

SUPPLEMENTAL MATERIAL

Supplemental Methods:

Serving Sizes of Major Protein Sources on Food Frequency Questionnaires in the Nurses' Health Study, 1980-2002

	1980	1984	1986	1990	1994	1998	2002
Skim or low fat milk	8oz	8oz	8oz	8oz			
Whole milk	8oz	8oz	8oz	8oz	8oz	8oz	8oz
1% or 2% milk					8oz		8oz
Skim milk					8oz		8oz
Skim or 1% milk						8oz	
2% milk						8oz	
Cream		1 tbs	1 tbs	1 tbs	1 tbs	1 tbs	1 tbs
Sour cream		1 tbs	1 tbs	1 tbs	1 tbs	1 tbs	1 tbs
Sherbet or ice milk or frozen yogurt or non-fat ice cream		½ cup	½ cup	½ cup	½ cup	½ cup	½ cup
Yogurt	1 cup	1 cup	1 cup	1 cup			

Hot dog	1 hot dog	1 hot dog	1 hot dog	1 hot dog	1 hot dog	1 hot dog	1 hot dog
Chicken or turkey dog					1 chicken or turkey dog	1 chicken or turkey dog	1 chicken or turkey dog
Processed meats	1 piece or slice	1 piece or slice	1 piece or slice	1 piece or slice	1 piece or slice		
* Sandwich						1 sandwich	1 sandwich
* Other (sausage, kielbasa, et)						2oz	2oz
Bacon	2 slices	2 slices	2 slices	2 slices	2 slices	2 slices	2 slices
Beef, pork, lamb sandwich or mixed dish (stew, casserole, lasagna, etc)	Not quantified	Not quantified	Not quantified	Not quantified	Not quantified	Not quantified	Not quantified
Beef, pork, lamb as main dish (steak, roast, ham, etc.)	6-8oz	4-6oz	4-6oz				
Pork as a main dish (eg, ham or chops)				4-6oz	4-6oz	4-6oz	4-6oz

Beef or lamb as a main dish (eg, steak or roast)				4-6oz	4-6oz	4-6oz	4-6oz
Eggs	1 egg	1 egg	1 egg	1 egg	1 egg	1 egg	1 egg
Fish	6-8oz						
* Canned tuna		3-4oz	3-4oz	3-4oz	3-4oz	2-3oz	2-3oz
* Dark meat fish (mackerel, salmon, sardines, bluefish, swordfish)		3-5oz	3-5oz	3-5oz	3-5oz	3-5oz	3-5oz
* Other fish (eg, Cod, Haddock, Halibut)							
* Breaded fish cakes, pieces, or fish sticks		3-5oz	3-5oz	3-5oz	3-5oz	3-5oz	3-5oz
					1 svg	1 svg	1 svg
Nuts (incl. peanuts,	1oz	Small packet	Small packet	Small packet	Small packet	Small packet	Small packet

Supplemental Methods:

Serving Sizes of Major Protein Sources on Food Frequency Questionnaires in the Health Professionals' Follow-up Study, 1986-2006

	1986	1990	1994	1998	2002	2006
Skim or low fat milk or 1% milk	8oz	8oz	8oz	8oz		
Whole milk	8oz	8oz	8oz	8oz	8oz	8oz
2% milk			8oz	8oz		
1% or 2% milk					8oz	8oz
Skim milk					8oz	8oz
Cream	1 tbs	1 tbs	1 tbs	1 tbs	1 tbs	1 tbs
Sour cream	1 tbs	1 tbs				
Sherbet or ice milk or frozen yogurt or non-fat ice cream	1 cup	½ cup	½ cup	½ cup	½ cup	1 cup
Yogurt	1 cup	1 cup				
Low carb, artificially sweetened, or plain yogurt			1 cup	1 cup	1 cup	1 cup
Sweetened or flavored yogurt			1 cup	1 cup	1 cup	1 cup

