

Appendix: Supplementary tables

Supplementary table 1. Spearman correlations among individual saturated fatty acids

	NHS				HPFS			
	12:0	14:0	16:0	18:0	12:0	14:0	16:0	18:0
4:0-10:0	0.82	0.91	0.46	0.38	0.84	0.90	0.48	0.41
12:0		0.82	0.44	0.45		0.81	0.46	0.43
14:0			0.70	0.65			0.75	0.67
16:0				0.93				0.92

All P values <0.001.

Supplementary table 2. Stratified analysis of associations between saturated fatty acids and CHD risk in NHS (1984-2012) and HPFS (1986-2010). *

		Hazard ratio of CHD				P
		Age				interaction
		<65yrs	P	≥65yrs	P	
Polyunsaturated fat to replace	12:0-14:0	0.91 (0.77, 1.08)	0.28	1.10 (0.96, 1.27)	0.18	0.82
	16:0	0.97 (0.84, 1.11)	0.63	0.82 (0.74, 0.92)	<0.001	0.79
	18:0	0.92 (0.79, 1.07)	0.27	0.91 (0.81, 1.02)	0.11	0.84
	12:0-18:0	0.93 (0.87, 0.98)	0.01	0.92 (0.88, 0.96)	<0.001	0.82
Monounsaturated fat to replace	12:0-14:0	0.97 (0.83, 1.13)	0.65	1.15 (1.01, 1.31)	0.03	0.48
	16:0	1.02 (0.87, 1.20)	0.81	0.86 (0.76, 0.97)	0.02	0.44
	18:0	0.97 (0.81, 1.15)	0.70	0.96 (0.84, 1.09)	0.55	0.49
	12:0-18:0	0.96 (0.87, 1.05)	0.36	0.95 (0.89, 1.01)	0.11	0.40
Whole-grain carbohydrate to replace	12:0-14:0	0.92 (0.78, 1.09)	0.35	1.13 (0.98, 1.30)	0.09	0.57
	16:0	0.98 (0.86, 1.11)	0.75	0.85 (0.77, 0.94)	0.001	0.61
	18:0	0.93 (0.80, 1.09)	0.36	0.93 (0.82, 1.04)	0.21	0.56
	12:0-18:0	0.94 (0.89, 0.99)	0.03	0.94 (0.90, 0.98)	0.002	0.62
Plant protein to replace	12:0-14:0	0.94 (0.79, 1.12)	0.52	1.10 (0.95, 1.27)	0.19	0.36
	16:0	1.00 (0.88, 1.15)	0.96	0.83 (0.75, 0.92)	<0.001	0.33
	18:0	0.95 (0.81, 1.11)	0.51	0.90 (0.80, 1.02)	0.10	0.37
	12:0-18:0	0.96 (0.89, 1.03)	0.24	0.91 (0.86, 0.96)	0.001	0.33
		BMI				
		<30kg/m²	P	≥30kg/m²	P	
Polyunsaturated fat to replace	12:0-14:0	1.04 (0.92, 1.17)	0.53	0.89 (0.68, 1.16)	0.38	0.69
	16:0	0.88 (0.80, 0.97)	0.01	0.91 (0.74, 1.13)	0.41	0.70
	18:0	0.93 (0.84, 1.03)	0.15	0.90 (0.72, 1.12)	0.33	0.67
	12:0-18:0	0.93 (0.90, 0.97)	0.001	0.89 (0.82, 0.97)	0.01	0.69
Monounsaturated fat to replace	12:0-14:0	1.09 (0.97, 1.22)	0.14	0.98 (0.77, 1.25)	0.87	0.69
	16:0	0.92 (0.83, 1.03)	0.14	1.00 (0.78, 1.28)	>0.99	0.73
	18:0	0.98 (0.87, 1.10)	0.71	0.97 (0.75, 1.26)	0.83	0.68
	12:0-18:0	0.96 (0.91, 1.02)	0.24	0.94 (0.82, 1.08)	0.38	0.75
Whole-grain carbohydrate to replace	12:0-14:0	1.06 (0.94, 1.20)	0.34	0.90 (0.69, 1.17)	0.44	0.52
	16:0	0.90 (0.83, 0.99)	0.02	0.94 (0.77, 1.14)	0.52	0.53
	18:0	0.94 (0.85, 1.05)	0.28	0.91 (0.72, 1.15)	0.42	0.52
	12:0-18:0	0.95 (0.92, 0.99)	0.01	0.91 (0.84, 0.99)	0.02	0.54
Plant protein to replace	12:0-14:0	1.04 (0.92, 1.18)	0.54	0.97 (0.74, 1.28)	0.83	0.38
	16:0	0.88 (0.81, 0.97)	0.01	1.00 (0.81, 1.24)	0.97	0.37
	18:0	0.92 (0.83, 1.03)	0.13	0.98 (0.77, 1.24)	0.86	0.38
	12:0-18:0	0.93 (0.89, 0.97)	0.002	0.97 (0.87, 1.08)	0.60	0.37
		Physical activity				
		<18 METs/wk	P	≥18 METs/wk	P	
Polyunsaturated fat	12:0-14:0	0.96 (0.84, 1.09)	0.50	1.17 (0.96, 1.44)	0.13	0.61

