix. Cancer incidence data from Texas were collected by the Texas Cancer Registry, Cancer Epidemiology and Surveillance Branch, Texas Department of State Health Services, Austin. Cancer incidence data from Nevada were collected by the Nevada Central Cancer Registry, Division of Public and Behavioral Health, State of Nevada Department of Health and Human Services, Carson City. Dr Huang was supported by the National Natural Science Foundation of China (82100949), the Outstanding Young Investigator Award of Hunan Province (2022JJ10094), and Central South University Research Programme of Advanced Interdisciplinary Studies (2023QYJC008). Dr Albanes was supported by the Intramural Research Program of the NIH National Cancer Institute.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The views expressed herein are solely those of the authors and do not necessarily reflect those of the Florida Cancer Data System or Florida Department of Health. The Pennsylvania Department of Health disclaims responsibility for any analyses, interpretations, or conclusions.

Data Sharing Statement: See Supplement 2.

Additional Contributions: We thank the participants in the National Institutes of Health–AARP Diet and Health Study for their outstanding cooperation. We also thank Sigurd Hermansen and Kerry Grace Morrissey, MPH, from Westat for study outcomes ascertainment and management and Leslie Carroll at Information Management Services for data support and analysis.

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