Ice cream	1 cup	½ cup	½ cup	½ cup	½ cup	½ cup
Cottage or ricotta cheese	½ cup	½ cup	½ cup	½ cup	½ cup	½ cup
Hard cheese	1 slice or 1oz svg	1 slice or 1oz svg	1 slice or 1oz svg	1 slice or 1oz svg	1 slice or 1oz svg	1 slice or 1oz svg
Cream cheese	1 oz	1 oz	1 oz	1 oz	1 oz	1 oz
Butter	1 pat	1 pat	1 pat	1 pat	1 pat	1 pat
Chicken or turkey w/o skin	4-6oz	4-6oz	4-6oz	3oz	3oz	3oz
Chicken or turkey w/skin	4-6oz	4-6oz	4-6oz	3oz	3oz	3oz
Chicken or turkey sandwich				Not quantified	Not quantified	Not quantified
Hamburger (incl. regular and lean)	1 patty	1 patty	1 patty	1 patty	1 patty	1 patty
Hot dog	1 hot dog	1 hot dog	1 hot dog	1 hot dog	1 hot dog	1 hot dog
Chicken or turkey dog			1 chicken or turkey dog	1 chicken or turkey dog	1 chicken or turkey dog	1 chicken or turkey dog
Processed meats * Sandwich	1 piece or slice	1 piece or slice	1 piece or slice	Not quantified	Not quantified	Not quantified

* Other (sausage, kielbasa, et)				2oz or 2 small links	2oz or 2 small links	2oz or 2 small links
Bacon	2 slices	2 slices	2 slices	2 slices	2 slices	2 slices
Beef, pork, lamb sandwich or mixed dish (stew, casserole, lasagna, etc)	Not quantified	Not quantified	Not quantified	Not quantified	Not quantified	Not quantified
Beef, pork, lamb as main dish (steak, roast, ham, etc.)	4-6oz					
Pork as a main dish (eg, ham or chops)		4-6 oz	4-6oz	4-6oz	4-6oz	4-6oz
Beef or lamb as a main dish (eg, steak or roast)		4-6 oz	4-6oz	4-6oz	4-6oz	4-6oz
Eggs	1 egg	1 egg	1 egg	1 egg	1 egg	1 egg
Fish						
* Canned tuna	3-4oz	3-4oz	3-4oz	3-4oz	3-4oz	3-4oz
* Dark meat fish (mackerel, salmon, sardines, bluefish,	3-5oz	3-5oz	3-5oz	3-5oz	3-5oz	3-5oz

swordfish)						
* Other fish (eg, Cod, Haddock, Halibut)	3-5 oz	3-5oz	3-5oz	3-5oz	3-5oz	3-5oz
* Breaded fish cakes, pieces, or fish sticks				1 svg	1 svg	1 svg
Nuts (incl. peanuts, walnuts, other nuts)	Small packet or 1oz	Small packet or 1oz	Small packet or 1oz	Small packet or 1oz	Small packet or 1oz	Small packet or 1oz
Beans or lentils, baked or dry	½ cup	½ cup	½ cup	½ cup	½ cup	½ cup
String beans	½ cup	½ cup	½ cup	½ cup	½ cup	½ cup
Peas	½ cup	½ cup	½ cup	½ cup	½ cup	½ cup
Soybeans or tofu	3-4 oz	3-4 oz	3-4 oz	3-4 oz		
Tofu, soy burger, or other soy protein					Not quantified	Not quantified

Supplemental Methods:

