Online supplementary material

Replacing the consumption of red meat with other major dietary protein sources and risk of type 2 diabetes mellitus: a prospective cohort study

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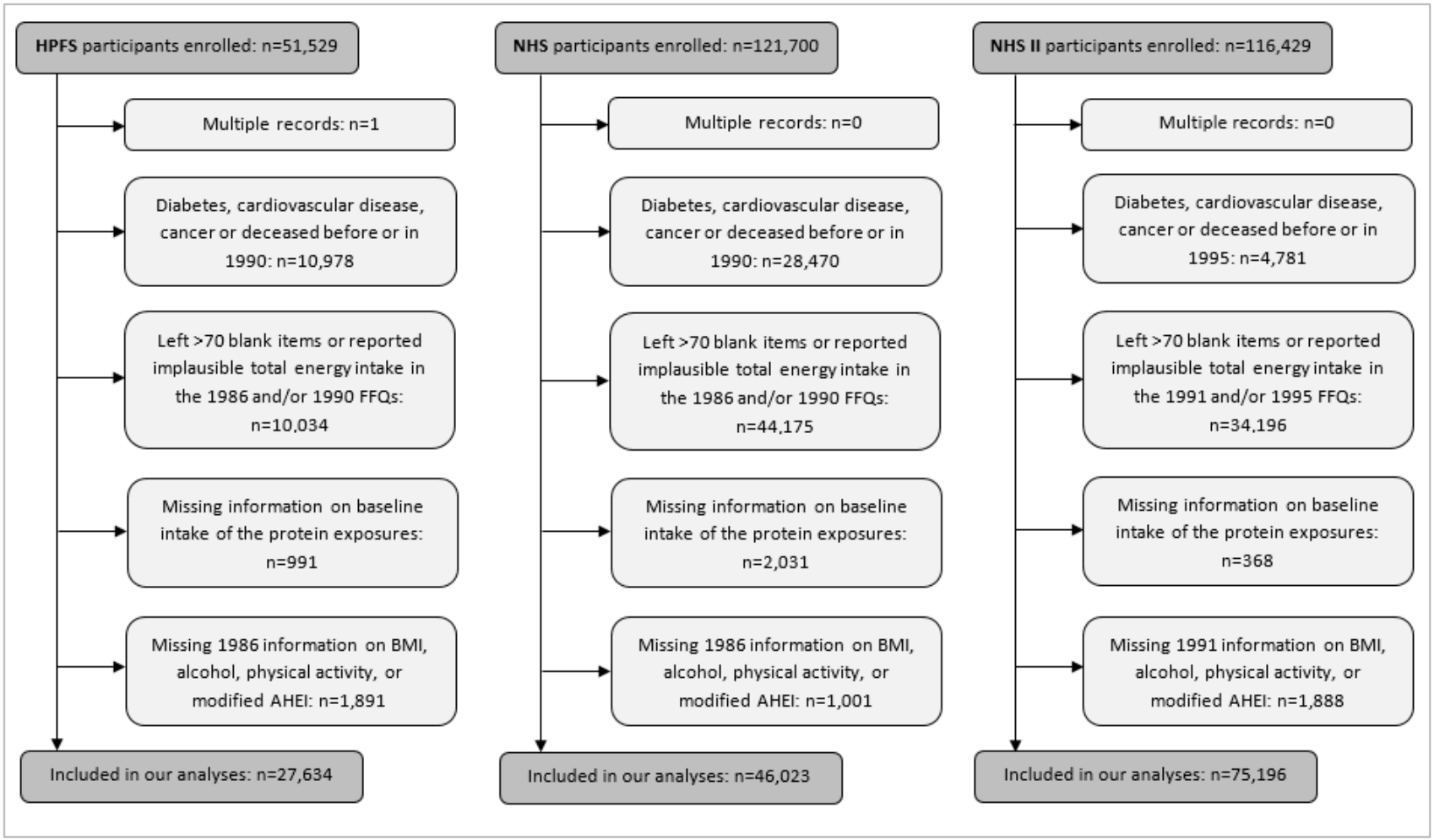


Supplemental Figure 1. Flowchart of participant exclusions (sequential) at baseline in HPFS (1986-1990), NHS (1986-1990) and NHS II (1991-1995) for the investigation of protein substitutions and T2DM. Abbreviations: AHEI, Alternative Healthy Eating Index; FFQ, food frequency questionnaire; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NHS II, Nurses' Health Study II.

