

SUPPLEMENTARY DATA

Supplementary Table S1. Top food sources of linoleic acid, arachidonic acid, and *trans* fats

	NHS 1984*		NHSII 1991		HPFS 1986	
LA	Mayonnaise	14.6	Mayonnaise	16.0	Mayonnaise	13.6
	Margarine	9.8	Margarine	8.5	Margarine	8.0
	Italian salad dressing	9.1	Potato chips	7.6	Peanut	6.2
	Potato chips	5.5	Spaghetti sauce	6.1	Potato chips	5.6
	Peanut	4.7	Chicken without skin	5.1	Peanut butter	5.0
AA	Chicken without skin	20.7	Chicken without skin	25.0	Eggs	26.0
	Eggs	17.1	Turkey	23.1	Chicken with skin	10.6
	Chicken with skin	13.8	Chicken with skin	9.2	Tuna	7.8
	Beef	8.2	Eggs	8.1	Chicken without skin	7.2
	Ham	8.1	Ham	6.5	Mayonnaise	5.5
<i>Trans</i>						
fats	Margarine	16.7	Fried food away from home	20.8	Beef	10.9
	Beef	9.6	French fries	8.6	French fries	9.0
	Italian salad dressing	5.9	Margarine	8.3	Italian salad dressing	6.5
	French fries	4.8	Danish pastry	6.4	Ham	4.9
	Oatmeal cookies	4.4	Chocolate chips	4.8	Sandwich beef	4.5
	NHS 1994		NHSII 1999		HPFS 1998	
LA	Margarine	9.8	Olive oil	10.5	Mayonnaise	4.8
	Mayonnaise	8.0	Potato chips	5.1	Olive oil	4.7
	Chicken without skin	6.5	Mayonnaise	4.8	Mixed nuts	4.7
	Tomato sauce	5.9	Chicken without skin	3.8	Chicken without skin	4.4
	Potato chips	4.6	Margarine	3.7	Potato chips	4.0
AA	Chicken without skin	37.0	Chicken without skin	23.8	Eggs	18.0
	Eggs	9.8	Chicken sandwich	14.6	Dark meat fish	8.4
	Chicken with skin	9.1	Eggs	12.3	Chicken without skin	5.7
	Lean beef patty	4.5	Chicken with skin	6.9	Tuna	5.0
	Pork	4.3	Pork	5.4	Cheddar cheese	4.2
<i>Trans</i>						
fats	Fried food away from home	12.8	French fries	14.2	Potato chips	11.2
	Cracker	9.1	Beef	10.9	Beef	9.8
	Danish pastry	8.2	Fried food away from home	6.0	Fried food away from home	9.4
	Margarine	7.9	Cracker	5.1	Cracker	8.2

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	Chocolate chips	6.6	Cheese(other than cottage or cream cheese)	4.8	Danish pastry	4.8
	NHS 2010		NHSII 2011		HPFS 2010	
LA	Walnuts	9.9	Walnuts	8.9	Walnuts	8.7
	Italian salad dressing	6.4	Mixed nuts	6.5	Mixed nuts	6.0
	Mayonnaise	5.6	Italian salad dressing	5.8	Peanut	5.5
	Mixed nuts	4.8	Olive oil	4.6	Italian salad dressing	5.0
	Peanut butter	4.7	French fries	4.4	French fries	4.7
AA	Dark meat fish	22.6	Dark meat fish	21.3	Dark meat fish	31.6
	Eggs	17.6	Chicken without skin	17.5	Eggs	14.6
	Fish oil	4.8	Eggs	13.9	Beef	4.2
	Chicken without skin	4.6	Chicken sandwich	10.9	Fish oil	3.6
	Beef as main dish	4.1	Chicken with skin	5.4	Chicken with skin	3.1
<i>Trans</i> fats	Cheese(other than cottage or cream cheese)	7.6	Cheese(other than cottage or cream cheese)	8.8	French fries	11.1
	Beef	5.6	Beef	6.6	Fried food away from home	9.0
	Danish pastry	4.9	Lean beef patty	4.7	Apple pie	7.0
	Ice cream	4.5	Frozen pizza	4.3	Home or ready-made cake	5.6
	Lean beef patty	4.4	Coffee whitener	4.1	Cheese(other than cottage or cream cheese)	4.2

Abbreviations: AA, arachidonic acid; HPFS, the Health Professionals Follow-Up Study; LA, linoleic acid; NHS, Nurses' Health Study; NHSII, Nurses' Health Study; PUFA, polyunsaturated fatty acids.