Many previous prospective cohort studies have stopped updating a study participant's diet when he or she developed an intermediate outcome on the causal pathway between diet and cardiovascular disease, such as diabetes, hypertension, hypercholesterolemia, angina, or coronary artery bypass surgery (CABG)/percutaneous coronary intervention (PCI). This has been done because changes in diet after these interim diagnoses or events may bias the diet-disease association; i.e., these diagnoses can be confounders. Rather than stop updating diet at all of these intermediates, we first assessed whether the occurrence of an intermediate outcome or event was associated with change in dietary protein intake. To do so, we fit multiple generalized linear models accounting for within-person repeated dietary measures. Three models were fit with data from the Nurses' Health Study and three were fit with data from the Health Professionals' Follow-Up Study. Within each Study, one model had as its continuous dependent variable the change in calorie-adjusted animal protein intake at each point in time (e.g., the "change" in animal protein intake in 1986 in the NHS was the calorie-adjusted 1984 intake subtracted from the calorie-adjusted 1990 intake), another model had as its continuous dependent variable the change in calorie-adjusted vegetable protein intake (defined in the same way as for animal protein), and a third model had as its outcome the change in calorie-adjusted red meat intake. The independent variables for each of the six models included binary indicators for a new diagnosis of each intermediate (yes/no for diabetes, hypertension, hypercholesterolemia, angina, or CABG/PCI), a binary indicator for a new diagnosis of cancer (yes/no), a binary indicator for a new diagnosis of myocardial infarction (yes/no), an indicator for the current follow-up cycle (ten 2-year follow-up cycles between 1986 and 2006), and interaction terms between the intermediate outcomes or cancer or myocardial infarction and the follow-up cycle. The correlation structure for the generalized linear models was autoregressive. From these models, we observed that new diagnoses of high cholesterol, high blood pressure, angina, and PCI/CABG were associated with statistically significant but very small changes in subsequent animal and vegetable protein intake (e.g., 0.1 to 1.2 g/day following diagnosis) and red meat intake (e.g., 0.01 to 0.1 servings/day following diagnosis) in men and women. As these diagnoses appeared to be only weak time-dependent confounders, and to avoid the potential for misclassification of each participant's long-term diet by stopping the updating of diet at one of these diagnoses, we continued updating a study participant's dietary intake throughout follow-up using data from all repeated FFQs.

Table S3. RR and 95% CI for stroke by quintiles of intake of processed and unprocessed red meat ^{*,†,‡}

		Quintiles					P for trend	RR for 1 serving/day
		1st	2nd	3rd	4th	5th		
Total Red Meat								
Men	Multivariable model	1.00	0.97 (0.81,1.17)	1.07 (0.88,1.30)	1.20 (0.98,1.48)	1.25 (1.00,1.58)	0.02	1.14 (1.02,1.26)
Women	Multivariable model	1.00	1.09 (0.97,1.23)	1.08 (0.94,1.23)	1.11 (0.95,1.28)	1.12 (0.94,1.33)	0.28	1.06 (0.95,1.19)
	Pooled	1.00	1.05 (0.95,1.17)	1.08 (0.96,1.20)	1.14 (1.01,1.29)	1.17 (1.02,1.34)	0.01	1.10 (1.02,1.19)
Processed Red Meat								
Men	Multivariable model	1.00	0.98 (0.82,1.19)	0.89 (0.73,1.08)	1.09 (0.89,1.32)	1.23 (1.00,1.51)	<0.01	1.48 (1.13,1.95)
Women	Multivariable model	1.00	0.96 (0.85,1.08)	1.03 (0.91,1.18)	1.04 (0.91,1.18)	1.03 (0.89,1.19)	0.53	1.08 (0.86,1.35)
	Pooled	1.00	0.97 (0.87,1.07)	0.99 (0.89,1.10)	1.05 (0.94,1.17)	1.09 (0.97,1.23)	0.02	1.23 (1.03,1.46)
Unprocessed Red Meat								
Men	Multivariable model	1.00	1.09 (0.91,1.31)	1.05 (0.86,1.28)	1.22 (0.99,1.50)	1.10 (0.87,1.38)	0.56	1.07 (0.86,1.33)

Women	Multivariable model	1.00	1.07 (0.95,1.21)	1.03 (0.90,1.17)	1.11 (0.96,1.28)	1.16 (0.99,1.37)	0.07	1.19 (0.98,1.43)
	Pooled	1.00	1.08 (0.97,1.19)	1.04 (0.93,1.16)	1.14 (1.02,1.28)	1.14 (1.00,1.30)	0.08	1.14 (0.98,1.31)