Supplemental Table 1. HR (95% CI) for type 2 diabetes mellitus associated with one daily serving decreased intake of unprocessed or processed red meat and concomitant increased intake of another major dietary protein source in pooled analyses of all three cohorts (n=148,853)

Substituted protein (one serving/day)	Model 1[1]	Model 2[2]	Model 3[3]	Model 4[4]
Unprocessed red meat[5]				
Poultry	0.86 (0.78, 0.94)	0.88 (0.81, 0.97)	0.85 (0.76, 0.95)	0.88 (0.79, 0.98)
Seafood	0.86 (0.77, 0.97)	0.89 (0.79, 0.99)	0.90 (0.79, 1.03)	0.95 (0.83, 1.08)
Low-fat dairy	0.92 (0.86, 0.98)	0.92 (0.87, 0.99)	0.85 (0.79, 0.91)	0.87 (0.81, 0.94)
High-fat dairy	0.93 (0.86, 0.99)	0.93 (0.87, 0.99)	0.85 (0.79, 0.91)	0.87 (0.80, 0.93)
Eggs	0.97 (0.88, 1.08)	0.95 (0.86, 1.05)	0.92 (0.83, 1.03)	0.95 (0.85, 1.06)
Legumes	0.94 (0.86, 1.03)	0.95 (0.87, 1.04)	0.93 (0.83, 1.03)	0.96 (0.87, 1.07)
Nuts	0.87 (0.81, 0.94)	0.91 (0.84, 0.98)	0.86 (0.79, 0.93)	0.88 (0.81, 0.96)
Processed red meat[5]				
Poultry	0.82 (0.73, 0.91)	0.88 (0.80, 0.97)	0.78 (0.69, 0.87)	0.81 (0.72, 0.91)
Seafood	0.83 (0.73, 0.93)	0.89 (0.79, 1.00)	0.82 (0.72, 0.94)	0.87 (0.76, 0.99)
Low-fat dairy	0.88 (0.81, 0.96)	0.93 (0.86, 1.00)	0.78 (0.72, 0.85)	0.81 (0.74, 0.88)
High-fat dairy	0.88 (0.81, 0.96)	0.92 (0.85, 1.00)	0.77 (0.71, 0.85)	0.79 (0.73, 0.87)
Eggs	0.93 (0.82, 1.05)	0.95 (0.85, 1.07)	0.85 (0.75, 0.96)	0.88 (0.78, 1.00)
Legumes	0.90 (0.81, 1.00)	0.95 (0.86, 1.05)	0.85 (0.76, 0.95)	0.89 (0.80, 1.00)
Nuts	0.84 (0.77, 0.92)	0.91 (0.84, 1.00)	0.79 (0.71, 0.87)	0.81 (0.74, 0.90)

[1] Model 1: Cox proportional hazards models including all protein foods simultaneously, adjusted for age, calendar time, and calories (initial and change, both quintiles). For each substitution of one food item for another, we exponentiated the difference between the beta-coefficients of the two foods to estimate the HR, and we used the variances and covariance of the two food items to estimate the 95% CI.

