

Table S1 Healthy lifestyle factor definitions

Healthy lifestyle factor	Source and definition	Self-reported UK Biobank field code
No current smoking	UK Biobank Touchscreen questionnaire at baseline; Smoking status was defined as current, previous, never smoker; Former smokers who had quit smoking more than 30 years were also considered as no current smoking	20116, 2897
Regular physical activity	UK Biobank Touchscreen questionnaire at baseline; ≥ 150 minutes moderate activity per week OR ≥ 75 minutes vigorous activity per week OR equivalent combination OR moderate physical activity at least 5 days a week and vigorous activity once a week	884, 894, 904, 914
Healthy diet	UK Biobank Food Frequency Questionnaire at baseline; At least 4 of the following 6 food groups: 1. Fruits: ≥ 4 servings/day 2. Vegetables: ≥ 4 servings/day 3. Fish: ≥ 2 times/week 4. Processed meats: ≤ 1 times/week 5. Unprocessed red meats: ≤ 1.5 times/week 6. Whole grains: ≥ 3 servings/day (Amount per serving: fresh fruit—1 piece; dried fruit—5 pieces; cooked/raw vegetables—3 heaped tablespoons; bran/oat/muesli cereal—1 bowl/day; wholemeal/wholegrain bread—1 slice/day)	1309, 1319, 1289, 1299, 1329, 1339, 1349, 1369, 1379, 1389, 1438, 1448, 1458, 1468
No alcohol consumption	UK Biobank Touchscreen questionnaire at baseline; never alcohol use	20117
Moderate BMI	UK Biobank Physical measures at baseline; 18.5–30	21001

Adapted from “Genetic Risk for Overall Cancer and the Benefit of Adherence to a Healthy Lifestyle,” by ZhuM, WangT, HuangY, *et al.*, 2021, *Cancer Research*, 81(17), p. 4618. Copyright 2021 by American Association for Cancer Research. Adapted with permission.

Table S2 The ICD-10 codes for gastrointestinal cancer

Cancer type	ICD-10 base code	Included subcodes
Esophageal cancer	C15	0–5, 8–9
Gastric cancer	C16	0–6, 8–9
Colorectal Cancer	C18	2–9
Colorectal Cancer	C21	0–2, 8
Liver cancer	C22	0–2, 7, 9
Bile duct cancer	C24	0–1, 8–9
Pancreatic cancer	C25	0–3, 7–9

Subcodes represent the fourth-digit extensions of ICD-10 classifications. Ranges indicate contiguous codes (e.g., 0–5 = C15.0, C15.1...C15.5), while individual numbers denote specific subcategories (e.g., C22.7).

Table S3 Baseline characteristics of participants by quartiles of plasma SFAs in the UK Biobank cohort

Demographics	Quartile of plasma SFAs				P value
	Q1 (N=22,811)	Q2 (N=22,809)	Q3 (N=22,812)	Q4 (N=22,807)	
Age (years)	53.9 (8.59)	55.4 (8.11)	56.6 (7.75)	56.7 (7.57)	<0.001
Sex					<0.001
Female	11,052 (48.5%)	12,940 (56.7%)	13,145 (57.6%)	12,157 (53.3%)	
Male	11,759 (51.5%)	9,869 (43.3%)	9,667 (42.4%)	10,650 (46.7%)	
BMI (kg/m ²)	26.6 (4.80)	26.9 (4.69)	27.5 (4.70)	28.6 (4.68)	<0.001
Family history					<0.001
No	15,550 (68.2%)	15,037 (65.9%)	14,719 (64.5%)	14,644 (64.2%)	
Gastrointestinal cancer	2,154 (9.44%)	2,444 (10.7%)	2,596 (11.4%)	2,549 (11.2%)	
Other cancer	5,107 (22.4%)	5,328 (23.4%)	5,497 (24.1%)	5,614 (24.6%)	
Education					<0.001
Other	14,102 (61.8%)	14,749 (64.7%)	15,179 (66.5%)	15,919 (69.8%)	
College or above	8,709 (38.2%)	8,060 (35.3%)	7,633 (33.5%)	6,888 (30.2%)	
Smoking					<0.001
Never	13,690 (60.0%)	13,229 (58.0%)	12,638 (55.4%)	11,722 (51.4%)	
Previous	7,017 (30.8%)	7,459 (32.7%)	7,868 (34.5%)	8,270 (36.3%)	
Current	2,104 (9.22%)	2,121 (9.30%)	2,306 (10.1%)	2,815 (12.3%)	
Alcohol					<0.001
Unknown	28 (0.12%)	25 (0.11%)	28 (0.12%)	19 (0.08%)	
Never	1,301 (5.70%)	1,052 (4.61%)	923 (4.05%)	810 (3.55%)	
Previous	1,067 (4.68%)	734 (3.22%)	710 (3.11%)	704 (3.09%)	
Current	20,415 (89.5%)	20,998 (92.1%)	21,151 (92.7%)	21,274 (93.3%)	
DM					<0.001
No	20,639 (90.5%)	21,257 (93.2%)	21,176 (92.8%)	20,390 (89.4%)	
Yes	2,172 (9.52%)	1,552 (6.80%)	1,636 (7.17%)	2,417 (10.6%)	
TDI	-1.05 (3.24)	-1.38 (3.08)	-1.43 (3.02)	-1.35 (3.04)	<0.001
Lifestyle score					<0.001
1	559 (2.45%)	566 (2.48%)	608 (2.67%)	855 (3.75%)	
2	1,652 (7.24%)	1,838 (8.06%)	2,008 (8.80%)	2,396 (10.5%)	
3	4,329 (19.0%)	4,506 (19.8%)	4,733 (20.7%)	5,288 (23.2%)	
4	7,106 (31.2%)	7,189 (31.5%)	7,192 (31.5%)	7,227 (31.7%)	
5	9,165 (40.2%)	8,710 (38.2%)	8,271 (36.3%)	7,041 (30.9%)	

Values are shown as mean (SD) unless otherwise specified. Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). BMI, body mass index; DM, diabetes mellitus; SFA, saturated fatty acid; TDI, Townsend deprivation index.

