Circulating Very-Long Chain Saturated Fatty Acid Levels are Inversely Associated with Incident Type 2 Diabetes in U.S. Men and Women
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Online Supplementary Material

Supplemental table 1. Baseline characteristics of 1,392 women in the Nurses' Health Study (1990) according to quartiles of plasma fatty acids of VLCSFA[1]

	Quartiles of 20:0			
	Q1	Q2	Q3	Q4
Plasma 20:0	0.14 ± 0.02	0.18 ± 0.01	0.22 ± 0.01	0.27 ± 0.03
Age, years	60.5 ± 6.1	61.1 ± 6.1	60.4 ± 6.3	59.3 ± 6.9
Race, Caucasian (%)	99.7	99.2	98.9	99.4
BMI (kg/m^2)	26.1 ± 4.7	25.4 ± 4.4	24.9 ± 4.5	24.6 ± 3.8
Current smoker (%)	16.5	17.4	19.6	19.9
Physical activity, MET, hours/week	14.1 ± 18.1	18.2 ± 22.2	16.2 ± 17.9	16.6 ± 18.4
Hypertension (%)	33.7	21.7	18.1	14.8
Hypercholesterolemia (%)	40.9	39.9	34.3	27.3
Family history of diabetes (%)	31.0	26.8	23.0	26.4
Total energy (kcal/day)	1715 ± 462	1797 ± 503	1788 ± 532	1760 ± 492
AHEI	47.8 ± 9.7	49.1 ± 10.5	48.5 ± 10.1	49.0 ± 10.7
Peanuts (g/day)	2.2 ± 4.3	2.2 ± 4.3	2.2 ± 4.8	2.2 ± 6.5
Peanut butter (g/day)	4.0 ± 9.1	4.0 ± 9.2	4.1 ± 8.9	4.2 ± 8.9
Coffee (ml/day)	308 ± 335	354 ± 338	401 ± 399	403 ± 400
Alcohol (g/day)	5.7 ± 10.3	5.5 ± 10.1	5.6 ± 9.3	3.8 ± 6.0
Vegetable fat (g/day)	27.4 ± 11.5	29.3 ± 13.5	28.9 ± 12.8	30.0 ± 14.3
Dairy fat (g/day)	10.9 ± 6.2	11.1 ± 6.5	12.3 ± 7.8	12.2 ± 7.6

	Quartiles of 22:0			
	Q1	Q2	Q3	Q4
Plasma 22:0	0.32 ± 0.07	0.46 ± 0.03	0.57 ± 0.04	0.76 ± 0.10
Age, years	60.6 ± 6.3	60.8 ± 5.8	60.4 ± 6.6	59.5 ± 6.7
Race, Caucasian (%)	99.2	100	98.8	99.0
BMI (kg/m^2)	26.3 ± 5.2	24.9 ± 4.1	25.1 ± 4.2	24.8 ± 3.9
Current smoker (%)	17.1	18.9	17.6	19.6
Physical activity, MET, hours/week	15.4 ± 20.2	16.8 ± 19.8	16.2 ± 18.2	16.6 ± 18.7
Hypertension (%)	32.6	22.7	16.1	17.3
Hypercholesterolemia (%)	39.7	36.8	34.0	32.6
Family history of diabetes (%)	31.3	26.5	23.8	25.6
Total energy (kcal/day)	1746 ± 491	1774 ± 504	1805 ± 480	1730 ± 515
AHEI	48.5 ± 10.3	48.4 ± 10.3	48.7 ± 10.2	39.1 ± 9.9
Peanuts (g/day)	2.0 ± 4.3	2.2 ± 4.3	2.2 ± 4.3	2.8 ± 8.8
Peanut butter (g/day)	3.5 ± 10.1	4.0 ± 10.2	4.2 ± 9.9	4.8 ± 10.9
Coffee (ml/day)	331 ± 358	354 ± 360	402 ± 380	422 ± 398
Alcohol (g/day)	6.9 ± 12.8	5.6 ± 9.6	5.1 ± 9.1	4.1 ± 7.5
Vegetable fat (g/day)	27.2 ± 12.1	27.9 ± 12.3	29.9 ± 12.6	29.7 ± 14.9