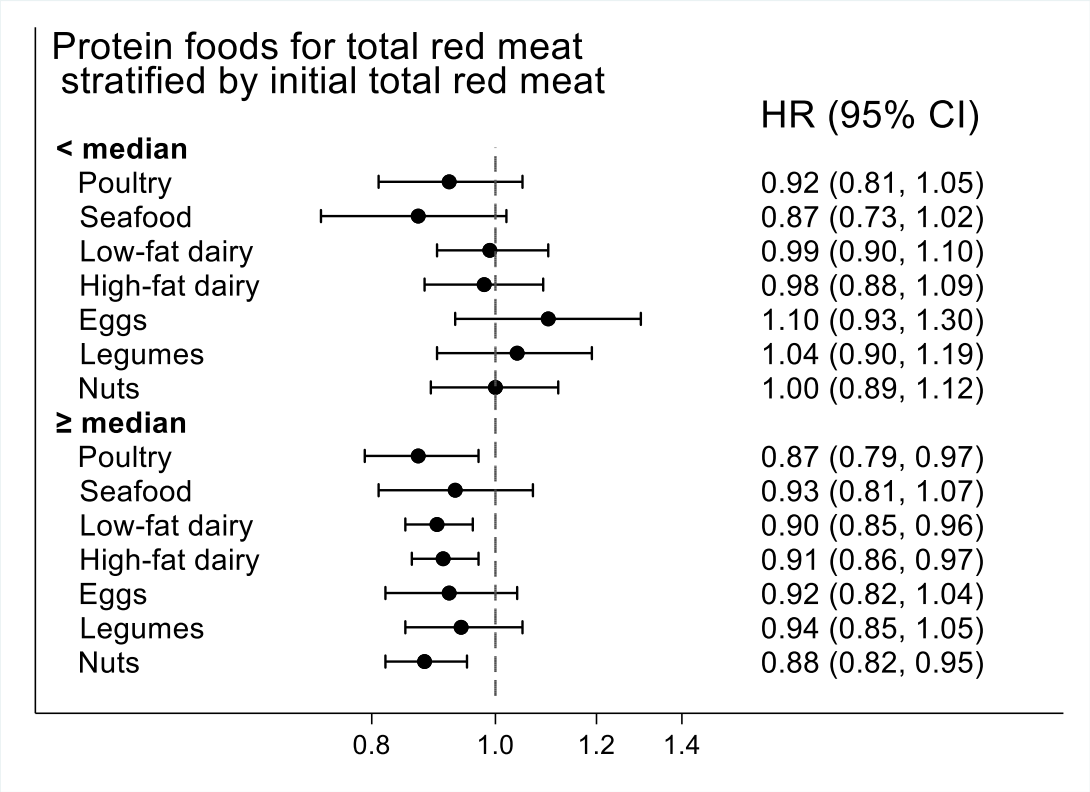
[2] Model 2: model 1 + marital status (with spouse, yes or no), race (white, African American, Asian/other), family history of diabetes (yes, no), history of hypertension (yes, no), history of hypercholesterolemia (yes, no), BMI (<20.0, 20.0-<23.0, 23.0-<25.0, 25.0-<30.0, ≥30.0 kg/m^2) alcohol intake, both as initial intake (0, 0.1-4.9, 5-14.9, 15-29.9, ≥30 grams/day) and change (quintiles), modified AHEI (initial and change, both quintiles), smoking status change (never to never, current to past, past to current, never to current, past to past, current to current), physical activity (metabolic equivalents initially and change, both quintiles) and for women initial menopausal status and use of postmenopausal hormones (premenopausal, postmenopausal + never hormone use, postmenopausal + past hormone use, postmenopausal + current hormone use)

[3] Model 3: model 2 + initial intake of red meat, poultry, seafood, low-fat dairy, high-fat dairy, eggs, legumes, and nuts (servings/day)

[4] Model 4: model 3 + simultaneous weight change (kg)

[5] The results across the three cohorts were pooled using an inverse variance weighted, fixed-effect meta-analysis