Table S4 Baseline characteristics of participants by quartiles of plasma MUFAs in the UK Biobank cohort

Demographics	Quartile of plasma MUFAs				P value
	Q1 (N=22,810)	Q2 (N=22,810)	Q3 (N=22,809)	Q4 (N=22,810)	
Age (years)	53.9 (8.50)	55.7 (8.03)	56.6 (7.83)	56.4 (7.72)	<0.001
Sex:					<0.001
Female	12,758 (55.9%)	13,079 (57.3%)	12,626 (55.4%)	10,831 (47.5%)	
Male	10,052 (44.1%)	9,731 (42.7%)	10,183 (44.6%)	11,979 (52.5%)	
BMI (kg/m ²)	25.8 (4.43)	26.8 (4.60)	27.8 (4.71)	29.2 (4.74)	<0.001
Family history:					<0.001
No	15,467 (67.8%)	15,034 (65.9%)	14,818 (65.0%)	14,631 (64.1%)	
Gastrointestinal cancer	2,201 (9.65%)	2,382 (10.4%)	2,555 (11.2%)	2,605 (11.4%)	
Other cancer	5,142 (22.5%)	5,394 (23.6%)	5,436 (23.8%)	5,574 (24.4%)	
Education					<0.001
Other	13,642 (59.8%)	14,708 (64.5%)	15,421 (67.6%)	16,178 (70.9%)	
College or above	9,168 (40.2%)	8,102 (35.5%)	7,388 (32.4%)	6,632 (29.1%)	
Smoking					<0.001
Never	13,843 (60.7%)	13,305 (58.3%)	12,646 (55.4%)	11,485 (50.4%)	
Previous	7,068 (31.0%)	7,449 (32.7%)	7,870 (34.5%)	8,227 (36.1%)	
Current	1,899 (8.33%)	2,056 (9.01%)	2,293 (10.1%)	3,098 (13.6%)	
Alcohol					0.001
Unknown	29 (0.13%)	24 (0.11%)	24 (0.11%)	23 (0.10%)	
Never	1,098 (4.81%)	1,040 (4.56%)	1,022 (4.48%)	926 (4.06%)	
Previous	871 (3.82%)	749 (3.28%)	790 (3.46%)	805 (3.53%)	
Current	20,812 (91.2%)	20,997 (92.1%)	20,973 (92.0%)	21,056 (92.3%)	
DM					<0.001
No	21,261 (93.2%)	21,263 (93.2%)	20,999 (92.1%)	19,939 (87.4%)	
Yes	1,549 (6.79%)	1,547 (6.78%)	1,810 (7.94%)	2,871 (12.6%)	
TDI	-1.20 (3.19)	-1.39 (3.06)	-1.40 (3.04)	-1.21 (3.09)	<0.001
Lifestyle score					<0.001
1	497 (2.18%)	544 (2.38%)	644 (2.82%)	903 (3.96%)	
2	1,578 (6.92%)	1,792 (7.86%)	2,037 (8.93%)	2,487 (10.9%)	
3	4,298 (18.8%)	4,495 (19.7%)	4,674 (20.5%)	5,389 (23.6%)	
4	7,162 (31.4%)	7,250 (31.8%)	7,236 (31.7%)	7,066 (31.0%)	
5	9,275 (40.7%)	8,729 (38.3%)	8,218 (36.0%)	6,965 (30.5%)	

Values are shown as mean (SD) unless otherwise specified. Q1: ≤25th percentile (lowest concentration); Q2: >25th to ≤50th percentile; Q3: >50th to ≤75th percentile; Q4: >75th percentile (highest concentration). BMI, body mass index; DM, diabetes mellitus; MUFA, monounsaturated fatty acids; TDI, Townsend deprivation index.

Table S5 Baseline characteristics of participants by quartiles of plasma OMEGA3 PUFAs in the UK Biobank cohort

