

Dietary Fatty Acids and Colorectal Cancer Risk in Men: A Report from the Shanghai Men's Health Study and a Meta-Analysis

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Supplementary Materials and Methods

Medical Subject Heading (MESH) search strategy

Strategy: Terms 1 AND Terms 2 AND Terms 3

- **Terms 1:** Colorectal Neoplasms OR Colonic Neoplasms OR Rectal Neoplasms
- **Terms 2:** Fatty Acids OR Fatty Acids, Monounsaturated OR Fatty Acids, Unsaturated OR Fatty Acids, Omega-6 OR Fatty Acids, Omega-3 OR Dietary Fats OR Dietary Fats, Unsaturated
- **Terms 3:** Cohort Studies OR Prospective Studies OR Case-Control Studies OR Follow-Up Studies

Search on PubMed database:

((("Colorectal Neoplasms"[Mesh]) OR "Colonic Neoplasms" [Mesh]) OR "Rectal Neoplasms"[Mesh]) AND (((((((("Fatty Acids"[Mesh]) OR "Fatty Acids, Monounsaturated"[Mesh]) OR "Fatty Acids, Unsaturated"[Mesh]) OR "Fatty Acids, Omega-6"[Mesh]) OR "Fatty Acids, Omega-3"[Mesh]) OR "Dietary Fats"[Mesh]) OR "Dietary Fats, Unsaturated"[Mesh]) AND (((("Cohort Studies"[Mesh]) OR "Prospective Studies"[Mesh]) OR "Case-Control Studies"[Mesh]) OR "Follow-Up Studies"[Mesh]))

Prospective cohort studies on dietary fatty acid intake and CRC risk

Author (year); Ethnicity (Country) (No. of reference)	Cohort study; Follow-up (median years)	Sex	Types	Cases	Participants	Fatty acids	Adjusted RR or HR (95% CI) (highest vs lowest intake)	Adjustment for confounding
Stemmermann (1984); Japanese (U.S.A) ¹⁴	Japan-Hawaii cancer Study; 1965-1983 (Average 15.0)	Men	CC	106	7074	SFA	0.49 (0.27-0.91)	Age at time of examination.
			RC	59	7074	SFA	1.51 (0.65-3.54)	Age at time of examination and ethanol intake (g per day).
Willett (1990); Caucasian (U.S.A) ⁷	Nurses' Health Study Cohort; 1980-1986 (NA)	Women	CC	150	88751	TFA SFA MUFA LA	2.0 (1.1-3.63) 1.39 (0.83-2.33) 1.72 (1.01-2.93) 0.93 (0.55-1.58)	Age and total energy.
			CC	212	35216	TFA SFA	0.86 (0.54-1.33) 1.21 (0.78-1.89)	Age, total energy intake, height, parity, total vitamin

Bostick (1994); Caucasian (U.S.A) ¹⁵	IoWa Women's Health Study; 1986- 1990 (NA)					MUFA PUFA Total n-3 PUFA	0.85 (0.54-1.35) 0.74 (0.49-1.12) 0.7 (0.45-1.09)	E intake, a total vitamin E by age interaction term, and Vitamin A supplement intake.
Giovannucci (1994); Caucasian (U.S.A) ¹⁶	Health Professionals Follow-up Study Cohort; 1986-1992 (NA)	Men	CC	205	47949	TFA SFA MUFA LA	1.19 (0.74-1.9) 0.88 (0.56-1.37) 1.07 (0.68-1.69) 0.79 (0.51-1.22)	Age and total energy intake using residual method
Chyou (1996); Japanese (U.S.A) ¹⁸	Hawaii Tumor Registry; 1965-1995 (NA)	Men	CC	330	7954	TFA MUFA	0.67 (0.5-0.9) 0.73 (0.53-1.0)	Age
			RC	123	7954	TFA MUFA	1.07 (0.61-1.86) 1.47 (0.88-2.47)	
Gaard (1996); Caucasian (Norway) ¹⁹	Norwegian Cancer Registry; 1977-1991 (Average 11.4)	Men & Women	CC	143	50535	TFA SFA MUFA	1.02 (0.57-1.81) 1.33 (0.82-2.14) 0.84 (0.5-1.41)	Age
Kato (1997); Caucasian (U.S.A) ²⁰	New York Women's Health Study; 1985- 1994 (Median 7.1)	Women	CRC	100	14727	TFA SFA	1.05 (0.6-1.84) 1.05 (0.59-1.88)	Age, total energy intake, place at enrolment, and educational levels
Pietinen (1999); Caucasian (Finland) ²¹	Alpha-Tocophenol, Beta-carotene cancer Prevention Study (ATBC); 1995 (Median 8.0)	Men	CRC	185	27111	TFA SFA MUFA PUFA Trans fatty acid LA ALA Total n-3 PUFA	0.9 (0.6-1.3) 0.9 (0.6-1.4) 1.2 (0.8-1.8) 1.4 (0.9-2.1) 1.1 (0.7-1.6) 1.3 (0.8-2) 1.4 (0.9-2.1) 1.2 (0.8-1.9)	Age, supplement group, smoking years, body mass index, alcohol, education, physical activity at work, and calcium intake.
Jarvinen (2001); Caucasian (Finland) ²²	Finnish Mobile Clinic Health Examination Survey; 1967-1999 (NA)	Men & Women	CRC	109	9959	TFA SFA MUFA PUFA	1.47 (0.52-4.2) 1.47 (0.56-3.83) 2.37 (0.86-6.51) 1.13 (0.56-2.26)	Age, sex, body mass index, occupation, smoking, geographical area, energy intake, and consumption of vegetables, fruit, and cereals.
			CC	63	9959	TFA SFA MUFA PUFA	1.86 (0.46-7.43) 1.56 (0.44-5.48) 2.37 (0.61-9.19) 0.97 (0.38-2.46)	
			RC	46	9959	TFA SFA MUFA PUFA	1.09 (0.22-5.41) 1.39 (0.31-6.14) 2.38 (0.52-10.85) 1.35 (0.47-3.89)	
Terry (2001); Caucasian (Sweden) ²³	1987-1998 (MA)	Women	CRC	460	61463	SFA LA ALA EPA DHA	1.08 (0.8-1.47) 1.06 (0.78-1.45) 0.99 (0.75-1.32) 0.96 (0.72-1.28) 0.9 (0.67-1.2)	Age, body mass index, educational level, energy intake, intakes of red meat and alcohol, energy, dietary fiber, calcium, Vitamin C,