to replace	16:0	0.89 (0.80, 0.99)	0.03	0.82 (0.71, 0.96)	0.01	0.59
	18:0	0.94 (0.84, 1.05)	0.28	0.90 (0.76, 1.06)	0.19	0.62
	12:0-18:0	0.92 (0.88, 0.96)	<0.001	0.92 (0.87, 0.98)	0.01	0.60
Monounsaturated fat to replace	12:0-14:0	1.02 (0.91, 1.15)	0.74	1.21 (1.00, 1.46)	0.05	0.63
	16:0	0.94 (0.83, 1.06)	0.33	0.84 (0.71, 1.00)	0.05	0.62
	18:0	1.00 (0.88, 1.14)	0.98	0.93 (0.78, 1.12)	0.45	0.63
Whole-grain carbohydrate to replace	12:0-18:0	0.96 (0.90, 1.03)	0.29	0.93 (0.85, 1.02)	0.12	0.59
	12:0-14:0	0.98 (0.86, 1.12)	0.77	1.18 (0.96, 1.45)	0.11	0.40
	16:0	0.91 (0.83, 1.01)	0.08	0.83 (0.73, 0.96)	0.01	0.40
Plant protein to replace	18:0	0.96 (0.85, 1.08)	0.51	0.90 (0.76, 1.06)	0.21	0.40
	12:0-18:0	0.94 (0.90, 0.98)	0.01	0.92 (0.87, 0.98)	0.01	0.40
	12:0-14:0	0.97 (0.85, 1.11)	0.69	1.18 (0.96, 1.46)	0.12	0.65
Plant protein to replace	16:0	0.91 (0.82, 1.01)	0.07	0.83 (0.72, 0.96)	0.01	0.66
	18:0	0.95 (0.84, 1.08)	0.44	0.89 (0.76, 1.06)	0.20	0.65
	12:0-18:0	0.93 (0.88, 0.99)	0.01	0.92 (0.86, 0.99)	0.02	0.67

Current smoking						
		No	<i>P</i>	Yes	<i>P</i>	
Polyunsaturated fat to replace	12:0-14:0	1.02 (0.90, 1.15)	0.77	1.04 (0.81, 1.33)	0.76	0.19
	16:0	0.87 (0.80, 0.96)	0.004	0.92 (0.75, 1.14)	0.46	0.20
	18:0	0.91 (0.83, 1.01)	0.08	0.99 (0.78, 1.26)	0.96	0.18
	12:0-18:0	0.92 (0.88, 0.95)	<0.001	0.98 (0.90, 1.08)	0.74	0.20
Monounsaturated fat to replace	12:0-14:0	1.08 (0.96, 1.21)	0.19	1.00 (0.81, 1.25)	0.99	0.93
	16:0	0.92 (0.82, 1.02)	0.12	0.90 (0.69, 1.16)	0.42	0.94
	18:0	0.97 (0.86, 1.08)	0.56	0.97 (0.73, 1.31)	0.86	0.94
	12:0-18:0	0.95 (0.89, 1.01)	0.08	0.96 (0.82, 1.13)	0.64	0.96
Whole-grain carbohydrate to replace	12:0-14:0	1.04 (0.92, 1.17)	0.55	1.03 (0.81, 1.31)	0.80	0.44
	16:0	0.89 (0.82, 0.97)	0.01	0.92 (0.75, 1.13)	0.43	0.44
	18:0	0.93 (0.84, 1.03)	0.15	0.99 (0.77, 1.27)	0.93	0.44
	12:0-18:0	0.93 (0.90, 0.97)	<0.001	0.98 (0.89, 1.07)	0.60	0.43
Plant protein to replace	12:0-14:0	1.03 (0.91, 1.17)	0.63	1.01 (0.78, 1.30)	0.95	0.72
	16:0	0.89 (0.81, 0.97)	0.01	0.90 (0.73, 1.12)	0.35	0.71
	18:0	0.92 (0.83, 1.02)	0.13	0.96 (0.74, 1.25)	0.78	0.72
	12:0-18:0	0.93 (0.88, 0.97)	0.001	0.96 (0.85, 1.08)	0.48	0.75

*, Other covariates adjusted were the same as figure 2.