Demographics	Quartile of plasma OMEGA3 PUFAs				P value
	Q1 (N=22,813)	Q2 (N=22,808)	Q3 (N=22,808)	Q4 (N=22,810)	
Age (years)	53.2 (8.25)	55.0 (8.16)	56.4 (7.80)	58.0 (7.34)	<0.001
Sex					<0.001
Female	10,302 (45.2%)	11,707 (51.3%)	12,813 (56.2%)	14,472 (63.4%)	
Male	12,511 (54.8%)	11,101 (48.7%)	9,995 (43.8%)	8,338 (36.6%)	
BMI (kg/m ²)	27.3 (5.18)	27.5 (4.86)	27.6 (4.70)	27.2 (4.35)	<0.001
Family history					<0.001
No	15,385 (67.4%)	15,182 (66.6%)	14,749 (64.7%)	14,634 (64.2%)	
Gastrointestinal cancer	2,288 (10.0%)	2,356 (10.3%)	2,484 (10.9%)	2,615 (11.5%)	
Other cancer	5,140 (22.5%)	5,270 (23.1%)	5,575 (24.4%)	5,561 (24.4%)	
Education					<0.001
Other	15,293 (67.0%)	14,931 (65.5%)	14,981 (65.7%)	14,744 (64.6%)	
College or above	7,520 (33.0%)	7,877 (34.5%)	7,827 (34.3%)	8,066 (35.4%)	
Smoking					<0.001
Never	12,733 (55.8%)	12,751 (55.9%)	12,780 (56.0%)	13,015 (57.1%)	
Previous	6,806 (29.8%)	7,620 (33.4%)	8,011 (35.1%)	8,177 (35.8%)	
Current	3,274 (14.4%)	2,437 (10.7%)	2,017 (8.84%)	1,618 (7.09%)	
Alcohol					<0.001
Unknown	32 (0.14%)	25 (0.11%)	19 (0.08%)	24 (0.11%)	
Never	1,253 (5.49%)	998 (4.38%)	944 (4.14%)	891 (3.91%)	
Previous	1,082 (4.74%)	764 (3.35%)	706 (3.10%)	663 (2.91%)	
Current	20,446 (89.6%)	21,021 (92.2%)	21,139 (92.7%)	21,232 (93.1%)	
DM					<0.001
No	20,774 (91.1%)	20,799 (91.2%)	20,855 (91.4%)	21,034 (92.2%)	
Yes	2,039 (8.94%)	2,009 (8.81%)	1,953 (8.56%)	1,776 (7.79%)	
TDI	-0.94 (3.21)	-1.22 (3.12)	-1.45 (3.06)	-1.60 (2.96)	<0.001
Lifestyle score					<0.001
1	884 (3.87%)	644 (2.82%)	606 (2.66%)	454 (1.99%)	
2	2,312 (10.1%)	2,018 (8.85%)	1,914 (8.39%)	1,650 (7.23%)	
3	4,880 (21.4%)	4,972 (21.8%)	4,639 (20.3%)	4,365 (19.1%)	
4	7,051 (30.9%)	7,211 (31.6%)	7,201 (31.6%)	7,251 (31.8%)	
5	7,686 (33.7%)	7,963 (34.9%)	8,448 (37.0%)	9,090 (39.9%)	

Values are shown as mean (SD) unless otherwise specified. Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). BMI, body mass index; DM, diabetes mellitus; OMEGA3 PUFA, OMEGA3 polyunsaturated fatty acids; TDI, Townsend deprivation index.

Table S6 Baseline characteristics of participants by quartiles of plasma OMEGA6 PUFAs in the UK Biobank cohort

Demographics	Quartile of plasma OMEGA6 PUFAs				p-value
	Q1 (N=22,812)	Q2 (N=22,812)	Q3 (N=22,807)	Q4 (N=22,808)	
Age (years)	55.1 (8.68)	55.1 (8.23)	55.8 (7.85)	56.5 (7.49)	<0.001
Sex					<0.001
Female	9,510 (41.7%)	11,961 (52.4%)	13,193 (57.8%)	14,630 (64.1%)	
Male	13,302 (58.3%)	10,851 (47.6%)	9,614 (42.2%)	8,178 (35.9%)	
BMI (kg/m ²)	27.6 (5.13)	27.2 (4.80)	27.3 (4.72)	27.4 (4.46)	<0.001
Family history:					<0.001
No	15,338 (67.2%)	15,054 (66.0%)	14,786 (64.8%)	14,772 (64.8%)	
Gastrointestinal cancer	2,316 (10.2%)	2,357 (10.3%)	2,520 (11.0%)	2,550 (11.2%)	
Other cancer	5,158 (22.6%)	5,401 (23.7%)	5,501 (24.1%)	5,486 (24.1%)	
Education					0.004
Other	14,891 (65.3%)	14,838 (65.0%)	15,052 (66.0%)	15,168 (66.5%)	
College or above	7,921 (34.7%)	7,974 (35.0%)	7,755 (34.0%)	7,640 (33.5%)	
Smoking					<0.001
Never	12,450 (54.6%)	12,943 (56.7%)	12,916 (56.6%)	12,970 (56.9%)	
Previous	7,829 (34.3%)	7,542 (33.1%)	7,647 (33.5%)	7,596 (33.3%)	
Current	2,533 (11.1%)	2,327 (10.2%)	2,244 (9.84%)	2,242 (9.83%)	
Alcohol					<0.001
Unknown	35 (0.15%)	20 (0.09%)	20 (0.09%)	25 (0.11%)	
Never	1,068 (4.68%)	944 (4.14%)	959 (4.20%)	1,115 (4.89%)	
Previous	1,000 (4.38%)	795 (3.49%)	708 (3.10%)	712 (3.12%)	
Current	20,709 (90.8%)	21,053 (92.3%)	21,120 (92.6%)	20,956 (91.9%)	
DM					<0.001
No	19,489 (85.4%)	21,042 (92.2%)	21,450 (94.1%)	21,481 (94.2%)	
Yes	3,323 (14.6%)	1,770 (7.76%)	1,357 (5.95%)	1,327 (5.82%)	
TDI	-1.09 (3.24)	-1.31 (3.10)	-1.42 (3.04)	-1.40 (3.01)	<0.001
Lifestyle score					0.04
1	729 (3.20%)	655 (2.87%)	591 (2.59%)	613 (2.69%)	
2	2,001 (8.77%)	1,989 (8.72%)	1,950 (8.55%)	1,954 (8.57%)	
3	4,719 (20.7%)	4,690 (20.6%)	4,705 (20.6%)	4,742 (20.8%)	
4	7,074 (31.0%)	7,145 (31.3%)	7,273 (31.9%)	7,222 (31.7%)	
5	8,289 (36.3%)	8,333 (36.5%)	8,288 (36.3%)	8,277 (36.3%)	