			CC	291	61463	LA ALA EPA DHA	0.88 (0.61-1.3) 0.9 (0.63-1.28) 0.85 (0.6-1.21) 0.88 (0.61-1.26)	folic acid, and vitamin D. Saturated fat, monounsaturated fat, and polyunsaturated fat were included in the same model.
			RC	159	61463	LA ALA EPA DHA	1.53 (0.87-2.69) 1.11 (0.7-1.78) 1.25 (0.75-2.06) 1.03 (0.62-1.71)	
Flood (2003); 88.8% Caucasian (U.S.A) ²⁴	BCDDP; 1989-1998 (Median 8.5)	Women	CRC	487	45496	TFA SFA UFA	1.14 (0.86-1.53) 1.02 (0.77-1.34) 1.07 (0.82-1.41)	Energy using multivariate nutrient density method and controlling total fat.
Brink (2004); Caucasian (Netherlands) ²⁵	Netherlands Cohort Study; 1989-1994 (Median 5.0)	M&F	CC	448	2948	TFA SFA MUFA PUFA ALA LA	0.95 (0.71-1.27) 0.93 (0.69-1.26) 0.98 (0.73-1.33) 1.21 (0.89-1.64) 1.01 (0.75-1.36) 1.31 (0.97-1.77)	Age, sex, Quetelet Index, smoking, energy intake (using residual method) and family history of CRC.
			RC	160	2948	TFA SFA MUFA PUFA ALA LA	0.86 (0.55-1.36) 0.73 (0.46-1.17) 0.87 (0.56-1.37) 0.83 (0.53-1.29) 0.91 (0.58-1.44) 1.03 (0.66-1.62)	
Lin (2004); Caucasian (U.S.A) ²⁶	Women's Health Study; 1993-2003 (Median 8.7)	Women	CRC	202	37547	TFA SFA MUFA Total n-6 PUFA Total n-3 PUFA Trans fatty acid FA4:0 FA6:0 – FA 10:0 FA12:0 - FA14:0 FA16:0 FA18:0 FA16:1 FA18:1 FA20:1 LA FA20:4 EPA DHA Trans FA 16:1 Trans FA18:1	1 (0.63-1.58) 0.92 (0.61-1.41) 1.09 (0.68-1.73) 1.6 (0.98-2.6) 1.11 (0.73-1.69) 1.3 (0.89-2.05) 1.19 (0.76-1.86) 1.22 (0.77-1.93) 0.99 (0.65-1.52) 0.99 (0.63-1.55) 0.87 (0.56-1.35) 0.67 (0.42-1.08) 1.16 (0.74-1.84) 1.04 (0.65-1.67) 1.42 (0.87-2.32) 0.9 (0.59-1.36) 0.79 (0.51-1.24) 1.09 (0.71-1.66) 0.8 (0.51-1.25) 1.33 (0.87-2.05)	Age, random treatment assignment, body mass index, family history of colorectal cancer, history of colorectal polyps, physical activity, cigarette smoking, alcohol consumption, postmenopausal hormone therapy, and total energy intake.

Oba (2006); Japanese (Japan) ²⁷	1993-2000 (Median 7.0)	Men	CC	111	13894	Trans FA18:2	1.29 (0.84-1.98)	Age, height, BMI, total pack-years of cigarette smoking, alcohol intake, and physical activity.
						TFA SFA MUFA PUFA Marine-derived PUFA	1.36 (0.83-2.24) 1.04 (0.65-1.66) 1.25 (0.78-1.99) 1.65 (1-2.74) 1.24 (0.8-1.95)	
Women	CC	102	16327	TFA SFA MUFA PUFA Marine-derived PUFA	0.77 (0.47-1.27) 0.85 (0.53-1.36) 0.87 (0.53-1.44) 0.72 (0.44-1.18) 0.89 (0.56-1.44)			
Hall (2008); Caucasian (U.S.A) ²⁹	Physicians' Health Study (PHS); 1984- 2006 (Median 17.6)	Men	CRC	500	21406	Total n-3 PUFA	0.76 (0.59-0.98)	Age, smoking (never smoked, past smoking, current smoking), body-mass index (<23, 23 to 24.99, 25 to 26.99, ≥ 27), multivitamin use (never use, past use, current use), history of diabetes, random assignment to aspirin or placebo, vigorous exercise (< once per week, 1-4 times per week, ≥ 5-6 times per week), alcohol intake (≤ once per week, 2-6 times per week, ≥ once-per day), and quartile of red meat intake.
Butler (2009); Chinese (Singapore) ⁸	Singapore Chinese Health Study; 1993- 2005 (Median 9.8)	Men	Localized CRC	210	27293	TFA SFA MUFA PUFA Total n-3 PUFA Marine PUFA Total n-6 PUFA Ratio n-3/ n-6 Ratio marine n-3 /n-6	0.9 (0.59-1.38) 0.85 (0.56-1.3) 1.07 (0.72-1.6) 0.97 (0.65-1.44) 0.78 (0.51-1.21) 1.4 (0.94-2.08) 0.92 (0.62-1.37) 0.93 (0.62-1.41) 1.08 (0.73-1.59)	Age at interview (yr), dialect group (Cantonese, Hokkien), interview year (1993-1995, 1996-1998), diabetes at baseline (no, yes), smoking history (never, "heavy" or ≥13 cigarettes per day starting age <15 years, "light" or non-heavy smokers), body mass index (<20, 20-23.9, 24-27.9, ≥28 m/kg ²), alcohol intake (0, <7, ≥7 drinks/week), education (no formal education, primary school, secondary school or higher),
			Advanced CRC	291	27293	TFA SFA MUFA PUFA Total n-3 PUFA Marine PUFA Total n-6 PUFA	0.7 (0.49-1) 0.76 (0.54-1.07) 0.78 (0.55-1.11) 0.86 (0.61-1.2) 1.09 (0.8-1.5) 1.27 (0.93-1.75) 0.85 (0.61-1.19)	

						Ratio n-3/ n-6 Ratio marine n-3 /n-6	1.32 (0.94-1.84) 1.54 (1.09-2.16)	any weekly physical activity (no, yes), first degree relative diagnosed with colorectal cancer (no, yes), and total daily energy intake (kcal).
		Women	Localized CRC	166	34028	TFA SFA MUFA PUFA Total n-3 PUFA Marine PUFA Total n-6 PUFA Ratio n-3/ n-6 Ratio marine n-3 /n-6	1.86 (1.18-2.92) 1.69 (1.08-2.63) 1.72 (1.09-2.7) 0.91 (0.58-1.43) 1.19 (0.75-1.89) 0.7 (0.45-1.07) 0.91 (0.58-1.42) 0.82 (0.53-1.28) 0.86 (0.56-1.32)	
			Advanced CRC	236	34028	TFA SFA MUFA PUFA Total n-3 PUFA Marine PUFA Total n-6 PUFA Ratio n-3/ n-6 Ratio marine n-3 /n-6	0.88 (0.6-1.3) 0.88 (0.61-1.28) 1.07 (0.74-1.54) 1.03 (0.7-1.51) 1.09 (0.75-1.59) 1.46 (1-2.12) 1.01 (0.69-1.47) 1.15 (0.8-1.65) 1.32 (0.9-1.95)	
		Men & Women	Localized CRC	376	61321	PUFA Total n-3 PUFA Marine PUFA Total n-6 PUFA Ratio n-3/ n-6 Ratio marine n-3 /n-6	0.94 (0.7-1.26) 0.97 (0.71-1.32) 1.02 (0.76-1.37) 0.92 (0.68-1.23) 0.88 (0.65-1.19) 0.98 (0.73-1.3)	
			Advanced CRC	527	61321	PUFA Total n-3 PUFA Marine PUFA Total n-6 PUFA Ratio n-3/ n-6 Ratio marine n-3 /n-6	0.91 (0.71-1.17) 1.07 (0.84-1.36) 1.33 (1.05-1.7) 0.9 (0.7-1.16) 1.24 (0.97-1.59) 1.45 (1.12-1.87)	
Daniel (2009); Caucasia (U.S.A) ³⁰	Cancer Prevention Study-II Nutrition Cohort; 1999-2005 (Median 6.0)	Women	CRC	417	55972	Total n-6 PUFA Total n-3 PUFA ALA Marine PUFA Ratio n-6/n-3 Ratio n-6/n-3 marine	1.17 (0.88-1.55) 1.38 (1.02-1.85) 1.38 (1.02-1.85) 0.94 (0.72-1.24) 0.96 (0.72-1.3) 1.11 (0.84-1.45)	
		Men	CRC	452	43108	Total n-6 PUFA Total n-3 PUFA ALA Marine PUFA Ratio n-6/n-3	0.81 (0.61-1.07) 0.86 (0.66-1.13) 0.87 (0.66-1.14) 1 (0.75-1.33) 1.04 (0.78-1.38)	