Dairy fat (g/day)	10.8 ± 6.0	12.0 ± 7.2	11.9 ± 7.5	11.7 ± 7.4

	Quartiles of 24:0			
	Q1	**Q2**	**Q3**	**Q4**
Plasma 24:0	0.22 ± 0.05	0.34 ± 0.03	0.44 ± 0.03	0.62 ± 0.10
Age, years	60.4 ± 6.4	60.9 ± 5.9	60.1 ± 6.6	59.9 ± 6.7
Race, Caucasian (%)	99.5	99.4	99.1	99.1
BMI (kg/m^2)	26.4 ± 4.9	25.2 ± 4.5	25.0 ± 4.2	24.4 ± 3.7
Current smoker (%)	14.9	21.1	20.4	16.9
Physical activity, MET, hours/week	14.7 ± 19.9	16.3 ± 19.3	17.2 ± 19.2	17.0 ± 18.4
Hypertension (%)	30.6	22.5	18.6	16.9
Hypercholesterolemia (%)	38.4	37.3	34.0	33.4
Family history of diabetes (%)	30.6	26.2	24.0	26.3
Total energy (kcal/day)	1765 ± 470	1757 ± 523	1788 ± 485	1746 ± 515
AHEI	48.0 ± 10.3	48.8 ± 9.8	48.4 ± 10.4	49.4 ± 10.3
Peanuts (g/day)	2.0 ± 4.2	2.0 ± 0.20	2.6 ± 4.4	2.8 ± 8.8
Peanut butter (g/day)	3.2 ± 10.9	3.6 ± 11.2	4.3 ± 10.4	4.5 ± 8.9
Coffee (ml/day)	307 ± 349	346 ± 352	402 ± 375	425 ± 405
Alcohol (g/day)	5.5 ± 11.1	5.5 ± 10.2	6.0 ± 10.2	5.1 ± 8.4
Vegetable fat (g/day)	28.0 ± 12.2	27.2 ± 12.3	29.8 ± 12.7	29.6 ± 14.7
Dairy fat (g/day)	11.1 ± 6.0	11.7 ± 7.0	11.9 ± 7.8	11.7 ± 7.3

	Quartiles of 20:0+22:0+24:0			
	Q1	**Q2**	**Q3**	**Q4**
Plasma 20:0+22:0+24:0	0.70 ± 0.14	1.00 ± 0.06	1.22 ± 0.08	1.63 ± 0.20
Age, years	60.5 ± 6.4	61.0 ± 5.8	60.2 ± 6.6	59.7 ± 6.7
Race, Caucasian (%)	99.5	99.7	99.1	98.8
BMI (kg/m^2)	26.3 ± 4.9	25.0 ± 4.4	25.1 ± 4.3	24.6 ± 3.8
Current smoker (%)	16.3	18.7	19.8	18.4
Physical activity, MET, hours/week	14.5 ± 19.6	17.1 ± 19.7	16.7 ± 19.0	16.8 ± 18.7
Hypertension (%)	31.3	22.8	17.6	16.9
Hypercholesterolemia (%)	39.3	39.3	31	33.1
Family history of diabetes (%)	31.3	25.2	24.3	26.3
Total energy (kcal/day)	1763 ± 479	1744 ± 506	1804 ± 489	1748 ± 518
AHEI	47.9 ± 10.2	48.9 ± 10.1	48.6 ± 10.5	49.2 ± 10.1
Peanuts (g/day)	2.0 ± 4.3	2.0 ± 5.7	2.6 ± 4.4	2.8 ± 5.7
Peanut butter (g/day)	3.2 ± 11.9	3.7 ± 10.9	4.1 ± 10.8	4.4 ± 10.9
Coffee (ml/day)	329 ± 350	332 ± 351	427 ± 378	422 ± 424
Alcohol (g/day)	6.2 ± 12.3	5.4 ± 9.4	5.9 ± 10.1	4.4 ± 7.7
Vegetable fat (g/day)	27.7 ± 12.0	27.4 ± 12.1	29.7 ± 12.7	29.9 ± 15.1

| Dairy fat (g/day) | 11.0 ± 5.9 | 11.6 ± 7.3 | 12.0 ± 7.6 | 11.8 ± 7.3 |

[1] Values are mean and ± SD for continuous variables and percent for categorical variables.
Abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHL, METs, metabolic equivalent; NHS, Nurses' Health Study.