Values are shown as mean (SD) unless otherwise specified. Q1: ≤25th percentile (lowest concentration); Q2: >25th to ≤50th percentile; Q3: >50th to ≤75th percentile; Q4: >75th percentile (highest concentration). BMI, body mass index; DM, diabetes mellitus; OMEGA6 PUFA, OMEGA6 polyunsaturated fatty acids; TDI, Townsend deprivation index.

Table S7 Association between plasma SFAs and incident gastrointestinal cancer in the UK Biobank

Cancer	Quartile of plasma SFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	1.2 (0.99, 1.45)	1.28 (1.00, 1.63)	1.58 (1.17, 2.13)	0.051	1.19 (1.02, 1.39)	0.028
Esophageal cancer	1	1.35 (0.83, 2.21)	1.62 (0.87, 3.00)	2.54 (1.21, 5.33)	0.2	1.6 (1.10, 2.32)	0.014
Gastric cancer	1	0.56 (0.29, 1.07)	0.64 (0.30, 1.40)	0.47 (0.18, 1.24)	0.13	0.94 (0.56, 1.56)	0.8
Colorectal cancer	1	1.25 (0.95, 1.65)	1.23 (0.86, 1.75)	1.3 (0.84, 2.02)	0.2	1.03 (0.82, 1.29)	0.8
Liver cancer	1	2.23 (1.18, 4.24)	2.37 (1.01, 5.53)	4.32 (1.56, 12.0)	0.005	1.53 (0.93, 2.54)	0.1
Bile duct cancer	1	0.19 (0.04, 0.86)	0.32 (0.06, 1.72)	1.18 (0.17, 8.13)	0.9	2.67 (0.84, 8.51)	0.1
Pancreatic cancer	1	1.27 (0.77, 2.10)	1.38 (0.75, 2.55)	2.04 (0.98, 4.22)	0.056	1.21 (0.83, 1.75)	0.3

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma SFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer HR for 1 SD increase in plasma SFA (mmol/L). HR, hazards ratio; SFA, saturated fatty acid.

Table S8 Association between plasma MFAs and incident gastrointestinal cancer in the UK Biobank

Cancer	Quartile of plasma MFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	1 (0.83, 1.20)	1 (0.80, 1.25)	0.88 (0.67, 1.17)	0.4	1 (0.84, 1.18)	>0.9
Esophageal cancer	1	0.97 (0.60, 1.56)	1.02 (0.58, 1.82)	0.74 (0.36, 1.49)	0.4	0.78 (0.51, 1.19)	0.3
Gastric cancer	1	1.36 (0.74, 2.50)	2.38 (1.12, 5.04)	2.63 (1.06, 6.57)	0.3	1.35 (0.78, 2.33)	0.3
Colorectal cancer	1	0.97 (0.75, 1.25)	0.86 (0.62, 1.19)	0.95 (0.64, 1.42)	0.8	1.15 (0.89, 1.47)	0.3
Liver cancer	1	0.83 (0.44, 1.55)	0.68 (0.32, 1.48)	0.53 (0.20, 1.38)	0.2	0.79 (0.45, 1.40)	0.4
Bile duct cancer	1	1.72 (0.51, 5.79)	3.31 (0.65, 16.9)	0.71 (0.09, 5.57)	0.7	0.35 (0.09, 1.34)	0.12
Pancreatic cancer	1	0.9 (0.56, 1.43)	0.99 (0.57, 1.72)	0.62 (0.31, 1.23)	0.2	0.92 (0.61, 1.39)	0.7

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma MFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer HR for 1 SD increase in plasma MFA (mmol/L). HR, hazards ratio; MFA, monounsaturated fatty acids.

Table S9 Association between plasma OMEGA3 PUFAs and incident gastrointestinal cancer in the UK Biobank

Cancer	Quartile of plasma OMEGA3 PUFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	0.92 (0.79, 1.07)	0.93 (0.80, 1.09)	0.93 (0.78, 1.12)	0.5	0.89 (0.65, 1.22)	0.5
Esophageal cancer	1	1.05 (0.73, 1.51)	1.02 (0.69, 1.51)	0.88 (0.55, 1.40)	0.6	0.9 (0.41, 2.01)	0.8
Gastric cancer	1	0.7 (0.43, 1.12)	0.82 (0.50, 1.34)	0.71 (0.40, 1.29)	0.3	0.59 (0.20, 1.72)	0.3
Colorectal cancer	1	1.03 (0.82, 1.27)	0.95 (0.75, 1.20)	1.04 (0.80, 1.35)	0.8	1.05 (0.68, 1.64)	0.8
Liver cancer	1	0.59 (0.36, 0.96)	0.71 (0.43, 1.18)	0.64 (0.35, 1.18)	0.2	0.37 (0.11, 1.19)	0.1
Bile duct cancer	1	1.28 (0.46, 3.57)	0.87 (0.26, 2.89)	1.13 (0.30, 4.25)	0.9	1.79 (0.20, 16.2)	0.6
Pancreatic cancer	1	0.9 (0.60, 1.33)	1.09 (0.74, 1.61)	1.01 (0.65, 1.57)	>0.9	0.88 (0.42, 1.82)	0.7