						Ratio n-6/n-3 marine	0.87 (0.66-1.15)	
Murff (2009); Chinese (China) ³¹	Shanghai Women's Health Study; 1997- 2007 (Median 7.4)	Women	CRC	332	73242	LA AA Total n-6 PUFA ALA n-3 HUFA Total n-3 PUFA Ratio n-6/n-3	1.2 (0.62-2.34) 0.96 (0.62-1.5) 1.1 (0.57-2.12) 1.03 (0.52-2.05) 0.95 (0.62-1.45) 1.16 (0.56-2.39) 2.02 (0.85-4.8)	Age, energy intake in kcal, total energy-adjusted n-6 PUFA intake in g/d, total energy-adjusted n-3 PUFA intake in g/d, energy- adjusted ratio of total n-6 PUFA to n-3 PUFA intake, body mass index in kg/m2, current smoker, alcohol use, regular physical activity in past five years, total energy- adjusted red meat intake in g/d, menopausal status, hormone replacement therapy use, multivitamin use and aspirin use.
			CC	200	73242	LA AA Total n-6 PUFA ALA n-3 HUFA Total n-3 PUFA Ratio n-6/n-3	1.03 (0.53-2) 1.14 (0.67-1.94) 0.88 (0.4-1.92) 1.4 (0.58-3.37) 0.79 (0.46-1.34) 1.51 (0.61-3.74) 2.02 (0.85-4.8)	
			RC	132	73242	LA AA Total n-6 PUFA ALA n-3 HUFA Total n-3 PUFA Ratio n-6/n-3	2.05 (0.61-6.86) 0.68 (0.31-1.52) 1.37 (0.55-3.41) 0.64 (0.22-1.89) 1.39 (0.7-2.85) 0.75 (0.23-2.41) 1.62 (0.48-5.5)	
Lee (2009); Chinese (China) ³²	Shanghai Women's Health Study; 1997- 2007 (Median 7.4)	Women	CRC	394	73224	TFA SFA MUFA PUFA	1.1 (0.7-1.7) 1.1 (0.7-1.6) 0.9 (0.6-1.3) 0.8 (0.5-1.3)	Age, education, income, survey season, tea consumption, NSAID use, energy intake, and fiber intake
			CC	236	73224	TFA SFA MUFA PUFA	1.4 (0.8-2.3) 1.2 (0.8-2.1) 1 (0.6-1.7) 1.2 (0.7-2.1)	
			RC	158	73224	TFA SFA MUFA PUFA	0.8 (0.4-1.5) 0.8 (0.4-1.5) 0.7 (0.4-1.3) 0.5 (0.3-0.9)	
Sasazuki (2011); Japanese (Japan) ³³	Japan Public Health Center (JPHC) - based Prospective Study; 1995-2006 (Median 9.3)	Men	CC	521	41382	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	0.81 (0.5-1.3) 1.02 (0.61-1.7) 0.86 (0.53-1.38) 0.96 (0.57-1.61) 0.84 (0.56-1.28) 0.76 (0.48-1.18) 0.85 (0.57-1.25) 1.22 (0.81-1.85)	Age, area, BMI, smoking status, alcohol drinking, past history of or medication use for DM, METs, screening for CRC, total calorie, intake of calcium, vitamin D, fiber and red meat.
				142	41382	EPA	0.27 (0.11-0.66)	

			Proximal CC			DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	0.48 (0.18-1.29) 0.35 (0.14-0.88) 0.35 (0.14-0.88) 0.61 (0.27-1.34) 0.42 (0.18-0.98) 0.46 (0.21-0.99) 0.92 (0.42-2.01)	
			Distal CC	197	41382	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	1.34 (0.68-2.67) 1.83 (0.8-4.17) 1.8 (0.83-3.91) 1.82 (0.79-4.2) 1.31 (0.65-2.63) 1.07 (0.52-2.2) 1.59 (0.85-2.99) 1.23 (0.65-2.34)	
			RC	253	41382	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	1.06 (0.53-2.11) 1.12 (0.53-2.36) 1.34 (0.67-2.68) 1.07 (0.51-2.26) 1.1 (0.61-1.98) 1.33 (0.7-2.51) 0.86 (0.5-1.5) 1.62 (0.89-2.93)	
			Invasive RC	214	41382	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	1.13 (0.53-2.38) 1.13 (0.5-2.54) 1.37 (0.65-2.91) 1.14 (0.51-2.57) 0.92 (0.49-1.74) 1.13 (0.57-2.24) 0.77 (0.43-1.4) 1.56 (0.82-2.97)	
		Women	CC	350	47192	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	0.49 (0.27-0.89) 0.5 (0.28-0.9) 0.53 (0.29-1) 0.6 (0.31-1.14) 1.01 (0.65-1.57) 0.68 (0.41-1.12) 0.87 (0.57-1.31) 1.05 (0.61-1.79)	
			Proximal CC	171	47192	EPA DHA DPA N3 HUFA	0.45 (0.2-1.05) 0.47 (0.2-1.14) 0.37 (0.16-0.85) 0.59 (0.24-1.45)	

						ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	0.84 (0.45-1.59) 0.55 (0.27-1.11) 0.74 (0.4-1.35) 1.07 (0.5-2.3)	
			Distal CC	88	47192	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	0.57 (0.17-1.91) 0.62 (0.17-2.22) 0.74 (0.23-2.42) 0.61 (0.17-2.24) 0.92 (0.38-2.22) 0.81 (0.28-2.33) 0.7 (0.32-1.57) 1.2 (0.4-3.62)	
			RC	144	47192	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	0.74 (0.3-1.82) 1.14 (0.46-2.81) 1.49 (0.57-3.87) 1.62 (0.61-4.32) 1.02 (0.5-2.06) 1.13 (0.51-2.49) 0.81 (0.42-1.56) 1 (0.44-2.27)	
			Invasive RC	126	47192	EPA DHA DPA N3 HUFA ALA Total n-3 PUFA Total n-6 PUFA Ratio n-3/n-6	0.78 (0.3-2.03) 1.36 (0.49-3.77) 1.25 (0.48-3.29) 1.51 (0.53-4.28) 0.87 (0.41-1.82) 1.16 (0.51-2.67) 0.65 (0.32-1.32) 1.14 (0.48-2.7)	
Key (2011); (UK) ³⁴	United Kingdom dietary Cohort Consortium; 3.0 - 8.4	Men & Women	CRC	565	2516	Total n-6 PUFA Total n-3 PUFA Ratio n-6/n-3	1.09 (0.77-1.55) 0.82 (0.59-1.13) 1.22 (0.92-1.63)	Matched by age, date of diary and sex, and adjusted for exact age, height, weight, energy intake, alcohol intake, fiber intake, smoking, education, social class, physical activity.
Kantor (2013); (U.S.A) ³⁵	VITamins and Lifestyle (VITAL) cohort; 2000-2008 (Median 6.7)	Men & Women	CRC	488	68109	EPA DHA Marine PUFA Ratio marine n-3/n-6	0.91 (0.67-1.22) 0.86 (0.63-1.16) 0.88 (0.65-1.2) 0.85 (0.63-1.16)	Age, sex, race/ethnicity, education, BMI, energy intake, MET-hours per week of moderate/vigorous activity, alcohol intake, smoking history, multivitamin use, calcium