Supplemental table 2. Baseline characteristics of 1,462 men in the Health Professionals Follow-Up Study (1994) according to quartiles of plasma fatty acids of VLCSFA[1]

| | Quartiles of 20:0 | | | |
	Q1	Q2	Q3	Q4
Plasma 20:0	0.12 ± 0.02	0.17 ± 0.01	0.20 ± 0.01	0.25 ± 0.03
Age, years	66.1 ± 8.3	64.9 ± 8.6	63.2 ± 8.7	63.2 ± 8.8
Race, Caucasian (%)	94.6	93.1	91.7	94.7
BMI (kg/m^2)	26.3 ± 3.3	25.6 ± 3.3	25.4 ± 3.0	25.5 ± 3.0
Current smoker (%)	8.5	5.9	7.0	9.9
Physical activity, MET, hours/week	35.8 ± 42.2	37.3 ± 40.7	36.2 ± 36.9	34.9 ± 32.5
Hypertension (%)	30.1	26.9	22.9	17.1
Hypercholesterolemia (%)	32.5	23.8	25.5	23.4
Family history of diabetes (%)	25.7	21.8	23.0	19.4
Total energy (kcal/day)	2054 ± 598	2010 ± 598	2033 ± 633	2075 ± 595
AHEI	48.7 ± 10.3	47.9 ± 10.2	48.5 ± 10.4	47.7 ± 10.1
Peanuts (g/day)	5.2 ± 11.9	4.8 ± 9.9	4.6 ± 10.2	5.0 ± 10.1
Peanut butter (g/day)	1.8 ± 6.9	2.6 ± 7.2	1.8 ± 6.4	3.5 ± 6.3
Coffee (ml/day)	472 ± 370	450 ± 422	471 ± 425	498 ± 401
Alcohol (g/day)	14.2 ± 18.9	11.3 ± 15.2	10.9 ± 14.0	9.5 ± 12.2
Vegetable fat (g/day)	33.3 ± 16.7	31.7 ± 14.7	33.1 ± 16.5	35.7 ± 17.3
Dairy fat (g/day)	11.0 ± 8.3	11.0 ± 8.6	11.4 ± 7.9	12.4 ± 9.4

| | Quartiles of 22:0 | | | |
	Q1	Q2	Q3	Q4
Plasma 22:0	0.27 ± 0.07	0.42 ± 0.04	0.55 ± 0.03	0.73 ± 0.10
Age, years	66.5 ± 8.3	64.4 ± 8.4	63.4 ± 8.6	62.9 ± 8.7
Race, Caucasian (%)	93.6	94.5	92.8	93.4
BMI (kg/m^2)	26.3 ± 3.4	25.6 ± 3.1	25.6 ± 3.1	25.4 ± 3.0
Current smoker (%)	7.5	8.3	8.2	7.3
Physical activity, MET, hours/week	33.5 ± 36.9	37.0 ± 42.3	36.0 ± 38.0	38.9 ± 38.0
Hypertension (%)	32.3	24.0	23.5	16.6
Hypercholesterolemia (%)	32.3	21.1	29.5	22.5
Family history of diabetes (%)	24.2	21.3	25.2	20.3
Total energy (kcal/day)	2041 ± 619	2047 ± 621	2015 ± 579	2073 ± 590
AHEI	47.9 ± 10.3	49.7 ± 10.9	48.7 ± 9.6	46.5 ± 9.7
Peanuts (g/day)	4.6 ± 10.9	5.1 ± 9.9	5.1 ± 10.1	5.1 ± 10.2
Peanut butter (g/day)	2.9 ± 8.1	2.8 ± 9.2	2.8 ± 9.4	3.5 ± 7.4
Coffee (ml/day)	448 ± 401	447 ± 405	469 ± 423	496 ± 421
Alcohol (g/day)	13.4 ± 18.5	12.1 ± 16.2	10.9 ± 13.2	9.6 ± 12.9
Vegetable fat (g/day)	32.1 ± 16.1	33.3 ± 17.3	33.1 ± 15.8	35.8 ± 16.0