*, Data is not available for 1980 dietary data in NHS, thus 1984 dietary data is presented.

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Supplementary Table S2. Associations between arachidonic acid and type 2 diabetes risk in NHS, NHSII, and HPFS.*

		Quintiles of fatty acid intake (% energy)					
		Q1	Q2	Q3	Q4	Q5	P trend
AA							
NHS	Median (range)	0.05(0.005, 0.06)	0.07(0.06, 0.08)	0.08(0.08, 0.09)	0.10(0.09, 0.11)	0.13(0.11, 0.47)	
	Case/person-year	1421/449219	1652/448937	1798/448930	2041/448515	2463/447788	
	Model 1	1	1.17 (1.09, 1.26)	1.27 (1.19, 1.37)	1.44 (1.35, 1.54)	1.73 (1.62, 1.85)	<0.001
	Model 2	1	1.12 (1.04, 1.20)	1.14 (1.06, 1.22)	1.21 (1.13, 1.29)	1.31 (1.22, 1.40)	<.0001
	Model 3	1	1.12 (1.04, 1.20)	1.15 (1.07, 1.23)	1.23 (1.14, 1.32)	1.35 (1.25, 1.46)	<.0001
NHSII	Median (range)	0.04(0, 0.05)	0.06(0.05, 0.07)	0.08(0.07, 0.08)	0.09(0.08, 0.11)	0.13(0.11, 0.55)	
	Case/person-year	766/357258	954/357656	1042/357785	1168/358006	1530/357437	
	Model 1	1	1.24 (1.13, 1.36)	1.33 (1.21, 1.46)	1.46 (1.33, 1.60)	1.85 (1.70, 2.02)	<0.001
	Model 2	1	1.09 (0.99, 1.20)	1.08 (0.99, 1.19)	1.10 (1.00, 1.21)	1.23 (1.12, 1.35)	<0.001
	Model 3	1	1.08 (0.98, 1.18)	1.07 (0.97, 1.18)	1.09 (0.99, 1.19)	1.21 (1.10, 1.33)	<0.001
HPFS	Median (range)	0.05(0.004, 0.06)	0.06(0.06, 0.07)	0.08(0.07, 0.08)	0.09(0.08, 0.10)	0.12(0.10, 0.36)	
	Case/person-year	544/180960	692/181187	692/181254	758/180900	921/179939	
	Model 1	1	1.25 (1.12, 1.40)	1.24 (1.11, 1.39)	1.37 (1.23, 1.53)	1.64 (1.47, 1.82)	<0.001
	Model 2	1	1.15 (1.02, 1.29)	1.09 (0.98, 1.23)	1.16 (1.03, 1.29)	1.31 (1.17, 1.46)	<0.001
	Model 3	1	1.12 (1.00, 1.26)	1.06 (0.94, 1.19)	1.11 (0.99, 1.25)	1.26 (1.12, 1.42)	<0.001
Pooled†	Model 2	1	1.10 (1.05, 1.16)	1.09 (1.04, 1.15)	1.14 (1.08, 1.20)	1.25 (1.19, 1.31)	<0.001
	Model 3	1	1.10 (1.04, 1.15)	1.09 (1.03, 1.15)	1.14 (1.08, 1.20)	1.25 (1.19, 1.32)	<0.001

Abbreviations: AA, arachidonic acid; HPFS, the Health Professionals Follow-Up Study; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acid.

* Hazard ratios were calculated in Cox proportional hazards model; Model 1, adjusted for age. Model 2, further adjusted for ethnicity (Caucasian, African American, Asian, and other ethnicity), smoking status (never, former, current (1–14, 15–24, or ≥25 cigarettes/day), or missing), alcohol intake (gram/day: 0, 0.1–4.9, 5.0–14.9, and >15.0 in women, 0, 0.1–4.9, 5.0–29.9, and >30.0 in men, or missing), family history of diabetes (yes/no), menopausal status and post-menopausal hormone use (pre-menopause, post-menopause (never, former, or current hormone use), or missing, for women), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9, ≥27.0 metabolic equivalent of task hours/week, or missing), multivitamin use (yes/no), baseline hypertension, baseline hypercholesterolemia, updated body mass index (<23, 23–24.9, 25–29.9, 30–34.9, >35kg/m², or missing), total energy intake, and fruits and vegetables. Model 3, further adjusted for total fats, trans fats, monounsaturated fats, and other PUFAs.