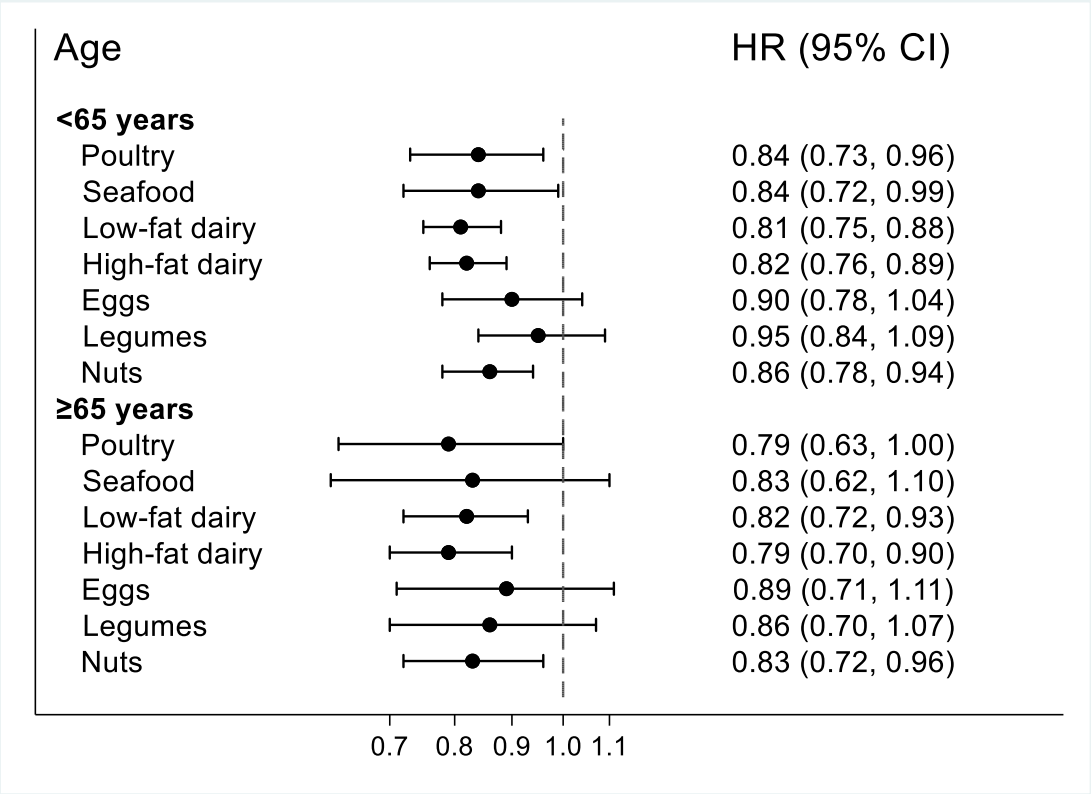
Abbreviations: CI, confidence interval; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; NHS, Nurses' Health Study; NHS II, Nurses' Health Study II.



Supplemental Figure 2. HR (95% CI) for type 2 diabetes mellitus associated with one daily serving decreased intake of red meat and concomitant increased intake of another major dietary protein source, stratified by baseline total red meat intake at the beginning of each 4-y period, in pooled analyses of all three cohorts (n=148,853).

Note: The Cox proportional hazards models included all protein foods simultaneously and were adjusted for age, calendar time, and calories (initial and change, both quintiles), marital status (with spouse, yes or no), race (white, African American, Asian/other), family history of diabetes (yes, no), history of hypertension (yes, no), history of hypercholesterolemia (yes, no), BMI (<20.0, 20.0-<23.0, 23.0-<25.0, 25.0-<30.0, ≥30.0 kg/m^2) alcohol intake, both as initial intake (0, 0.1-4.9, 5-14.9, 15-29.9, ≥30 grams/day) and change (quintiles), modified AHEI (initial and change, both quintiles), smoking status change (never to never, current to past, past to current, never to current, past to past, current to current), physical activity (metabolic equivalents initially and change, both quintiles) and for women initial menopausal status and use of postmenopausal hormones (premenopausal, postmenopausal + never hormone use, postmenopausal + past hormone use, postmenopausal + current hormone use). For each substitution of one food item for another, we exponentiated the difference between the beta-coefficients of the two foods to estimate the HR, and we used the variances and covariance of the two food items to estimate the 95% CI. The results across the three cohorts were pooled using an inverse variance weighted, fixed-effect meta-analysis.