								intake, dietary fiber intake, fruit and vegetable intake, red/processed meat intake, aspirin use, non-aspirin NSAID use, family history of colorectal cancer, history of sigmoidoscopy/colonoscopy, history of polyps, hormone replacement therapy, cardiovascular disease, memory loss, use of cholesterol-lowering drugs, and omega-6 (linoleic +arachidonic) intake.
Song (2014) (U.S.A) ³⁶	Nurses' Health Study Cohort; 1984-2010 (Median 20.0)	Women	CRC	1469	76386	ALA n-3 HUFA Total n-6 PUFA	1.05 (0.86-1.29) 1.03 (0.89-1.2) 0.89 (0.7-1.12)	Age, calendar year, family history of colorectal cancer, prior lower gastrointestinal endoscopy, pack-years of smoking before age 30, body mass index, physical activity, current multivitamin use, postmenopausal status and hormone use for women, regular aspirin or NSAID use (≥ 2 tablets/week), total caloric intake, red meat, process meat, alcohol consumption, and energy-adjusted intake of folate, calcium, vitamin D and total fiber.
			Proximal CC	713	76386	ALA n-3 HUFA Total n-6 PUFA	1.04 (0.78-1.4) 0.86 (0.69-1.08) 1.06 (0.76-1.48)	
			Distal CC	416	76386	ALA n-3 HUFA Total n-6 PUFA	1.18 (0.81-1.71) 1.36 (1.03-1.8) 0.74 (0.48-1.15)	
			RC	310	76386	ALA n-3 HUFA Total n-6 PUFA	0.84 (0.52-1.37) 1.06 (0.76-1.48) 0.72 (0.43-1.22)	
Song (2014); (U.S.A) ³⁶	Health Professionals Follow-up Study Cohort; 1986-2010 (Median 22.0)	Men	CRC	987	76386	ALA n-3 HUFA Total n-6 PUFA	0.89 (0.7-1.13) 1.05 (0.85-1.3) 1.17 (0.95-1.44)	
			Proximal CC	342	76386	ALA n-3 HUFA Total n-6 PUFA	0.81 (0.53-1.23) 1.03 (0.72-1.47) 1.25 (0.88-1.79)	
			Distal CC	302	76386	ALA n-3 HUFA Total n-6 PUFA	1.15 (0.75-1.75) 1.43 (0.97-2.11) 0.97 (0.66-1.41)	
			RC	215	76386	ALA n-3 HUFA Total n-6 PUFA	0.68 (0.41-1.15) 0.79 (0.51-1.22) 1.3 (0.84-2.03)	
Kraja (2015); Caucasian (Netherland) ³⁷	Rotterdam study; 1990-2011 (Median 14.6)	Men & Women	CRC	222	4967	UFA Total n-6 PUFA Total n-3 PUFA SFAs	0.95 (0.6-1.32) 0.89 (0.65-1.23) 1.44 (1.02-2.04) 1.13 (0.79-1.62)	Age, gender, energy-adjusted dietary fiber intake, and Dutch Healthy Diet index (excluding PUFA,

								fish, SFA, and dietary fiber components).
Hodge (2015); Caucasian (Australia) ⁴¹	Melbourne Collaborative Cohort study (MCCS); 1990- 2002 (Median: 9.0)	Men & Women	CRC	395	4205	FA 14:0 FA15:0 FA 16:0 FA 18:0 SFAs FA16:1 FA 18:1 MUFAs Trans fatty acid FA 18:2 FA 20:3 FA 20:4 n-6 PUFA FA 18:3 FA 20:5 FA 22:5 FA 22:6 n-3 PUFA Total PUFA	0.97 (0.68-1.39) 0.91 (0.62-1.32) 1.08 (0.76-1.52) 1.06 (0.75-1.51) 0.93 (0.66-1.32) 1.04 (0.74-1.47) 1.27 (0.89-1.81) 1.29 (0.91-1.83) 0.98 (0.69-1.40) 1.41 (0.99-1.99) 1.12 (0.79-1.60) 1.12 (0.79-1.58) 1.42 (1.00-2.01) 1.09 (0.77-1.53) 1.19 (0.84-1.68) 1.00 (0.71-1.42) 1.08 (0.76-1.53) 1.07 (0.76-1.50) 1.37 (0.97-1.93)	Education, alcohol intake, smoking status, physical activity, total energy intake, and stratified by sex, ethnicity (Southern- European migrant vs. Not)and family hityory of cancer.
Navarro (2016); (U.S.A) ⁴⁰	Women's Health Initiative; 1993-2010 (Median 11.7)	Women	CRC	1952	134017	TFA Total n-6 PUFA Total n-3 PUFA Marine PUFA	0.98 (0.76-1.27) 0.84 (0.68-1.05) 0.9 (0.74-1.09) 0.98 (0.84-1.13)	Total energy intake(continuous), age (continuous), body mass index (continuous), education (high school, technical school or some college, college graduate or post-graduate), family history of colorectal cancer (yes/no), history of colonoscopy (yes/no), current NSAID use (yes/no), alcohol intake (continuous), smoking history (never, former, current), physical activity (total metabolic equivalent-hours, continuous), ever use of hormone therapy (never, current/former), folate (dietary folate equivalents