Dairy fat (g/day)	10.8 ± 7.8	11.4 ± 9.6	11.0 ± 7.7	12.5 ± 8.9

	Quartiles of 24:0			
	Q1	**Q2**	**Q3**	**Q4**
Plasma 24:0	0.22 ± 0.05	0.35 ± 0.03	0.46 ± 0.03	0.62 ± 0.09
Age, years	66.6 ± 8.2	64.7 ± 8.5	63.0 ± 8.7	62.5 ± 8.6
Race, Caucasian (%)	92.3	95.3	92.3	94.2
BMI (kg/m^2)	26.3 ± 3.3	25.7 ± 3.2	25.6 ± 3.2	25.3 ± 3.0
Current smoker (%)	8.0	6.4	9.6	7.2
Physical activity, MET, hours/week	32.6 ± 37.6	38.6 ± 42.4	34.9 ± 37.4	40.4 ± 37.5
Hypertension (%)	33.1	22.8	22.4	16.3
Hypercholesterolemia (%)	30.2	25.1	24.9	16.3
Family history of diabetes (%)	24.0	22.3	22.9	24.9
Total energy (kcal/day)	2054 ± 617	2033 ± 617	2020 ± 592	2062 ± 581
AHEI	47.1 ± 10.2	50.3 ± 10.5	48.2 ± 9.8	48.0 ± 10.2
Peanuts (g/day)	4.9 ± 11.5	4.9 ± 10.9	4.9 ± 10.8	5.0 ± 9.1
Peanut butter (g/day)	2.1 ± 8.9	2.7 ± 11.2	2.1 ± 10.4	3.5 ± 8.2
Coffee (ml/day)	446 ± 377	446 ± 371	468 ± 446	520 ± 425
Alcohol (g/day)	12.3 ± 17.6	12.0 ± 15.7	11.2 ± 14.5	11.3 ± 13.8
Vegetable fat (g/day)	32.5 ± 16.0	33.0 ± 17.4	33.2 ± 15.8	35.6 ± 16.3
Dairy fat (g/day)	1.9 ± 1.6	1.9 ± 1.6	11.3 ± 8.3	2.2 ± 1.8

	Quartiles of 20:0+22:0+24:0			
	Q1	**Q2**	**Q3**	**Q4**
Plasma 20:0+22:0+24:0	0.63 ± 0.13	0.94 ± 0.08	1.20 ± 0.07	1.57 ± 0.20
Age, years	66.4 ± 8.2	64.8 ± 8.6	62.8 ± 8.5	63.1 ± 8.7
Race, Caucasian (%)	94.1	93.8	92.8	93.6
BMI (kg/m^2)	26.4 ± 3.3	25.6 ± 3.2	25.5 ± 3.0	25.3 ± 3.0
Current smoker (%)	7.9	7.3	8.2	7.8
Physical activity, MET, hours/week	32.8 ± 36.9	38.6 ± 44.2	35.3 ± 36.9	39.3 ± 36.4
Hypertension (%)	33.3	22.8	22.3	17.0
Hypercholesterolemia (%)	32.7	21.1	25.8	25.1
Family history of diabetes (%)	25.2	21.2	23.9	20.1
Total energy (kcal/day)	2059 ± 623	2021 ± 603	2016 ± 580	2074 ± 604
AHEI	47.7 ± 10.3	49.7 ± 9.8	48.3 ± 9.6	47.4 ± 10.1
Peanuts (g/day)	4.8 ± 11.9	4.9 ± 10.9	4.9 ± 10.8	5.0 ± 10.2
Peanut butter (g/day)	2.8 ± 7.6	2.6 ± 10.5	2.6 ± 10.2	3.5 ± 10.2
Coffee (ml/day)	448 ± 403	446 ± 405	471 ± 451	519 ± 424
Alcohol (g/day)	13.2 ± 18.5	12.1 ± 15.8	10.7 ± 13.3	10.2 ± 13.2
Vegetable fat (g/day)	32.5 ± 16.3	32.9 ± 16.9	33.0 ± 16.2	35.9 ± 15.8

Supplementary data

Dairy fat (g/day)	11.2 ± 8.7	11.0 ± 8.7	11.0 ± 7.6	12.3 ± 9.1

[1] **Supplemental table 3. Partial Spearman correlations between circulating plasma fatty acid biomarkers of 20:0, 22:0, and 24:0 among 708 participants in the Nurses' Health Study and 808 participants in the Health Professionals Follow-Up Study**

Values are mean and ± SD for continuous variables and percent for categorical variables.
Abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; METs, metabolic equivalent; NHS, Nurses' Health Study.