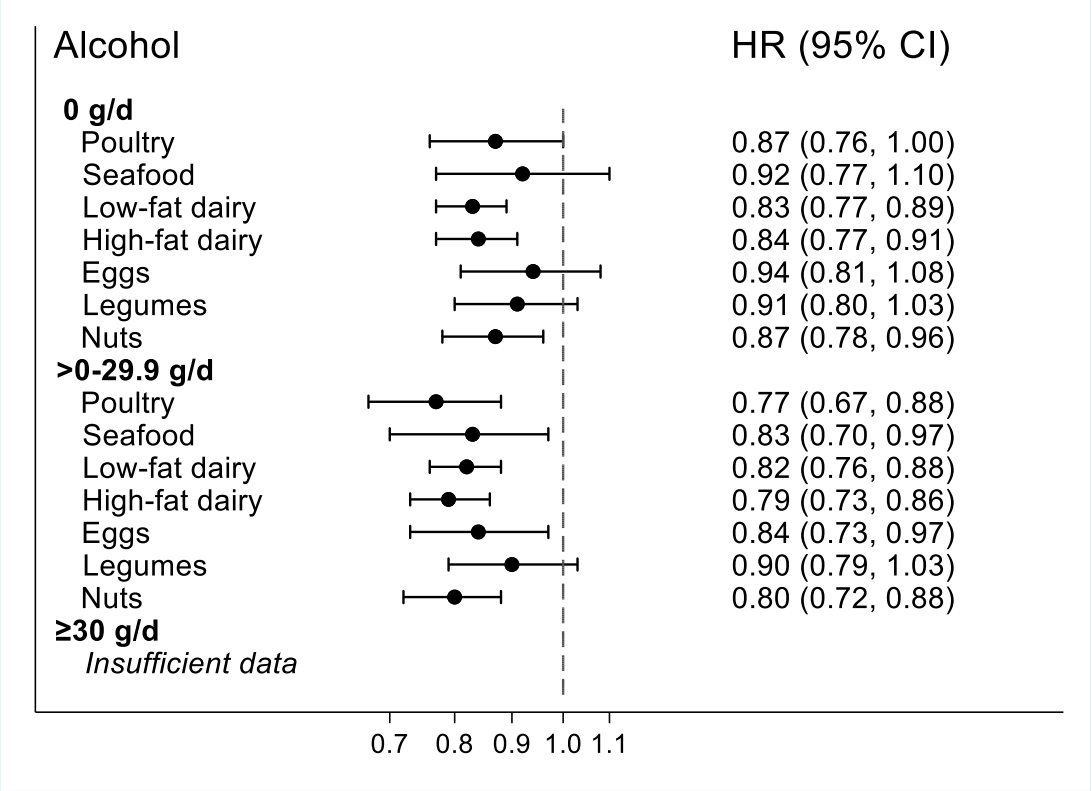
Abbreviations: CI, confidence interval; HR, hazard ratio.



Supplemental Figure 3. HR (95% CI) for type 2 diabetes mellitus associated with one daily serving decreased intake of total red meat and concomitant increased intake of another major dietary protein source stratified by baseline age in pooled analyses of the Nurses' Health Study and the Health Professionals Follow-up Study (n=73,657).