								g/day, continuous), calcium (mg/day, continuous), and red meat intake(g/day, continuous), and study component (observational study, clinical trial) and clinical trial randomization assignment and treatment arm.
Aglago (2019); Caucasian (Europe) ⁴²	European Prospective investigation into Cancer and Nutrition (EPIC) cohort; 1992-2014 (Median: 14.9)	Men & Women	CRC	6291	521324	EPA DPA DHA n-3HUFA Ratio n-6/n-3 HUFA	0.86 (0.78-0.95) 0.83 (0.75-0.92) 0.87 (0.78-0.96) 0.86 (0.78-0.95) 1.31 (1.18-1.45)	Body mass index, height, physical activity, smoking, education, and intakes of energy, alcohol, red and process meat, fiber, and dairy products and stratified age, sex, and center.
			CC	4197	521324	EPA DPA DHA n-3HUFA Ratio n-6/n-3 HUFA	0.87 (0.77-0.98) 0.83 (0.73-0.94) 0.87 (0.77-0.99) 0.85 (0.75-0.96) 1.32 (1.17-1.50)	
			Proximal CC	1877	521324	EPA DPA DHA n-3HUFA Ratio n-6/n-3 HUFA	0.84 (0.70-1.01) 0.85 (0.71-1.03) 0.89 (0.74-1.06) 0.86 (0.72-1.04) 1.39 (1.15-1.68)	
			Distal CC	1743	521324	EPA DPA DHA n-3HUFA Ratio n-6/n-3 HUFA	0.94 (0.78-1.13) 0.82 (0.68-1.00) 0.89 (0.74-1.08) 0.86 (0.72-1.04) 1.14 (0.94-1.39)	
			RC	2094	521324	EPA DPA DHA n-3HUFA Ratio n-6/n-3 HUFA	0.87 (0.74-1.04) 0.84 (0.71-1.01) 0.87 (0.73-1.04) 0.91 (0.77-1.08) 1.24 (1.04-1.48)	
Shin (2020); Swedish (Sweden) ⁴³	Swedish Women's Lifestyle and Health (WLH) cohort; 1991-2012 (Median: 21.3)	Women	CRC	334	48,233	Total n-3 PUFA ALA DPA EPA DHA Total n-6 PUFA LA AA	1.21 (0.88-1.67) 1.17 (0.86-1.59) 0.96 (0.71-1.29) 0.92 (0.69-1.24) 0.91 (0.67-1.22) 1.37 (1.00-1.87) 1.40 (1.02-1.92) 0.79 (0.58-1.07)	Body mass index, education, smoking history, and alcohol intake. Total caloric intake was adjusted by the residual method.
			CC	201	48,233	Total n-3 PUFA ALA	1.18 (0.79-1.78) 0.96 (0.65-1.41)	

						DPA	0.95 (0.64-1.40)	
						EPA	1.11 (0.76-1.62)	
						DHA	1.19 (0.80-1.78)	
						Total n-6 PUFA	1.09 (0.73-1.62)	
						LA	1.08 (0.73-1.62)	
						AA	0.79 (0.54-1.17)	
			RC	133	48,233	Total n-3 PUFA	1.25 (0.74-2.12)	
						ALA	1.61 (0.98-2.66)	
						DPA	0.97 (0.61-1.55)	
						EPA	0.69 (0.43-1.11)	
						DHA	0.62 (0.39-0.98)	
						Total n-6 PUFA	1.98 (1.17-3.32)	
						LA	2.11 (1.25-3.59)	
						AA	0.79 (0.49-1.29)	

TFA: Total fatty acids; SFAs: saturated fatty acids; MUFAs: monounsaturated fatty acids; PUFAs: polyunsaturated fatty acids; CRC: Colorectal cancer; CC: Colon cancer; RC: Rectal cancer; n-3 HUFAs: n-3 Highly unsaturated fatty acids.

Total fatty acids (TFA): SFA + MUFA + PUFA; Total *n*-6 PUFA: LA + AA; Total *n*-3 PUFA: EPA + DHA + DPA+ ALA or EPA + DHA + ALA; n-3 HUFA: EPA + DHA + DPA; Marine-derived PUFA: EPA + DHA.

Supplementary Tables

Supplementary Table 1. HRs (95% CIs) for colorectal cancer by quartile of specific fatty acid intake

	Q1	Q2	Q3	Q4	P trend
Saturated fatty acids (SFA)					
Caproic acid C6:0	1 (ref.)	0.98 (0.81-1.20)	0.90 (0.73-1.11)	0.88 (0.69-1.11)	0.20
Caprylic acid C8:0	1 (ref.)	0.86 (0.71-1.04)	0.93 (0.76-1.13)	0.86 (0.70-1.06)	0.23
Capric acid C10:0	1 (ref.)	1.08 (0.89-1.30)	0.93 (0.75-1.15)	0.85 (0.67-1.08)	0.08
Henedecanoic C11:0	1 (ref.)	0.94 (0.78-1.14)	0.90 (0.74-1.09)	1.01 (0.84-1.22)	0.79
Lauric acid C12:0	1 (ref.)	0.86 (0.71-1.04)	1.04 (0.87-1.26)	1.01 (0.83-1.22)	0.56
Tridecanoic acid C13:0	1 (ref.)	0.90 (0.74-1.09)	0.95 (0.77-1.16)	0.78 (0.62-0.99)	0.09
Myristic acid C14:0	1 (ref.)	1.07 (0.88-1.30)	0.94 (0.76-1.17)	0.90 (0.70-1.15)	0.25
Pentadecanoic C15:0	1 (ref.)	1.04 (0.85-1.26)	0.86 (0.69-1.06)	0.92 (0.72-1.16)	0.27
Palmitic acid C16:0	1 (ref.)	1.00 (0.83-1.22)	0.82 (0.66-1.01)	1.00 (0.81-1.24)	0.80
Margaric acid C17:0	1 (ref.)	0.94 (0.78-1.14)	1.08 (0.90-1.30)	1.00 (0.83-1.21)	0.72
Stearic acid C18:0	1 (ref.)	0.89 (0.74-1.08)	0.95 (0.77-1.16)	0.85 (0.68-1.07)	0.21
Nonadecylic acid C19:0	1 (ref.)	1.04 (0.86-1.26)	1.11 (0.91-1.35)	1.07 (0.88-1.32)	0.46
Arachidic acid C20:0	1 (ref.)	0.97 (0.80-1.17)	0.90 (0.74-1.10)	0.98 (0.81-1.19)	0.77
Behenic acid C22:0	1 (ref.)	1.13 (0.93-1.38)	1.06 (0.87-1.30)	0.97 (0.79-1.19)	0.34
Monounsaturated fatty acids (MUFA)					
Myristoleic acid C14:1	1 (ref.)	0.99 (0.81-1.20)	0.91 (0.74-1.13)	0.83 (0.65-1.06)	0.10
Pentadecenoic acid C15:1	1 (ref.)	0.95 (0.78-1.15)	0.86 (0.70-1.05)	0.88 (0.70-1.10)	0.20
Palmitoleic acid C16:1	1 (ref.)	0.90 (0.75-1.09)	1.02 (0.84-1.23)	0.93 (0.76-1.13)	0.66
Heptadecenoic C17:1	1 (ref.)	1.00 (0.83-1.21)	0.88 (0.72-1.09)	0.88 (0.71-1.11)	0.20
Oleic acid C18:1	1 (ref.)	0.92 (0.76-1.12)	0.91 (0.75-1.10)	0.98 (0.81-1.19)	0.89
Gadoleic acid C20:1	1 (ref.)	0.99 (0.82-1.19)	1.06 (0.88-1.27)	0.91 (0.74-1.11)	0.43
Erucic acid C22:1	1 (ref.)	0.99 (0.81-1.20)	1.02 (0.84-1.25)	0.91 (0.73-1.13)	0.33
Polyunsaturated fatty acids (PUFA)					
Hexadecadienoic C16:2	1 (ref.)	0.95 (0.79-1.15)	0.98 (0.81-1.18)	1.03 (0.85-1.25)	0.67
Linoleic acid C18:2	1 (ref.)	1.18 (0.96-1.44)	1.22 (0.99-1.49)	1.19 (0.96-1.48)	0.15
Alpha Linolenic acid C18:3	1 (ref.)	1.09 (0.89-1.33)	1.25 (1.02-1.52)	1.15 (0.92-1.43)	0.18
Eicosadienoic acid C20:2	1 (ref.)	0.99 (0.82-1.19)	1.03 (0.85-1.24)	1.05 (0.86-1.27)	0.58
Eicosatrienoic acid C20:3	1 (ref.)	0.94 (0.78-1.13)	0.90 (0.75-1.09)	0.87 (0.72-1.06)	0.16