Supplementary data

	Plasma fatty acids[1]		
	20:0	**22:0**	**24:0**
NHS			
20:0	1.0	0.77§	0.73§
22:0	0.77§	1.0	0.92§
24:0	0.69§	0.92§	1.0
14:0	-0.42§	-0.48§	-0.46§
16:0	-0.48§	-0.62§	-0.62§
18:0	0.45§	0.26§	0.19§
15:0	-0.20§	-0.25§	-0.31§
17:0	0.26§	0.12§	0.08†
trans 16:1n-7	-0.06	-0.12§	-0.23§
trans 18:1	0.09†	-0.01	-0.17§
trans 18:2	0.01	-0.08‡	-0.22§
18:2	0.24§	0.41§	0.38§
20:4	0.26§	0.39§	0.45§
EPA	0.11‡	0.11‡	0.20§
DHA	0.17§	0.23§	0.34§
HPFS			
20:0	1.0	0.71§	0.68§
22:0	0.71§	1.0	0.89§
24:0	0.68§	0.89§	1.0
14:0	-0.39§	-0.49§	-0.49§
16:0	-0.51§	-0.60§	-0.59§
18:0	0.36§	0.07†	0.09†
15:0	-0.10§	-0.23§	-0.29§
17:0	0.21§	0.03	-0.03
trans 16:1n-7	0.07†	-0.07†	-0.10§
trans 18:1	<0.01	-0.06	-0.13§
trans 18:2	-0.08†	-0.17§	-0.20§
18:2	0.27§	0.42§	0.43§
20:4	0.23§	0.40§	0.41§
EPA	0.07	0.05	0.14§
DHA	0.16§	0.15§	0.24§

[1]Fatty acid concentrations were assessed from the plasma fraction of NHS and HPFS participants.
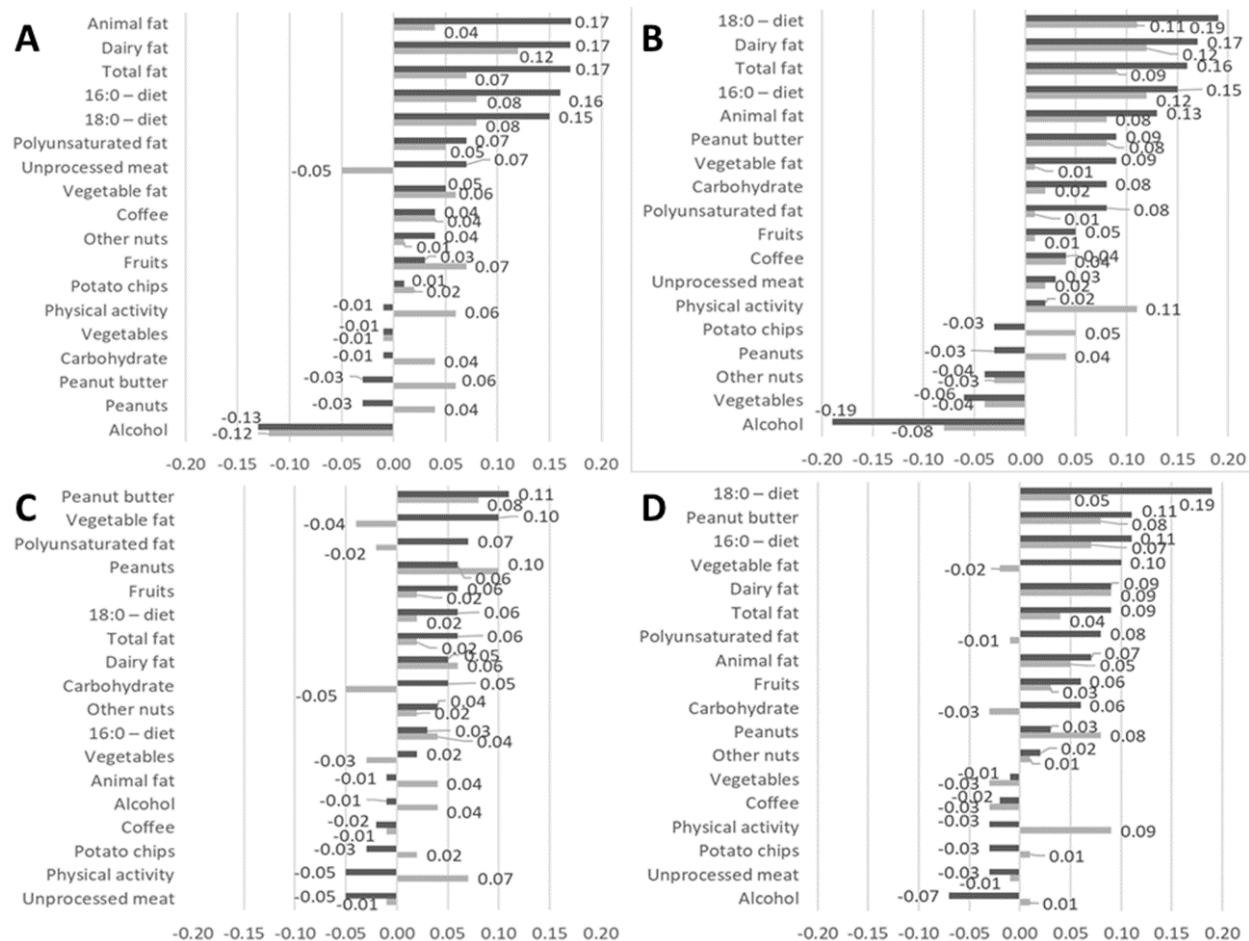†p-value for correlation coefficient < 0.05; ‡ p-value <0.01; § p-value <0.001.