* Median values shown for quintiles of servings/day

† Multivariable model stratified on age (months) and time period (13 periods in NHS, 11 in HPFS) and includes: body mass index (10 categories), cigarette smoking (never, past, current 1-14 cig/day, current 14-25 cig/day, current 25+ cig/day), physical exercise (<3, 3-9, 9-18, 18-27, 27+ metabolic equivalents/week), parental history of early myocardial infarction (before age 60), menopausal status in women (pre-menopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of yrs), vitamin E supplement use (yes/no), aspirin use at least once per week (yes/no), total energy (quintiles of Kcal), cereal fiber (quintiles of g/day), alcohol (quintiles of g/day), trans-fat (quintiles of g/day), fruit and vegetables (quintiles of servings/day), other protein sources (quintiles of servings/day), and history of myocardial infarction (yes/no), coronary artery bypass surgery or percutaneous coronary intervention (yes/no), angina (yes/no), diabetes (yes/no), hypertension (yes/no), and hypercholesterolemia (yes/no)

‡ Q statistic p value for between-study heterogeneity (null hypothesis is that *there is no* heterogeneity) for total red meat, processed meat, unprocessed meat > 0.05

Table S4: Relative Risks (RR) and 95% confidence intervals for hemorrhagic stroke in men and women by quintiles of intake of major sources of dietary protein *

		Quintiles					P for trend	RR for 1 serving/day
		1st	2nd	3rd	4th	5th		
Total Red Meat								
	Men	1.00	1.03 (0.61,1.73)	0.93 (0.53,1.63)	1.14 (0.63,2.06)	1.07 (0.55,2.08)	0.61	1.08 (0.80,1.48)
	Women	1.00	1.46 (0.97,2.22)	1.49 (0.94,2.34)	1.54 (0.94,2.51)	1.30 (0.72,2.34)	0.56	1.11 (0.78,1.60)
Processed Red Meat								
	Men	1.00	0.95 (0.55,1.67)	1.04 (0.59,1.84)	1.26 (0.72,2.21)	1.47 (0.80,2.72)	0.08	2.06 (0.92,4.62)
	Women	1.00	1.12 (0.74,1.68)	1.09 (0.70,1.71)	1.48 (0.97,2.27)	0.94 (0.56,1.57)	0.96	0.98 (0.46,2.09)
Unprocessed Red Meat								
	Men	1.00	0.72 (0.42,1.22)	1.09 (0.65,1.83)	0.60 (0.32,1.12)	0.70 (0.36,1.37)	0.35	0.73 (0.39,1.40)
	Women	1.00	1.12 (0.74,1.69)	0.94 (0.60,1.49)	1.39 (0.88,2.18)	0.93 (0.54,1.60)	0.92	1.03 (0.56,1.91)
Poultry								
	Men	1.00	0.87 (0.53,1.44)	0.93 (0.57,1.51)	0.93 (0.53,1.64)	0.66 (0.37,1.18)	0.19	0.55 (0.22,1.36)
	Women	1.00	0.74 (0.48,1.15)	0.87 (0.59,1.30)	0.71 (0.45,1.10)	0.79 (0.51,1.24)	0.45	0.67 (0.24,1.89)

Fish

Men	1.00	1.18 (0.72,1.94)	0.92 (0.53,1.61)	0.88 (0.50,1.55)	1.08 (0.60,1.94)	0.89	0.94 (0.37,2.40)
Women	1.00	0.61 (0.40,0.92)	0.61 (0.40,0.93)	0.63 (0.41,0.96)	0.65 (0.41,1.02)	0.21	0.47 (0.14,1.53)

Whole-fat dairy

Men	1.00	0.69 (0.41,1.17)	0.77 (0.46,1.30)	0.85 (0.51,1.43)	0.65 (0.36,1.15)	0.46	0.92 (0.73,1.15)
Women	1.00	0.78 (0.52,1.18)	0.91 (0.60,1.37)	0.73 (0.46,1.14)	1.23 (0.80,1.88)	0.10	1.15 (0.97,1.35)