Supplementary table 3. Associations between individual saturated fatty acids and CHD risk in NHS (1984-2012) and HPFS (1986-2010)

adjusting for baseline BMI as a covariate. *

		Hazard ratio of CHD					
		NHS	<i>P</i>	HPFS	<i>P</i>	Pooled ⁵	<i>P</i>
Polyunsaturated fat to replace	12:0-14:0	0.99 (0.83, 1.18)	0.88	1.02 (0.88, 1.16)	0.83	1.00 (0.90, 1.12)	0.94
	16:0	0.87 (0.76, 1.00)	0.05	0.91 (0.82, 1.01)	0.07	0.89 (0.82, 0.97)	0.01
	18:0	0.84 (0.72, 0.99)	0.03	0.98 (0.88, 1.09)	0.70	0.93 (0.85, 1.02)	0.12
	12:0-18:0	0.89 (0.84, 0.94)	<0.001	0.96 (0.92, 1.00)	0.05	0.93 (0.90, 0.96)	<0.001
Monounsaturated fat to replace	12:0-14:0	1.05 (0.89, 1.23)	0.57	1.07 (0.94, 1.21)	0.32	1.06 (0.96, 1.17)	0.25
	16:0	0.92 (0.79, 1.08)	0.32	0.94 (0.83, 1.07)	0.37	0.94 (0.85, 1.03)	0.19
	18:0	0.89 (0.74, 1.07)	0.21	1.03 (0.91, 1.17)	0.63	0.98 (0.88, 1.09)	0.74
	12:0-18:0	0.92 (0.84, 1.00)	0.05	0.99 (0.93, 1.06)	0.82	0.96 (0.91, 1.02)	0.17
Whole-grain carbohydrate to replace	12:0-14:0	1.03 (0.87, 1.23)	0.71	1.02 (0.89, 1.17)	0.74	1.03 (0.92, 1.14)	0.63
	16:0	0.92 (0.81, 1.04)	0.18	0.92 (0.83, 1.01)	0.09	0.92 (0.85, 0.99)	0.03
	18:0	0.88 (0.74, 1.03)	0.12	0.99 (0.88, 1.10)	0.80	0.95 (0.86, 1.04)	0.27
	12:0-18:0	0.93 (0.88, 0.98)	0.01	0.96 (0.92, 1.00)	0.08	0.95 (0.92, 0.98)	0.002
Plant protein to replace	12:0-14:0	1.04 (0.87, 1.25)	0.64	1.00 (0.86, 1.15)	0.96	1.01 (0.91, 1.13)	0.81
	16:0	0.92 (0.81, 1.06)	0.25	0.89 (0.80, 0.99)	0.03	0.90 (0.83, 0.98)	0.02
	18:0	0.89 (0.75, 1.05)	0.16	0.96 (0.85, 1.08)	0.49	0.94 (0.85, 1.03)	0.17
	12:0-18:0	0.93 (0.87, 1.00)	0.05	0.94 (0.89, 0.99)	0.01	0.93 (0.90, 0.98)	0.002

*, Other covariates adjusted were the same as figure 2.

Supplementary table 4. Associations between individual saturated fatty acids and CHD risk in NHS (1984-2012) and HPFS (1986-2010) adjusting for incident hypercholesterolemia, hypertension and diabetes during the follow-up. *