Supplementary data

Supplemental table 4. Partial Spearman correlations between circulating erythrocyte fatty acid biomarkers of 20:0, 22:0, and 24:0 among 669 participants in the Nurses' Health Study and 852 participants in the Health Professionals Follow-Up Study

	Erythrocyte fatty acids[1]		
	20:0	**22:0**	**24:0**
NHS			
20:0	1.0	0.53§	0.32§
22:0	0.53§	1.0	0.83§
24:0	0.32§	0.83§	1.0
14:0	-0.29§	-0.52§	-0.48§
16:0	-0.27§	-0.63§	-0.69§
18:0	0.21§	0.40§	0.43§
15:0	-0.05	-0.36§	-0.44§
17:0	0.08†	-0.48§	-0.54§
trans 16:1n-7	-0.03	-0.44§	-0.54§
trans 18:1	0.16§	-0.33§	-0.49§
trans 18:2	0.31§	0.25§	0.02
18:2	-0.05	0.28§	0.19§
20:4	0.05	0.52§	0.50§
EPA	-0.11‡	0.12‡	0.23§
DHA	-0.01	0.33§	0.44§
HPFS			
20:0	1.0	0.53§	0.31§
22:0	0.53§	1.0	0.76§
24:0	0.31§	0.76§	1.0
14:0	-0.17§	-0.39§	-0.38§
16:0	-0.31§	-0.64§	-0.60§
18:0	0.35§	0.01	0.04
15:0	-0.06	-0.13§	-0.22§
17:0	0.26§	<0.01	-0.16§
trans 16:1n-7	0.14§	-0.07†	-0.23§
trans 18:1	0.11§	0.06	-0.19§
trans 18:2	-0.09‡	-0.15§	-0.35§
18:2	-0.19‡	-0.09§	-0.21§
20:4	0.17§	0.43§	0.39§
EPA	<0.01	-0.06	0.09†
DHA	0.09†	0.11§	0.25§

[1]Fatty acid concentrations were assessed from the erythrocyte fraction of NHS and HPFS participants.
†p-value for correlation coefficient < 0.05; ‡ p-value <0.01; § p-value <0.001.

Supplemental Figure 1. Spearman partial correlations between circulating erythrocyte fatty acid biomarkers of 20:0 (A), 22:0 (B), 24:0 (C), and sum of VLCSFAs (D) and dietary factors at baseline among 659 participants in the Nurses' Health Study and 704 participants in the Health Professionals Follow-up Study.[1,2]

[1]Abbreviations: BMI, body mass index; HPFS, Health Professionals Follow-up Study; METs, metabolic equivalent; NHS, Nurses' Health Study.
[2]Correlations were adjusted for age, total energy intake, and BMI
 Fatty acid concentrations were assessed from the plasma fraction of HPFS and NHS participants
 Dietary and nutrient factors were assessed using the average of self-reported responses in 1990 and 1994 in the HPFS (black bars) and 1986 and 1990 in the NHS (grey bars).