Low-fat dairy

Men	1.00	0.93 (0.55,1.57)	0.90 (0.53,1.52)	0.63 (0.36,1.11)	1.10 (0.65,1.85)	0.55	1.06 (0.88,1.28)
Women	1.00	0.69 (0.45,1.05)	0.74 (0.49,1.14)	0.89 (0.58,1.36)	0.73 (0.45,1.16)	0.53	0.93 (0.76,1.15)

Eggs

Men	1.00	1.39 (0.76,2.55)	2.05 (1.15,3.62)	1.55 (0.86,2.79)	0.53 (0.22,1.25)	0.05	0.48 (0.23,1.01)
Women	1.00	0.98 (0.67,1.45)	1.17 (0.79,1.73)	0.98 (0.63,1.52)	0.76 (0.47,1.23)	0.22	0.64 (0.31,1.30)

Nuts

Men	1.00	0.76 (0.45,1.28)	0.84 (0.50,1.41)	0.93 (0.57,1.52)	0.79 (0.47,1.31)	0.51	0.77 (0.35,1.67)
Women	1.00	1.24 (0.84,1.85)	0.78 (0.49,1.22)	0.80 (0.51,1.27)	0.86 (0.55,1.35)	0.20	0.46 (0.14,1.50)

Legumes

Men	1.00	0.84 (0.49,1.45)	1.18 (0.71,1.96)	0.88 (0.51,1.53)	1.29 (1.75,2.20)	0.28	1.72 (0.65,4.58)
Women	1.00	0.80 (0.52,1.24)	1.31 (0.85,2.01)	0.96 (0.63,1.47)	1.07 (0.69,1.66)	0.80	1.16 (0.37,3.63)

* Multivariable model stratified on age (months) and time period (13 periods in NHS, 11 in HPFS) and includes: body mass index (10 categories), cigarette smoking (never, past, current 1-14 cig/day, current 14-25 cig/day, current 25+ cig/day), physical exercise (<3, 3-9, 9-18, 18-27, 27+ metabolic equivalents/week), parental history of early myocardial infarction (before age 60), menopausal status in women (pre-menopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of yrs), vitamin E supplement use (yes/no), aspirin use at least once per week (yes/no), total energy (quintiles of Kcal), cereal fiber (quintiles of g/day), alcohol (quintiles of g/day), trans-fat (quintiles of g/day), fruit and vegetables (quintiles of servings/day), and other protein sources (quintiles of servings/day)

Table S5: Relative Risks (RR) and 95% confidence intervals for ischemic stroke in men and women by quintiles of intake of major sources of dietary protein *

		Quintiles					P for trend	RR for 1 serving/day
		1st	2nd	3rd	4th	5th		
Total Red Meat								
	Men	1.00	1.03 (0.81,1.31)	1.09 (0.85,1.41)	1.34 (1.03,1.75)	1.31 (0.97,1.77)	0.06	1.14 (0.99,1.32)
	Women	1.00	1.09 (0.92,1.29)	1.09 (0.91,1.31)	1.10 (0.90,1.35)	1.16 (0.92,1.48)	0.27	1.09 (0.93,1.27)
Processed Red Meat								
	Men	1.00	1.07 (0.84,1.36)	0.87 (0.67,1.12)	1.10 (0.85,1.42)	1.31 (1.00,1.71)	0.01	1.59 (1.11,2.27)
	Women	1.00	0.98 (0.83,1.16)	1.06 (0.89,1.27)	0.98 (0.82,1.18)	1.07 (0.87,1.31)	0.54	1.10 (0.80,1.52)
Unprocessed Red Meat								
	Men	1.00	1.26 (0.99,1.60)	1.08 (0.84,1.40)	1.49 (1.14,1.94)	1.23 (0.91,1.67)	0.33	1.15 (0.86,1.53)
	Women	1.00	1.20 (1.01,1.43)	1.18 (0.98,1.42)	1.16 (0.95,1.42)	1.30 (1.03,1.63)	0.08	1.26 (0.97,1.64)
Poultry								
	Men	1.00	1.10 (0.88,1.38)	0.94 (0.75,1.18)	1.14 (0.89,1.46)	1.07 (0.84,1.37)	0.74	1.07 (0.72,1.58)
	Women	1.00	0.96 (0.80,1.15)	0.88 (0.74,1.04)	0.92 (0.76,1.10)	0.78 (0.64,0.95)	0.02	0.61 (0.39,0.94)