		Hazard ratio of CHD					
		NHS	<i>P</i>	HPFS	<i>P</i>	Pooled ⁵	<i>P</i>
Polyunsaturated fat to replace	12:0-14:0	0.98 (0.82, 1.16)	0.80	1.03 (0.89, 1.18)	0.71	1.01 (0.90, 1.12)	0.89
	16:0	0.89 (0.78, 1.02)	0.09	0.89 (0.80, 0.99)	0.03	0.89 (0.82, 0.96)	0.005
	18:0	0.85 (0.72, 0.99)	0.04	0.97 (0.87, 1.09)	0.62	0.93 (0.85, 1.02)	0.12
	12:0-18:0	0.89 (0.84, 0.95)	<0.001	0.95 (0.91, 0.99)	0.02	0.93 (0.90, 0.96)	<0.001
Monounsaturated fat to replace	12:0-14:0	1.04 (0.89, 1.22)	0.61	1.07 (0.95, 1.22)	0.27	1.06 (0.96, 1.17)	0.24
	16:0	0.95 (0.81, 1.11)	0.50	0.92 (0.81, 1.04)	0.20	0.93 (0.84, 1.03)	0.15
	18:0	0.90 (0.75, 1.08)	0.26	1.02 (0.90, 1.16)	0.71	0.98 (0.88, 1.09)	0.73
	12:0-18:0	0.94 (0.86, 1.02)	0.13	0.98 (0.92, 1.05)	0.64	0.96 (0.91, 1.02)	0.20
Whole-grain carbohydrate to replace	12:0-14:0	1.03 (0.87, 1.23)	0.73	1.03 (0.90, 1.19)	0.62	1.03 (0.93, 1.15)	0.55
	16:0	0.94 (0.83, 1.07)	0.34	0.90 (0.81, 0.99)	0.03	0.91 (0.84, 0.99)	0.02
	18:0	0.89 (0.76, 1.05)	0.17	0.98 (0.88, 1.10)	0.73	0.95 (0.87, 1.04)	0.29
	12:0-18:0	0.94 (0.89, 0.99)	0.03	0.96 (0.92, 1.00)	0.04	0.95 (0.92, 0.98)	0.003
Plant protein to replace	12:0-14:0	1.05 (0.87, 1.25)	0.63	1.01 (0.88, 1.16)	0.88	1.02 (0.92, 1.14)	0.68
	16:0	0.95 (0.83, 1.09)	0.48	0.88 (0.79, 0.97)	0.01	0.90 (0.83, 0.98)	0.02
	18:0	0.90 (0.76, 1.07)	0.24	0.96 (0.85, 1.08)	0.46	0.94 (0.85, 1.03)	0.20
	12:0-18:0	0.95 (0.89, 1.02)	0.17	0.93 (0.89, 0.98)	0.01	0.94 (0.90, 0.98)	0.004

*, Other covariates adjusted were the same as figure 2.

Supplementary table 5. Associations between individual saturated fatty acids and CHD risk in NHS (1984-2012) and HPFS (1986-2010) after excluding participants with probable fatal CHD. *

		Hazard ratio of CHD					
		NHS	P	HPFS	P	Pooled⁵	P
Substitution of PUFA	12:0-14:0	0.98 (0.81, 1.18)	0.81	1.12 (0.96, 1.31)	0.14	1.06 (0.94, 1.19)	0.32
	16:0	0.87 (0.75, 1.00)	0.05	0.88 (0.79, 0.99)	0.03	0.88 (0.80, 0.96)	0.003
	18:0	0.87 (0.74, 1.03)	0.10	0.93 (0.83, 1.04)	0.18	0.91 (0.83, 1.00)	0.04
	12:0-18:0	0.89 (0.84, 0.95)	<0.001	0.95 (0.90, 0.99)	0.02	0.93 (0.89, 0.96)	<0.001
Substitution of MUFA	12:0-14:0	1.03 (0.87, 1.22)	0.70	1.16 (1.01, 1.33)	0.04	1.11 (0.99, 1.23)	0.07
	16:0	0.91 (0.77, 1.08)	0.28	0.91 (0.80, 1.04)	0.17	0.91 (0.82, 1.01)	0.08
	18:0	0.92 (0.76, 1.11)	0.37	0.97 (0.85, 1.10)	0.61	0.95 (0.85, 1.06)	0.35
	12:0-18:0	0.92 (0.84, 1.01)	0.07	0.97 (0.90, 1.05)	0.44	0.95 (0.90, 1.01)	0.08
Substitution of whole grain carbohydrates	12:0-14:0	1.01 (0.84, 1.21)	0.93	1.12 (0.96, 1.30)	0.15	1.07 (0.95, 1.20)	0.24
	16:0	0.90 (0.78, 1.03)	0.12	0.88 (0.79, 0.98)	0.02	0.89 (0.82, 0.97)	0.01
	18:0	0.89 (0.75, 1.06)	0.20	0.92 (0.82, 1.04)	0.17	0.91 (0.83, 1.00)	0.06
	12:0-18:0	0.92 (0.87, 0.97)	0.003	0.94 (0.90, 0.99)	0.01	0.93 (0.90, 0.97)	<0.001
Substitution of plant proteins	12:0-14:0	1.04 (0.86, 1.26)	0.68	1.10 (0.94, 1.28)	0.24	1.08 (0.95, 1.21)	0.24
	16:0	0.93 (0.80, 1.07)	0.30	0.87 (0.78, 0.97)	0.01	0.89 (0.81, 0.97)	0.01
	18:0	0.92 (0.77, 1.10)	0.38	0.90 (0.80, 1.02)	0.10	0.91 (0.82, 1.01)	0.06
	12:0-18:0	0.94 (0.88, 1.02)	0.13	0.93 (0.88, 0.98)	0.01	0.93 (0.89, 0.97)	0.002

*, Other covariates adjusted were the same as figure 2.