Note: The Cox proportional hazards models included all protein foods simultaneously and were adjusted for age, calendar time, and calories (initial and change, both quintiles), marital status (with spouse, yes or no), race (white, African American, Asian/other), family history of diabetes (yes, no), history of hypertension (yes, no), history of hypercholesterolemia (yes, no), BMI (<20.0, 20.0-<23.0, 23.0-<25.0, 25.0-<30.0, ≥30.0 kg/m^2) alcohol intake, both as initial intake (0, 0.1-4.9, 5-14.9, 15-29.9, ≥30 grams/day) and change (quintiles), modified AHEI (initial and change, both quintiles), smoking status change (never to never, current to past, past to current, never to current, past to past, current to current), physical activity (metabolic equivalents initially and change, both quintiles) and for women initial menopausal status and use of postmenopausal hormones (premenopausal, postmenopausal + never hormone use, postmenopausal + past hormone use, postmenopausal + current hormone use), initial intake of red meat, poultry, seafood, low-fat dairy, high-fat dairy, eggs, legumes, and nuts (servings/day). For each substitution of one food item for another, we exponentiated the difference between the beta-coefficients of the two foods to estimate the HR, and we used the variances and covariance of the two food items to estimate the 95% CI. The results across the three cohorts were pooled using an inverse variance weighted, fixed-effect meta-analysis.

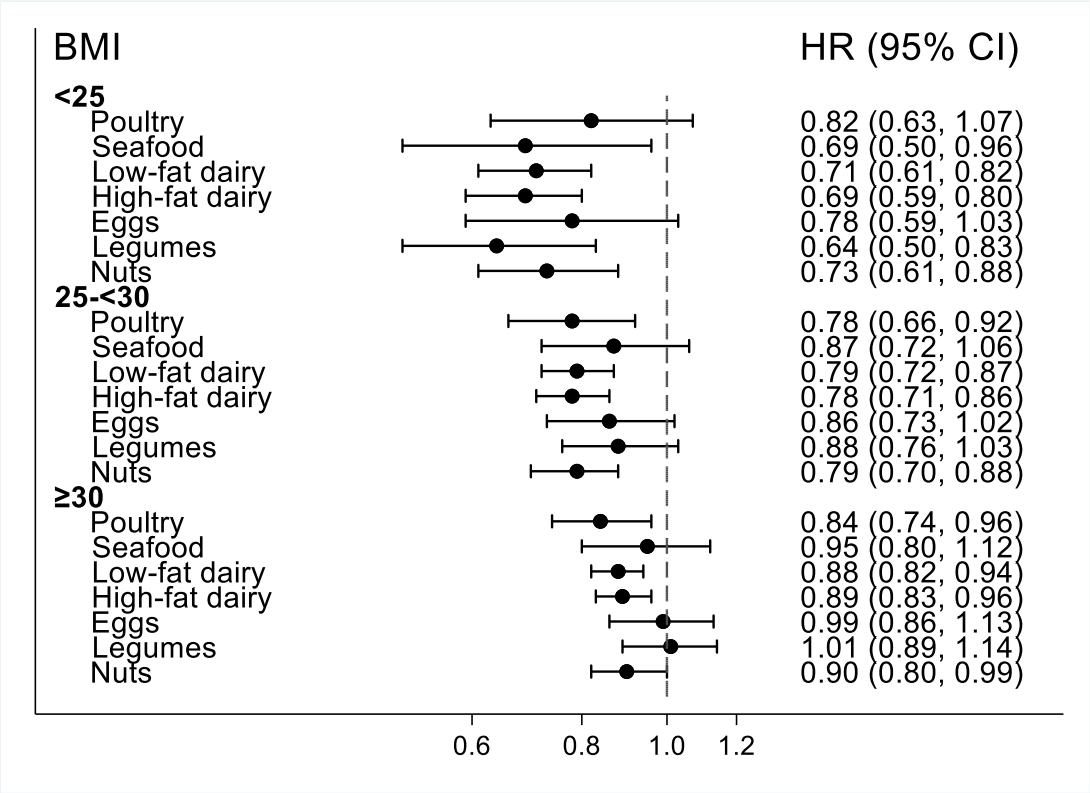
Abbreviations: CI, confidence interval; HR, hazard ratio.