Fish

Men	1.00	0.91 (0.73,1.13)	0.90 (0.71,1.15)	0.92 (0.73,1.17)	0.96 (0.74,1.23)	0.96	0.99 (0.66,1.49)
Women	1.00	1.03 (0.86,1.23)	0.98 (0.82,1.19)	1.09 (0.90,1.31)	0.94 (0.76,1.15)	0.54	0.86 (0.53,1.39)

Whole-fat dairy

Men	1.00	0.85 (0.68,1.07)	0.86 (0.68,1.09)	0.98 (0.78,1.25)	0.92 (0.72,1.19)	0.92	0.99 (0.90,1.10)
Women	1.00	0.93 (0.79,1.09)	0.87 (0.73,1.03)	0.83 (0.69,0.99)	0.85 (0.70,1.03)	0.12	0.94 (0.88,1.01)

Low-fat dairy

Men	1.00	0.88 (0.69,1.11)	0.97 (0.78,1.22)	0.92 (0.73,1.16)	0.96 (0.76,1.22)	0.83	0.99 (0.91,1.08)
Women	1.00	0.94 (0.78,1.12)	0.98 (0.81,1.18)	0.95 (0.79,1.15)	0.93 (0.76,1.13)	0.54	0.97 (0.89,1.06)

Eggs

Men	1.00	0.74 (0.58,0.93)	0.75 (0.59,0.94)	0.67 (0.53,0.85)	0.79 (0.61,1.04)	0.34	0.86 (0.63,1.17)
Women	1.00	0.89 (0.75,1.04)	0.92 (0.78,1.08)	0.90 (0.74,1.08)	0.95 (0.79,1.14)	0.72	0.95 (0.71,1.27)

Nuts

Men	1.00	1.04 (0.83,1.31)	1.02 (0.81,1.28)	1.06 (0.85,1.32)	0.97 (0.77,1.22)	0.51	0.89 (0.63,1.26)
Women	1.00	0.92 (0.77,1.10)	0.98 (0.81,1.18)	1.01 (0.84,1.21)	0.96 (0.80,1.16)	0.98	0.99 (0.63,1.57)

Legumes

Men	1.00	0.93 (0.74,1.16)	0.89 (0.70,1.12)	1.03 (0.82,1.30)	1.11 (0.88,1.41)	0.09	1.45 (0.94,2.24)
Women	1.00	0.98 (0.82,1.18)	1.14 (0.95,1.37)	1.04 (0.87,1.25)	1.16 (0.96,1.40)	0.12	1.45 (0.91,2.33)

* Multivariable model stratified on age (months) and time period (13 periods in NHS, 11 in HPFS) and includes: body mass index (10 categories), cigarette smoking (never, past, current 1-14 cig/day, current 14-25 cig/day, current 25+ cig/day), physical exercise (<3, 3-9, 9-18, 18-27, 27+ metabolic equivalents/week), parental history of early myocardial infarction (before age 60), menopausal status in women (pre-menopausal, postmenopausal with no history of hormone replacement, postmenopausal with history of hormone replacement, postmenopausal with current hormone replacement), multivitamin use (quintiles of yrs), vitamin E supplement use (yes/no), aspirin use at least once per week (yes/no), total energy (quintiles of Kcal), cereal fiber (quintiles of g/day), alcohol (quintiles of g/day), trans-fat (quintiles of g/day), fruit and vegetables (quintiles of servings/day), and other protein sources (quintiles of servings/day)