† Study estimates from three cohorts were pooled using a fixed effects model.

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Supplementary Table S3. Hazard ratios of type 2 diabetes using linoleic acid to substitute for energy from other macronutrients by further adjusting incident hypertension and hypercholesterolemia.*

	Hazard ratio of type 2 diabetes						P for heterogeneity		
	NHS	<i>P</i>	NHSII	<i>P</i>	HPFS	<i>P</i>	Pooled†	<i>P</i>	
SFAs	0.92 (0.81, 1.03)	0.16	0.84 (0.68, 1.03)	0.09	0.74 (0.62, 0.90)	0.002	0.86 (0.79, 0.95)	0.002	0.15
Trans fats	0.84 (0.73, 0.97)	0.02	0.95 (0.80, 1.13)	0.55	0.82 (0.68, 1.00)	0.05	0.86 (0.78, 0.95)	0.002	0.42
MUFAs	0.97 (0.81, 1.16)	0.75	0.78 (0.60, 1.00)	0.05	0.93 (0.69, 1.26)	0.66	0.90 (0.79, 1.02)	0.11	0.43
n-3 PUFA	1.44 (0.95, 2.19)	0.08	0.90 (0.53, 1.55)	0.71	0.80 (0.50, 1.28)	0.35	0.99 (0.75, 1.30)	0.93	0.38
Carbohydrates	0.94 (0.82, 1.07)	0.33	0.86 (0.71, 1.05)	0.13	0.94 (0.77, 1.14)	0.52	0.91 (0.83, 1.00)	0.05	0.80

Abbreviations: HPFS, the Health Professionals Follow-Up Study; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids; SFA, saturated fatty acid.

* Hazard ratios were calculated in Cox proportional hazards mode after adjusting for age, ethnicity (Caucasian, African American, Asian, and other ethnicity), smoking status (never, former, current (1–14, 15–24, or ≥25 cigarettes/day), or missing), alcohol intake (gram/day: 0, 0.1–4.9, 5.0–14.9, and >15.0 in women, 0, 0.1–4.9, 5.0–29.9, and >30.0 in men, or missing), family history of diabetes (yes/no), menopausal status and post-menopausal hormone use (pre-menopause, post-menopause (never, former, or current hormone use), or missing, for women), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9, ≥27.0 metabolic equivalent of task hours/week, or missing), current aspirin use (yes/no), multivitamin use (yes/no), incident hypertension, incident hypercholesterolemia, updated body mass index (<23, 23–24.9, 25–29.9, 30–34.9, >35kg/m², or missing), total energy intake, and fruits and vegetables; for fat-fat substitution, further adjusted for other fats and total fats; for carbohydrate substitution, further adjusted for energy from protein.

† Study estimates from three cohorts were pooled using a fixed effects model.

SUPPLEMENTARY DATA

Supplementary Table S4. Hazard ratios of type 2 diabetes using linoleic acid to substitute for energy from other macronutrients by using two most recent dietary data.*

	Hazard ratio of type 2 diabetes								P for heterogeneity
	NHS	<i>P</i>	NHSII	<i>P</i>	HPFS	<i>P</i>	Pooled†	<i>P</i>	
SFAs	0.94 (0.85, 1.04)	0.22	0.86 (0.73, 1.02)	0.09	0.80 (0.67, 0.95)	0.010	0.89 (0.83, 0.96)	0.004	0.26
Trans fats	0.87 (0.78, 0.97)	0.009	0.89 (0.78, 1.02)	0.10	0.87 (0.75, 1.02)	0.08	0.88 (0.81, 0.94)	<0.001	0.96
MUFAs	0.96 (0.84, 1.10)	0.53	0.81 (0.66, 0.99)	0.04	0.92 (0.72, 1.18)	0.51	0.91 (0.82, 1.01)	0.07	0.39
n-3 PUFA	1.10 (0.83, 1.44)	0.52	0.97 (0.65, 1.43)	0.87	0.84 (0.57, 1.23)	0.37	0.99 (0.82, 1.21)	0.95	0.53
Carbohydrates	0.97 (0.87, 1.07)	0.50	0.87 (0.74, 1.01)	0.07	0.96 (0.81, 1.13)	0.63	0.94 (0.87, 1.01)	0.11	0.51

Abbreviations: HPFS, the Health Professionals Follow-Up Study; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids; SFA, saturated fatty acid.