Arachidonic acid C20:4	1 (ref.)	0.89 (0.74-1.07)	0.89 (0.74-1.08)	0.89 (0.73-1.09)	0.30
Timnodonic acid C20:5	1 (ref.)	1.05 (0.88-1.25)	0.96 (0.79-1.16)	0.93 (0.75-1.14)	0.33
Docosatrienoic acid C22:3	1 (ref.)	0.95 (0.79-1.15)	1.01 (0.83-1.22)	0.85 (0.69-1.04)	0.15
Docosatetraenoic acid C22:4	1 (ref.)	1.01 (0.84-1.21)	0.94 (0.78-1.14)	0.92 (0.75-1.12)	0.32
Docosapentaenoic acid C22:5	1 (ref.)	1.12 (0.93-1.33)	1.00 (0.82-1.21)	0.99 (0.81-1.21)	0.63
Docosahexaenoic acid C22:6	1 (ref.)	1.02 (0.86-1.22)	0.95 (0.78-1.14)	0.92 (0.76-1.13)	0.34

Cox proportional hazards model was adjusted for age, total energy intake (residual method), education levels, alcohol consumption (continuous - drinks/day), family history of CRC, history of other diseases (cancer, myocardial infarction, stroke or diabetes mellitus), BMI (continuous - kg/m²), physical activity (continuous - MET-hour/week), fiber intake, calcium intake (kcal/day, continuous) and was stratified income levels and cigarette smoking.

Supplementary Table 2. HRs (95% CIs) for colon cancer by quartile of major subtypes and specific fatty acid intakes

	Q1	Q2	Q3	Q4	P trend
Major subtypes of fatty acids					
TFA	1 (ref.)	1.05 (0.82-1.34)	0.96 (0.74-1.24)	0.98 (0.75-1.28)	0.74
SFA	1 (ref.)	0.79 (0.62-1.02)	0.83 (0.64-1.08)	0.86 (0.65-1.12)	0.37
MUFA	1 (ref.)	0.89 (0.70-1.14)	1.01 (0.79-1.29)	0.91 (0.70-1.17)	0.63
PUFA	1 (ref.)	1.22 (0.95-1.57)	1.06 (0.81-1.38)	1.10 (0.84-1.45)	0.79
Ratio (PUFA + MUFA)/SFA	1 (ref.)	0.97 (0.76-1.23)	0.99 (0.76-1.28)	1.15 (0.88-1.50)	0.25
Total n-6 PUFA	1 (ref.)	1.16 (0.90-1.50)	1.16 (0.89-1.51)	1.12 (0.85-1.47)	0.56
Total n-3 PUFA	1 (ref.)	1.19 (0.93-1.52)	1.12 (0.86-1.45)	0.95 (0.71-1.28)	0.57
n-3 HUFA	1 (ref.)	1.04 (0.83-1.30)	0.91 (0.71-1.17)	0.95 (0.73-1.23)	0.53
Marine-derived PUFA	1 (ref.)	1.00 (0.80-1.25)	0.90 (0.70-1.14)	0.93 (0.72-1.20)	0.48
Ratio n-6PUFA/n-3 PUFA	1 (ref.)	0.98 (0.76-1.27)	0.95 (0.73-1.24)	1.19 (0.92-1.54)	0.14
Specific fatty acids					
Saturated fatty acids (SFA)					
Caproic acid C6:0	1 (ref.)	1.04 (0.80-1.35)	1.03 (0.79-1.36)	1.00 (0.74-1.35)	0.92
Caprylic acid C8:0	1 (ref.)	0.86 (0.67-1.10)	0.95 (0.74-1.22)	0.80 (0.61-1.05)	0.16
Capric acid C10:0	1 (ref.)	1.16 (0.90-1.49)	1.00 (0.76-1.32)	0.93 (0.68-1.27)	0.36
Henedecanoic C11:0	1 (ref.)	1.03 (0.81-1.31)	0.96 (0.75-1.23)	1.05 (0.82-1.34)	0.74
Lauric acid C12:0	1 (ref.)	0.84 (0.66-1.07)	1.01 (0.79-1.28)	0.94 (0.74-1.21)	0.94
Tridecanoic acid C13:0	1 (ref.)	0.93 (0.72-1.20)	0.99 (0.76-1.29)	0.79 (0.59-1.07)	0.22
Myristic acid C14:0	1 (ref.)	0.97 (0.75-1.25)	0.90 (0.68-1.18)	0.90 (0.66-1.23)	0.45
Pentadecanoic C15:0	1 (ref.)	1.07 (0.83-1.37)	0.81 (0.61-1.07)	0.93 (0.68-1.26)	0.37
Palmitic acid C16:0	1 (ref.)	0.97 (0.76-1.24)	0.83 (0.63-1.08)	0.99 (0.76-1.30)	0.89
Margaric acid C17:0	1 (ref.)	1.04 (0.82-1.31)	1.20(0.95-1.51)	0.89 (0.69-1.15)	0.55
Stearic acid C18:0	1 (ref.)	0.84 (0.65-1.08)	0.95 (0.73-1.23)	0.87 (0.65-1.16)	0.49
Nonadecylic acid C19:0	1 (ref.)	1.04 (0.81-1.33)	1.15 (0.90-1.48)	1.01 (0.78-1.32)	0.87
Arachidic acid C20:0	1 (ref.)	0.94 (0.73-1.19)	0.92 (0.71-1.18)	0.91 (0.71-1.18)	0.50
Behenic acid C22:0	1 (ref.)	1.27 (0.98-1.64)	0.96 (0.74-1.26)	1.12 (0.86-1.46)	0.84
Monounsaturated fatty acids (MUFA)					
Myristoleic acid C14:1	1 (ref.)	0.96 (0.75-1.24)	0.93 (0.71-1.22)	0.82 (0.60-1.12)	0.22
Pentadecenoic acid C15:1	1 (ref.)	0.95 (0.74-1.23)	0.94 (0.72-1.22)	0.95 (0.71-1.22)	0.73
Palmitoleic acid C16:1	1 (ref.)	0.88 (0.70-1.12)	1.06 (0.84-1.35)	0.89 (0.69-1.15)	0.63
Heptadecenoic C17:1	1 (ref.)	0.98 (0.77-1.26)	0.92 (0.71-1.20)	0.90 (0.68-1.21)	0.45