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma OMEGA3 PUFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer hazard ratios (HR) for 1 SD increase in plasma OMEGA3 PUFA (mmol/L). HR, hazards ratio; OMEGA3 PUFA, omega-3 polyunsaturated fatty acids.

Table S10 Association between plasma OMEGA6 PUFAs and incident gastrointestinal cancer in the UK Biobank

Cancer	Quartile of plasma OMEGA6 PUFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	0.87 (0.73, 1.02)	0.84 (0.68, 1.04)	0.93 (0.69, 1.26)	0.7	1.12 (0.82, 1.53)	0.5
Esophageal cancer	1	0.77 (0.51, 1.17)	0.86 (0.50, 1.46)	0.82 (0.38, 1.77)	0.6	1.11 (0.50, 2.46)	0.8
Gastric cancer	1	0.94 (0.54, 1.65)	1.15 (0.57, 2.35)	1.43 (0.52, 3.91)	0.5	1.69 (0.58, 4.94)	0.3
Colorectal cancer	1	0.91 (0.71, 1.15)	0.79 (0.58, 1.07)	0.9 (0.58, 1.38)	0.6	0.95 (0.61, 1.48)	0.8
Liver cancer	1	0.74 (0.42, 1.31)	0.66 (0.31, 1.41)	1.04 (0.37, 2.89)	>0.9	2.73 (0.84, 8.88)	0.1
Bile duct cancer	1	0.67 (0.22, 2.06)	0.4 (0.08, 1.89)	0.29 (0.03, 2.87)	0.3	0.56 (0.06, 5.06)	0.6
Pancreatic cancer	1	0.98 (0.64, 1.49)	1.15 (0.69, 1.92)	1.14 (0.55, 2.37)	0.7	1.14 (0.55, 2.38)	0.7

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma OMEGA6 PUFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer hazard ratios (HR) for 1 SD increase in plasma OMEGA6 PUFA (mmol/L). HR, hazards ratio; OMEGA6 PUFA, omega-6 polyunsaturated fatty acids.

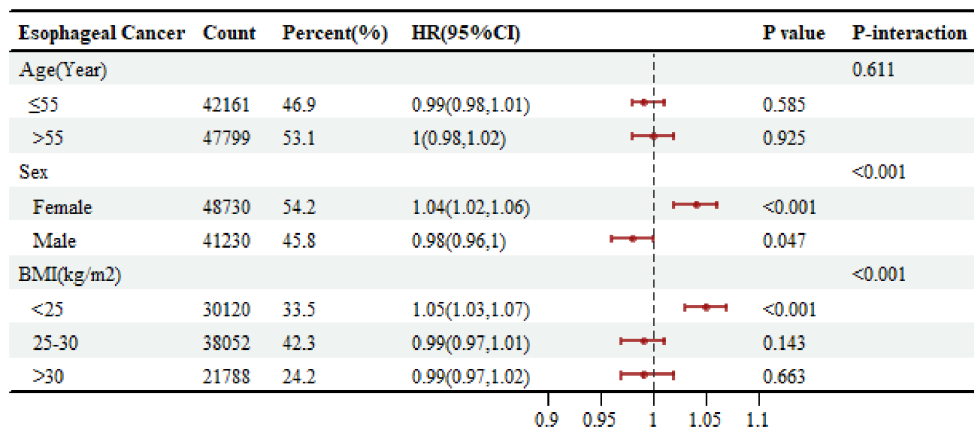


Figure S1 Association between plasma PUFAs and incidence of esophageal cancers in different subgroups.

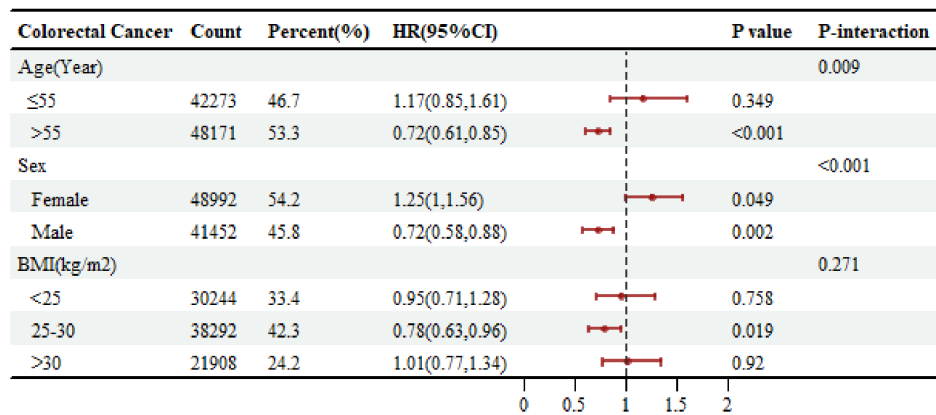


Figure S2 Association between plasma PUFAs and incidence of colorectal cancers in different subgroups.