* Hazard ratios were calculated in Cox proportional hazards mode after adjusting for age, ethnicity (Caucasian, African American, Asian, and other ethnicity), smoking status (never, former, current (1–14, 15–24, or ≥25 cigarettes/day), or missing), alcohol intake (gram/day: 0, 0.1–4.9, 5.0–14.9, and >15.0 in women, 0, 0.1–4.9, 5.0–29.9, and >30.0 in men, or missing), family history of diabetes (yes/no), menopausal status and post-menopausal hormone use (pre-menopause, post-menopause (never, former, or current hormone use), or missing, for women), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9, ≥27.0 metabolic equivalent of task hours/week, or missing), current aspirin use (yes/no), multivitamin use (yes/no), baseline hypertension, baseline hypercholesterolemia, updated body mass index (<23, 23–24.9, 25–29.9, 30–34.9, >35kg/m², or missing), total energy intake, and fruits and vegetables; for fat-fat substitution, further adjusted for other fats and total fats; for carbohydrate substitution, further adjusted for energy from protein.

† Study estimates from three cohorts were pooled using a fixed effects model.

SUPPLEMENTARY DATA

Supplementary Table S5. Hazard ratios of type 2 diabetes using LA to substitute for energy from other macronutrients by using baseline dietary data.*

	Hazard ratio of type 2 diabetes								P for heterogeneity
	NHS	<i>P</i>	NHSII	<i>P</i>	HPFS	<i>P</i>	Pooled†	<i>P</i>	
SFAs	0.93 (0.82, 1.05)	0.25	0.93 (0.79, 1.09)	0.35	0.77 (0.66, 0.90)	0.001	0.94 (0.88, 1.02)	0.12	0.009
Trans fats	0.83 (0.72, 0.96)	0.01	0.96 (0.84, 1.11)	0.60	0.96 (0.88, 1.05)	0.39	0.96 (0.90, 1.02)	0.21	0.99
MUFAs	0.95 (0.80, 1.14)	0.59	0.71 (0.56, 0.90)	0.005	0.88 (0.71, 1.09)	0.23	0.90 (0.82, 0.99)	0.03	0.08
n-3 PUFA	1.23 (0.81, 1.87)	0.34	0.71 (0.46, 1.11)	0.13	1.00 (0.91, 1.09)	0.97	0.97 (0.89, 1.06)	0.56	0.10
Carbohydrates	0.92 (0.81, 1.05)	0.22	0.84 (0.72, 0.99)	0.04	0.83 (0.70, 0.99)	0.03	0.89 (0.83, 0.96)	0.002	0.39

Abbreviations: HPFS, the Health Professionals Follow-Up Study; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids; SFA, saturated fatty acid.

* Hazard ratios were calculated in Cox proportional hazards mode after adjusting for age, ethnicity (Caucasian, African American, Asian, and other ethnicity), smoking status (never, former, current (1–14, 15–24, or ≥25 cigarettes/day), or missing), alcohol intake (gram/day: 0, 0.1–4.9, 5.0–14.9, and >15.0 in women, 0, 0.1–4.9, 5.0–29.9, and >30.0 in men, or missing), family history of diabetes (yes/no), menopausal status and post-menopausal hormone use (pre-menopause, post-menopause (never, former, or current hormone use), or missing, for women), physical activity (<3, 3.0–8.9, 9.0–17.9, 18.0–26.9, ≥27.0 metabolic equivalent of task hours/week, or missing), current aspirin use (yes/no), multivitamin use (yes/no), baseline hypertension, baseline hypercholesterolemia, updated body mass index (<23, 23–24.9, 25–29.9, 30–34.9, >35kg/m², or missing), total energy intake, and fruits and vegetables; for fat-fat substitution, further adjusted for other fats and total fats; for carbohydrate substitution, further adjusted for energy from protein.

† Study estimates from three cohorts were pooled using a fixed effects model.