Oleic acid C18:1	1 (ref.)	0.98 (0.77-1.25)	0.99 (0.77-1.26)	0.98 (0.76-1.26)	0.88
Gadoleic acid C20:1	1 (ref.)	1.15 (0.91-1.45)	1.21 (0.95-1.54)	0.95 (0.73-1.23)	0.68
Erucic acid C22:1	1 (ref.)	0.98 (0.76-1.26)	1.13 (0.87-1.45)	0.86 (0.65-1.14)	0.25
Polyunsaturated fatty acids (PUFA)					
Hexadecadienoic C16:2	1 (ref.)	0.95 (0.75-1.22)	1.05 (0.83-1.35)	1.09 (0.85-1.40)	0.37
Linoleic acid C18:2	1 (ref.)	1.17 (0.90-1.51)	1.18 (0.91-1.54)	1.12 (0.85-1.47)	0.57
Alpha Linolenic acid C18:3	1 (ref.)	1.16 (0.90-1.49)	1.21 (0.93-1.57)	0.98 (0.74-1.31)	0.82
Eicosadienoic acid C20:2	1 (ref.)	1.04 (0.82-1.31)	1.06 (0.83-1.34)	0.95 (0.74-1.23)	0.72
Eicosatrienoic acid C20:3	1 (ref.)	1.00 (0.78-1.27)	0.97 (0.75-1.24)	0.94 (0.73-1.20)	0.57
Arachidonic acid C20:4	1 (ref.)	0.89 (0.70-1.13)	0.90 (0.70-1.15)	0.93 (0.72-1.20)	0.64
Timnodonic acid C20:5	1 (ref.)	1.00 (0.80-1.25)	0.90 (0.71-1.16)	0.95 (0.74-1.23)	0.61
Docosatrienoic acid C22:3	1 (ref.)	0.93 (0.73-1.18)	1.03 (0.81-1.31)	0.80 (0.62-1.04)	0.13
Docosatetraenoic acid C22:4	1 (ref.)	0.95 (0.75-1.21)	0.93 (0.73-1.19)	0.93 (0.72-1.20)	0.59
Docosapentaenoic acid C22:5	1 (ref.)	1.18 (0.94-1.48)	0.95 (0.74-1.23)	1.03 (0.80-1.34)	0.80
Docosahexaenoic acid C22:6	1 (ref.)	1.02 (0.81-1.27)	0.92 (0.72-1.18)	0.95 (0.73-1.22)	0.56

Cox proportional hazards model was adjusted for age, total energy intake (residual method), education levels, alcohol consumption (continuous - drinks/day), family history of CRC, history of other diseases (cancer, myocardial infarction, stroke or diabetes mellitus), BMI (continuous - kg/m²), physical activity (continuous - MET-hour/week), fiber intake, calcium intake (kcal/day, continuous) and was stratified income levels and cigarette smoking.

Total fatty acids (TFA): SFA + MUFA + PUFA; Total n-6 PUFA: LA + AA; Total n-3 PUFA: EPA + DHA + ALA + DPA; n-3 HUFA: EPA + DHA + DPA; Marine-derived PUFA: EPA + DHA.

Supplementary Table 3. HRs (95% CIs) for rectal cancer by quartile of major subtypes and specific fatty acid intakes

	Q1	Q2	Q3	Q4	P trend
Major subtypes of fatty acids					
TFA	1 (ref.)	1.13 (0.83-1.52)	0.83 (0.60-1.16)	1.14 (0.82-1.57)	0.69
SFA	1 (ref.)	1.03 (0.76-1.39)	0.87 (0.62-1.21)	1.03 (0.73-1.44)	0.97
MUFA	1 (ref.)	0.90 (0.67-1.21)	0.74 (0.54-1.03)	1.03 (0.76-1.39)	0.95
PUFA	1 (ref.)	1.06 (0.77-1.45)	1.18 (0.85-1.63)	1.31 (0.94-1.84)	0.08
Ratio (PUFA + MUFA)/SFA	1 (ref.)	0.90 (0.66-1.23)	1.01 (0.73-1.39)	1.13 (0.82-1.57)	0.29
Total n-6 PUFA	1 (ref.)	1.16 (0.84-1.59)	1.27 (0.92-1.76)	1.30 (0.92-1.83)	0.12
Total n-3 PUFA	1 (ref.)	0.90 (0.65-1.24)	1.24 (0.90-1.71)	1.32 (0.94-1.87)	0.04
n-3 HUFA	1 (ref.)	1.16 (0.87-1.54)	0.99 (0.73-1.34)	0.94 (0.68-1.30)	0.49
Marine-derived PUFA	1 (ref.)	1.11 (0.84-1.47)	0.98 (0.72-1.33)	0.90 (0.65-1.25)	0.39
Ratio n-6PUFA/n-3 PUFA	1 (ref.)	0.93 (0.67-1.29)	1.11 (0.81-1.52)	0.98 (0.71-1.36)	0.90
Specific fatty acids					
Saturated fatty acids (SFA)					
Caproic acid C6:0	1 (ref.)	0.92 (0.68-1.23)	0.74 (0.53-1.03)	0.72 (0.50-1.05)	0.05
Caprylic acid C8:0	1 (ref.)	0.86 (0.63-1.17)	0.89 (0.65-1.22)	0.95 (0.69-1.32)	0.85
Capric acid C10:0	1 (ref.)	0.98 (0.73-1.31)	0.84 (0.60-1.17)	0.75 (0.51-1.10)	0.09
Henecanoic C11:0	1 (ref.)	0.82 (0.61-1.11)	0.82 (0.61-1.10)	0.96 (0.71-1.28)	0.99
Lauric acid C12:0	1 (ref.)	0.88 (0.65-1.21)	1.11 (0.82-1.49)	1.11 (0.82-1.51)	0.30
Tridecanoic acid C13:0	1 (ref.)	0.86 (0.64-1.16)	0.89 (0.64-1.23)	0.76 (0.52-1.11)	0.24
Myristic acid C14:0	1 (ref.)	1.23 (0.91-1.67)	1.02 (0.72-1.44)	0.89 (0.59-1.33)	0.38
Pentadecanoic C15:0	1 (ref.)	1.00 (0.73-1.35)	0.94 (0.67-1.31)	0.90 (0.61-1.32)	0.53
Palmitic acid C16:0	1 (ref.)	1.07 (0.79-1.44)	0.80 (0.57-1.12)	1.02 (0.73-1.42)	0.83
Margaric acid C17:0	1 (ref.)	0.80 (0.59-1.09)	0.90 (0.67-1.22)	1.15 (0.86-1.54)	0.19
Stearic acid C18:0	1 (ref.)	0.98 (0.73-1.33)	0.95 (0.69-1.32)	0.82 (0.57-1.18)	0.26
Nonadecylic acid C19:0	1 (ref.)	1.04 (0.76-1.41)	1.04 (0.76-1.43)	1.18 (0.86-1.63)	0.32
Arachidic acid C20:0	1 (ref.)	1.03 (0.76-1.39)	0.87 (0.63-1.20)	1.10 (0.80-1.49)	0.71
Behenic acid C22:0	1 (ref.)	0.96 (0.70-1.31)	1.22 (0.90-1.64)	0.75 (0.54-1.05)	0.07
Monounsaturated fatty acids (MUFA)					
Myristoleic acid C14:1	1 (ref.)	1.03 (0.76-1.39)	0.89 (0.64-1.26)	0.85 (0.58-1.26)	0.28
Pentadecenoic acid C15:1	1 (ref.)	0.94 (0.70-1.26)	0.75 (0.54-1.05)	0.78 (0.54-1.13)	0.11