Supplemental Figure 4. HR (95% CI) for type 2 diabetes mellitus associated with one daily serving decreased intake of total red meat and concomitant increased intake of another major dietary protein source stratified by baseline alcohol intake in pooled analyses of all three cohorts (n=148,853).

Note: The Cox proportional hazards models included all protein foods simultaneously and were adjusted for age, calendar time, and calories (initial and change, both quintiles), marital status (with spouse, yes or no), race (white, African American, Asian/other), family history of diabetes (yes, no), history of hypertension (yes, no), history of hypercholesterolemia (yes, no), BMI (<20.0, 20.0-<23.0, 23.0-<25.0, 25.0-<30.0, ≥30.0 kg/m^2) alcohol intake, both as initial intake (0, 0.1-4.9, 5-14.9, 15-29.9, ≥30 grams/day) and change (quintiles), modified AHEI (initial and change, both quintiles), smoking status change (never to never, current to past, past to current, never to current, past to past, current to current), physical activity (metabolic equivalents initially and change, both quintiles) and for women initial menopausal status and use of postmenopausal hormones (premenopausal, postmenopausal + never hormone use, postmenopausal + past hormone use, postmenopausal + current hormone use), initial intake of red meat, poultry, seafood, low-fat dairy, high-fat dairy, eggs, legumes, and nuts (servings/day). For each substitution of one food item for another, we exponentiated the difference between the beta-coefficients of the two foods to estimate the HR, and we used the variances and covariance of the two food items to estimate the 95% CI. The results across the three cohorts were pooled using an inverse variance weighted, fixed-effect meta-analysis.

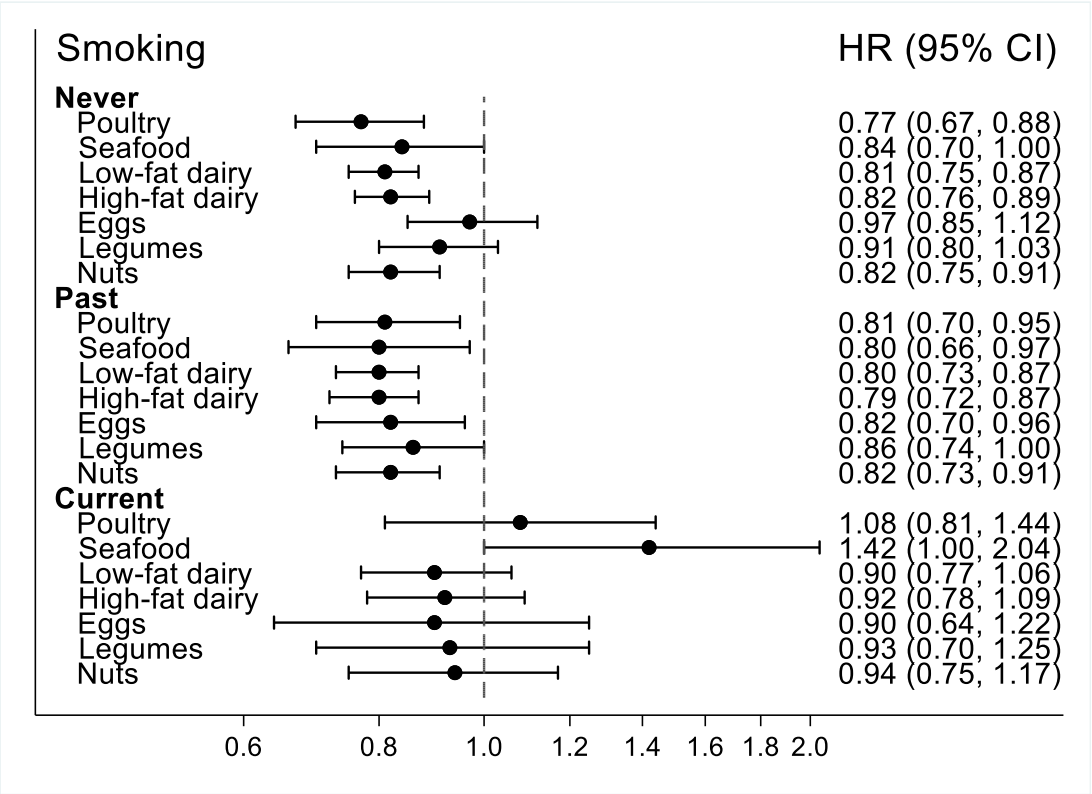
Abbreviations: CI, confidence interval; HR, hazard ratio.