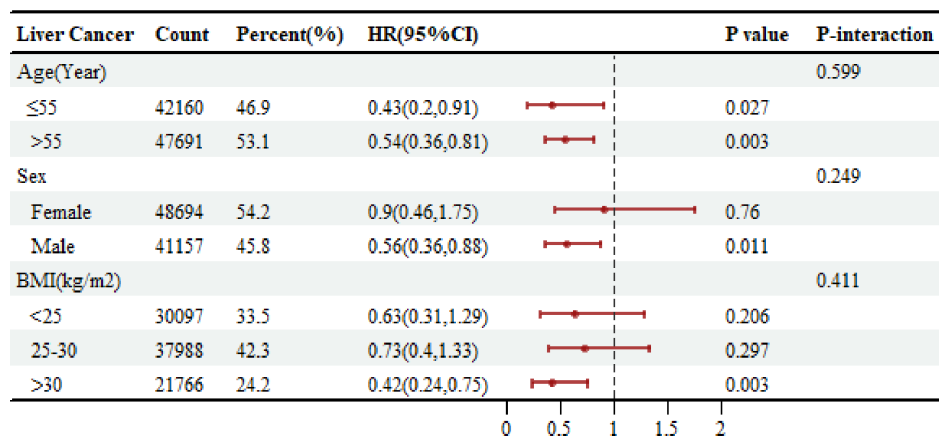


Figure S3 Association between plasma PUFAs and incidence of liver cancers in different subgroups.

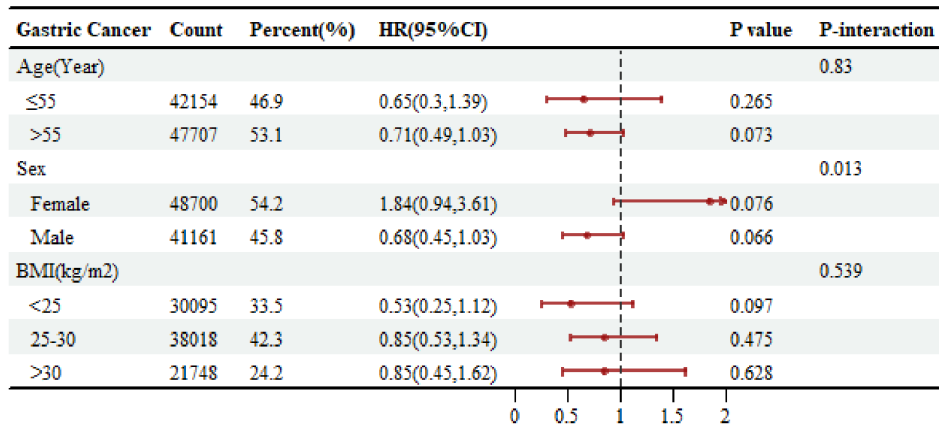


Figure S4 Association between plasma PUFAs and incidence of gastric cancers in different subgroups.

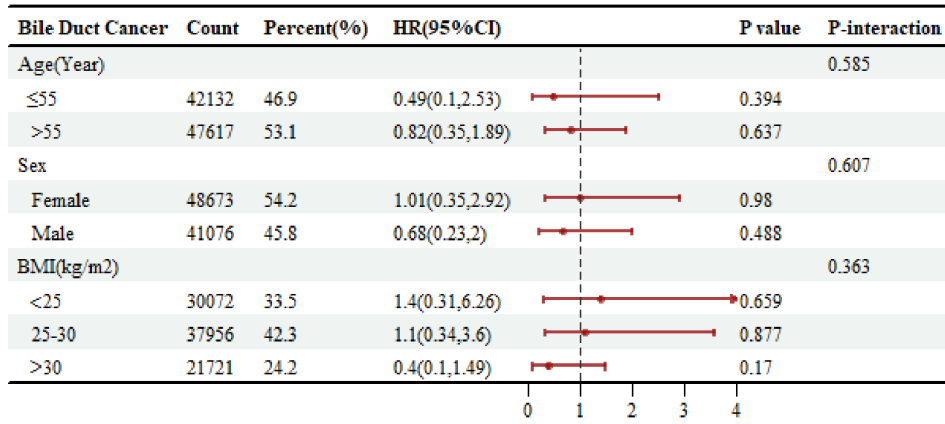


Figure S5 Association between plasma PUFAs and incidence of bile duct cancers in different subgroups.

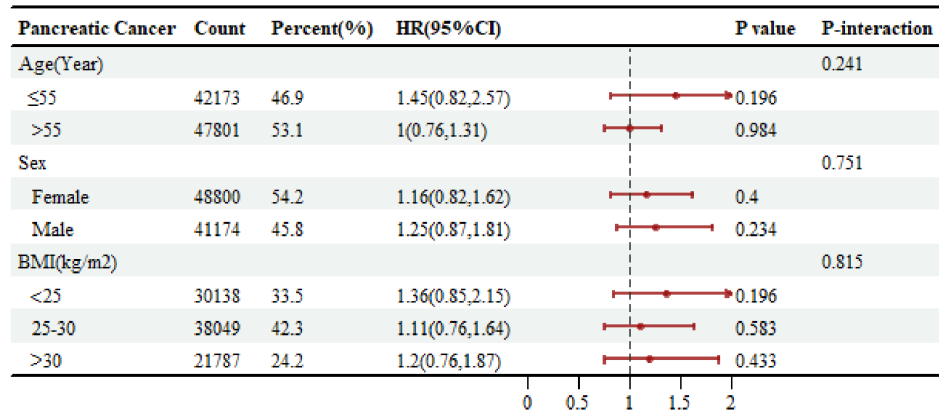


Figure S6 Association between plasma PUFAs and incidence of pancreatic cancers in different subgroups.