Supplemental Figure 5. HR (95% CI) for type 2 diabetes mellitus associated with one daily serving decreased intake of total red meat and concomitant increased intake of another major dietary protein source stratified by baseline BMI in pooled analyses of all three cohorts (n=148,853).

Note: The Cox proportional hazards models included all protein foods simultaneously and were adjusted for age, calendar time, and calories (initial and change, both quintiles), marital status (with spouse, yes or no), race (white, African American, Asian/other), family history of diabetes (yes, no), history of hypertension (yes, no), history of hypercholesterolemia (yes, no), BMI (<20.0, 20.0-<23.0, 23.0-<25.0, 25.0-<30.0, ≥30.0 kg/m^2) alcohol intake, both as initial intake (0, 0.1-4.9, 5-14.9, 15-29.9, ≥30 grams/day) and change (quintiles), modified AHEI (initial and change, both quintiles), smoking status change (never to never, current to past, past to current, never to current, past to past, current to current), physical activity (metabolic equivalents initially and change, both quintiles) and for women initial menopausal status and use of postmenopausal hormones (premenopausal, postmenopausal + never hormone use, postmenopausal + past hormone use, postmenopausal + current hormone use), initial intake of red meat, poultry, seafood, low-fat dairy, high-fat dairy, eggs, legumes, and nuts (servings/day). For each substitution of one food item for another, we exponentiated the difference between the beta-coefficients of the two foods to estimate the HR, and we used the variances and covariance of the two food items to estimate the 95% CI. The results across the three cohorts were pooled using an inverse variance weighted, fixed-effect meta-analysis.

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



Supplemental Figure 6. HR (95% CI) for type 2 diabetes mellitus associated with one daily serving decreased intake of total red meat and concomitant increased intake of another major dietary protein source stratified by baseline smoking in pooled analyses of all three cohorts (n=148,853).

Note: The Cox proportional hazards models included all protein foods simultaneously and were adjusted for age, calendar time, and calories (initial and change, both quintiles), marital status (with spouse, yes or no), race (white, African American, Asian/other), family history of diabetes (yes, no), history of hypertension (yes, no), history of hypercholesterolemia (yes, no), BMI (<20.0, 20.0-<23.0, 23.0-<25.0, 25.0-<30.0, ≥30.0 kg/m^2) alcohol intake, both as initial intake (0, 0.1-4.9, 5-14.9, 15-29.9, ≥30 grams/day) and change (quintiles), modified AHEI (initial and change, both quintiles), smoking status change (never to never, current to past, past to current, never to current, past to past, current to current), physical activity (metabolic equivalents initially and change, both quintiles) and for women initial menopausal status and use of postmenopausal hormones (premenopausal, postmenopausal + never hormone use, postmenopausal + past hormone use, postmenopausal + current hormone use), initial intake of red meat, poultry, seafood, low-fat dairy, high-fat dairy, eggs, legumes, and nuts (servings/day). For each substitution of one food item for another, we exponentiated the difference between the beta-coefficients of the two foods to estimate the HR, and we used the variances and covariance of the two food items to estimate the 95% CI. The results across the three cohorts were pooled using an inverse variance weighted, fixed-effect meta-analysis.

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