Table S11 Association between plasma PUFAs and incident gastrointestinal cancer in the UK Biobank after adjustment

Cancer	Quartile of plasma PUFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	0.72 (0.61, 0.85)	0.69 (0.57, 0.83)	0.67 (0.54, 0.84)	<0.001	0.79 (0.71, 0.88)	<0.001
Esophageal cancer	1	0.73 (0.49, 1.10)	0.64 (0.40, 1.01)	0.51 (0.30, 0.87)	0.013	0.68 (0.52, 0.89)	0.004
Gastric cancer	1	0.76 (0.43, 1.32)	0.88 (0.47, 1.63)	0.84 (0.41, 1.74)	0.6	0.78 (0.54, 1.12)	0.2
Colorectal cancer	1	0.71 (0.56, 0.91)	0.68 (0.51, 0.89)	0.71 (0.52, 0.98)	0.037	0.82 (0.70, 0.96)	0.012
Liver cancer	1	0.53 (0.31, 0.89)	0.32 (0.16, 0.61)	0.48 (0.24, 0.93)	0.031	0.67 (0.47, 0.96)	0.028
Bile duct cancer	1	0.53 (0.14, 1.95)	0.87 (0.22, 3.48)	0.39 (0.07, 2.04)	0.3	0.66 (0.29, 1.48)	0.3
Pancreatic cancer	1	0.85 (0.54, 1.32)	0.98 (0.61, 1.59)	0.90 (0.52, 1.55)	0.7	0.93 (0.72, 1.21)	0.6

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma PUFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer hazard ratios (HR) for 1 SD increase in plasma PUFA (mmol/L). HR, hazards ratio; PUFA, polyunsaturated fatty acid.

Table S12 Association between plasma SFAs and incident gastrointestinal cancer in the UK Biobank after adjustment

Cancer	Quartile of plasma SFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	1.23 (1.01, 1.51)	1.41 (1.08, 1.82)	1.78 (1.30, 2.44)	<0.001	1.26 (1.07, 1.48)	0.005
Esophageal cancer	1	1.49 (0.88, 2.51)	1.91 (0.99, 3.67)	3.16 (1.45, 6.87)	0.004	1.73 (1.18, 2.53)	0.005
Gastric cancer	1	0.57 (0.28, 1.13)	0.62 (0.27, 1.43)	0.40 (0.14, 1.14)	0.087	0.97 (0.56, 1.66)	>0.9
Colorectal cancer	1	1.33 (0.99, 1.77)	1.36 (0.93, 1.98)	1.45 (0.91, 2.31)	0.12	1.12 (0.88, 1.43)	0.3
Liver cancer	1	2.09 (1.06, 4.13)	2.37 (0.97, 5.79)	4.58 (1.58, 13.3)	0.005	1.55 (0.92, 2.59)	0.1
Bile duct cancer	1	0.14 (0.02, 0.79)	0.37 (0.06, 2.15)	1.39 (0.18, 10.5)	0.9	2.44 (0.74, 8.09)	0.14
Pancreatic cancer	1	1.20 (0.70, 2.06)	1.50 (0.78, 2.88)	2.30 (1.06, 4.98)	0.035	1.18 (0.79, 1.76)	0.4

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma SFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer hazard ratios (HR) for 1 SD increase in plasma SFA (mmol/L). HR, hazards ratio; SFA, saturated fatty acid.

Table S13 Association between plasma MFAs and incident gastrointestinal cancer in the UK Biobank after adjustment

Cancer	Quartile of plasma MFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	0.98 (0.81, 1.20)	0.96 (0.75, 1.22)	0.81 (0.60, 1.09)	0.2	0.94 (0.79, 1.13)	0.5
Esophageal cancer	1	0.87 (0.53, 1.44)	0.91 (0.50, 1.67)	0.63 (0.30, 1.31)	0.2	0.73 (0.47, 1.13)	0.2
Gastric cancer	1	1.19 (0.62, 2.27)	2.05 (0.92, 4.55)	2.38 (0.90, 6.28)	0.081	1.24 (0.69, 2.23)	0.5
Colorectal cancer	1	0.94 (0.72, 1.24)	0.83 (0.59, 1.17)	0.89 (0.58, 1.36)	0.6	1.05 (0.81, 1.36)	0.7
Liver cancer	1	0.90 (0.46, 1.76)	0.73 (0.32, 1.67)	0.58 (0.21, 1.60)	0.3	0.82 (0.45, 1.47)	0.5
Bile duct cancer	1	2.13 (0.60, 7.54)	3.22 (0.56, 18.6)	0.74 (0.09, 6.36)	0.8	0.37 (0.09, 1.50)	0.2
Pancreatic cancer	1	0.98 (0.59, 1.62)	1.03 (0.56, 1.88)	0.57 (0.27, 1.19)	0.13	0.94 (0.60, 1.45)	0.8

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma MFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer hazard ratios (HR) for 1 SD increase in plasma MFA (mmol/L). HR, hazards ratio; MFA, monounsaturated fatty acids.

Table S14 Association between plasma OMEGA3 PUFAs and incident gastrointestinal cancer in the UK Biobank after adjustment

Cancer	Quartile of plasma OMEGA3 PUFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	0.98 (0.83, 1.14)	0.99 (0.84, 1.17)	1 (0.83, 1.21)	>0.9	0.96 (0.69, 1.32)	0.8
Esophageal cancer	1	1.12 (0.76, 1.64)	1.12 (0.74, 1.69)	0.95 (0.58, 1.55)	0.8	0.92 (0.40, 2.10)	0.8
Gastric cancer	1	0.66 (0.40, 1.11)	0.80 (0.47, 1.35)	0.75 (0.40, 1.40)	0.4	0.63 (0.20, 1.97)	0.4
Colorectal cancer	1	1.08 (0.86, 1.37)	1.01 (0.79, 1.30)	1.13 (0.86, 1.50)	0.4	1.22 (0.77, 1.93)	0.4
Liver cancer	1	0.69 (0.41, 1.15)	0.84 (0.49, 1.43)	0.76 (0.40, 1.44)	0.4	0.51 (0.16, 1.71)	0.3
Bile duct cancer	1	1.37 (0.47, 4.00)	0.75 (0.21, 2.71)	1.08 (0.27, 4.29)	>0.9	1.77 (0.19, 16.9)	0.6
Pancreatic cancer	1	0.95 (0.63, 1.43)	1.09 (0.72, 1.65)	1.00 (0.62, 1.60)	>0.9	0.73 (0.33, 1.62)	0.4

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma OMEGA3 PUFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer hazard ratios (HR) for 1 SD increase in plasma OMEGA3 PUFA (mmol/L). HR, hazards ratio; OMEGA3 PUFA, omega-3 polyunsaturated fatty acids.

Table S15 Association between plasma OMEGA6 PUFAs and incident gastrointestinal cancer in the UK Biobank after adjustment

Cancer	Quartile of plasma OMEGA6 PUFAs				P value ¹	HR (95% CI)	P value ²
	Q1	Q2	Q3	Q4			
Gastrointestinal cancer	1	0.87 (0.73, 1.03)	0.85 (0.68, 1.06)	0.91 (0.66, 1.25)	0.6	1.05 (0.76, 1.45)	0.8
Esophageal cancer	1	0.84 (0.54, 1.30)	0.91 (0.52, 1.59)	0.86 (0.38, 1.93)	0.7	1.09 (0.48, 2.51)	0.8
Gastric cancer	1	1.01 (0.55, 1.84)	1.32 (0.62, 2.83)	1.72 (0.59, 5.03)	0.3	1.58 (0.51, 4.90)	0.4
Colorectal cancer	1	0.88 (0.68, 1.13)	0.75 (0.54, 1.03)	0.8 (0.51, 1.26)	0.3	0.82 (0.52, 1.30)	0.4
Liver cancer	1	0.68 (0.38, 1.24)	0.70 (0.32, 1.50)	0.96 (0.33, 2.78)	>0.9	1.94 (0.59, 6.44)	0.3
Bile duct cancer	1	0.76 (0.24, 2.39)	0.43 (0.09, 2.12)	0.29 (0.03, 3.10)	0.3	0.56 (0.06, 5.39)	0.6
Pancreatic cancer	1	1.00 (0.64, 1.57)	1.21 (0.70, 2.10)	1.30 (0.60, 2.82)	0.5	1.36 (0.62, 3.01)	0.4

Data are presented as HR (95% CI). Q1: \leq 25th percentile (lowest concentration); Q2: >25th to \leq 50th percentile; Q3: >50th to \leq 75th percentile; Q4: >75th percentile (highest concentration). P value¹: based on the median value of each quartile of plasma OMEGA6 PUFA concentration as a continuous variable in the models. P value²: based on gastrointestinal cancer hazard ratios (HR) for 1 SD increase in plasma OMEGA6 PUFA (mmol/L). HR, hazards ratio; OMEGA6 PUFA, omega-6 polyunsaturated fatty acids.

Table S16 Multivariable hazard ratios for colon cancer and rectal cancer from heterogeneity analysis

Plasma fatty acids	Rectal cancer (N=37)	Colon cancer (N=687)	P heterogeneity
	HR (95% CI)	HR (95% CI)	
PUFA	1.09 (0.77, 1.53)	0.99 (0.91, 1.09)	0.624
SFA	1.09 (0.82, 1.44)	0.98 (0.91, 1.06)	0.477
MFA	1.12 (0.83, 1.52)	0.97 (0.89, 1.06)	0.373
OMEGA3 PUFA	1.24 (0.22, 6.97)	1.07 (0.77, 1.49)	0.870
OMEGA6 PUFA	1.10 (0.75, 1.61)	0.98 (0.89, 1.09)	0.595

HR, hazards ratio; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; MFA, monounsaturated fatty acids; OMEGA3 PUFA, omega-3 polyunsaturated fatty acid; OMEGA6 PUFA, omega-6 polyunsaturated fatty acid.