Palmitoleic acid C16:1	1 (ref.)	0.94 (0.70-1.27)	0.95 (0.70-1.29)	0.98 (0.71-1.33)	0.91
Heptadecenoic C17:1	1 (ref.)	1.04 (0.77-1.39)	0.83 (0.60-1.16)	0.86 (0.60-1.24)	0.29
Oleic acid C18:1	1 (ref.)	0.85 (0.63-1.15)	0.80 (0.58-1.09)	0.99 (0.73-1.34)	0.96
Gadoleic acid C20:1	1 (ref.)	0.77 (0.58-1.04)	0.86 (0.64-1.16)	0.86 (0.63-1.17)	0.48
Erucic acid C22:1	1 (ref.)	1.00 (0.74-1.35)	0.87 (0.62-1.20)	0.99 (0.71-1.39)	0.91
Polyunsaturated fatty acids (PUFA)					
Hexadecadienoic C16:2	1 (ref.)	0.95 (0.71-1.28)	0.87 (0.64-1.18)	0.95 (0.70-1.29)	0.68
Linoleic acid C18:2	1 (ref.)	1.19 (0.87-1.64)	1.28 (0.92-1.77)	1.34 (0.95-1.88)	0.10
Alpha Linolenic acid C18:3	1 (ref.)	0.99 (0.72-1.37)	1.31 (0.95-1.81)	1.45 (1.03-2.05)	0.01
Eicosadienoic acid C20:2	1 (ref.)	0.91 (0.67-1.24)	0.99 (0.73-1.34)	1.18 (0.88-1.59)	0.18
Eicosatrienoic acid C20:3	1 (ref.)	0.87 (0.65-1.16)	0.82 (0.61-1.11)	0.78 (0.58-1.06)	0.12
Arachidonic acid C20:4	1 (ref.)	0.89 (0.66-1.20)	0.88 (0.65-1.19)	0.84 (0.61-1.16)	0.30
Timnodonic acid C20:5	1 (ref.)	1.13 (0.85-1.51)	1.06 (0.78-1.43)	0.89 (0.64-1.24)	0.38
Docosatrienoic acid C22:3	1 (ref.)	0.99 (0.74-1.33)	0.97 (0.71-1.31)	0.94 (0.68-1.30)	0.69
Docosatetraenoic acid C22:4	1 (ref.)	1.10 (0.82-1.47)	0.96 (0.70-1.31)	0.89 (0.65-1.24)	0.37
Docosapentaenoic acid C22:5	1 (ref.)	1.02 (0.76-1.36)	1.06 (0.79-1.43)	0.93 (0.67-1.28)	0.66
Docosahexaenoic acid C22:6	1 (ref.)	1.03 (0.78-1.37)	0.98 (0.73-1.33)	0.89 (0.65-1.23)	0.44

Cox proportional hazards model was adjusted for age, total energy intake (residual method), education levels, alcohol consumption (continuous - drinks/day), family history of CRC, history of other diseases (cancer, myocardial infarction, stroke or diabetes mellitus), BMI (continuous - kg/m²), physical activity (continuous - MET-hour/week), fiber intake, calcium intake (kcal/day, continuous) and was stratified income levels and cigarette smoking.

Total fatty acids (TFA): SFA + MUFA + PUFA; Total n-6 PUFA: LA + AA; Total n-3 PUFA: EPA + DHA + ALA + DPA; n-3 HUFA: EPA + DHA + DPA; Marine-derived PUFA: EPA + DHA.

Supplementary Table 4: Spearman rank correlation (*r*) between dietary fatty acid intake and food groups*

Fatty acids	Grains	Fruit	Vegetable	Dairy	Fish	Nut bean	Legume	Red meat	Poultry	Eggs
Major subtypes of fatty acids										
TFA	-0.59	0.07	0.09	0.20	0.27	0.27	0.11	0.55	0.39	0.20
SFA	-0.59	0.09	0.07	0.37	0.28	0.17	0.06	0.51	0.40	0.23
MUFA	-0.53	0.05	0.04	0.15	0.23	0.15	0.06	0.65	0.40	0.18
PUFA	-0.54	0.08	0.18	0.05	0.26	0.56	0.23	0.33	0.32	0.13
Ratio (PUFA + MUFA)/SFA	0.17	-0.09	0.04	-0.70	-0.12	0.31	0.14	0.02	-0.10	-0.21
Total n-6 PUFA	-0.54	0.08	0.18	0.04	0.23	0.58	0.24	0.29	0.31	0.14
Total n-3 PUFA	-0.60	0.11	0.21	0.12	0.44	0.51	0.24	0.38	0.30	0.09
n-3 HUFA	-0.39	0.10	0.12	0.02	0.73	0.12	0.10	0.14	0.19	0.03
Marine-derived PUFA	-0.39	0.10	0.12	0.02	0.72	0.12	0.10	0.14	0.19	0.03
Ratio n-6PUFA/n-3 PUFA	0.28	-0.10	-0.09	-0.19	-0.49	0.05	-0.04	-0.26	-0.05	0.07
Saturated fatty acids (SFA)										
Caproic acid C6:0	-0.37	0.22	0.04	0.94	0.06	-0.02	-0.00	-0.68	0.07	0.17
Caprylic acid C8:0	-0.42	0.08	-0.02	0.55	0.06	-0.03	-0.02	0.40	0.15	0.11
Capric acid C10:0	-0.41	0.21	0.04	0.93	0.08	-0.02	-0.00	0.04	0.11	0.17
Henedecanoic C11:0	-0.35	-0.06	-0.07	-0.02	0.05	0.01	-0.04	0.43	0.13	0.21
Lauric acid C12:0	-0.39	0.03	-0.03	0.19	0.10	-0.00	-0.00	0.68	0.23	0.08
Tridecanoic acid C13:0	-0.40	0.26	0.08	0.92	0.17	-0.00	0.03	-0.04	0.11	0.17
Myristic acid C14:0	-0.53	0.21	0.07	0.82	0.28	0.03	0.03	0.20	0.23	0.19
Pentadecanoic C15:0	-0.56	0.20	0.10	0.75	0.38	0.04	0.04	0.21	0.27	0.20
Palmitic acid C16:0	-0.58	0.07	0.08	0.29	0.29	0.20	0.07	0.49	0.42	0.25
Margaric acid C17:0	-0.31	-0.03	-0.04	-0.05	0.09	-0.00	-0.00	0.74	0.23	0.03
Stearic acid C18:0	-0.61	0.12	0.09	0.48	0.28	0.17	0.07	0.43	0.40	0.27
Nonadecylic acid C19:0	-0.51	0.07	0.13	0.04	0.29	0.45	0.09	0.32	0.38	0.09
Arachidic acid C20:0	-0.54	0.08	0.08	0.24	0.24	0.17	0.12	0.61	0.41	0.09
Behenic acid C22:0	-0.43	0.18	0.20	0.17	0.20	0.41	0.27	0.13	0.26	0.10
Monounsaturated fatty acids (MUFA)										
Myristoleic acid C14:1	-0.43	0.25	0.08	0.92	0.23	0.00	0.03	-0.01	0.13	0.18
Pentadecenoic acid C15:1	-0.43	0.21	0.10	0.77	0.31	0.05	0.02	0.04	0.16	0.16

Palmitoleic acid C16:1	-0.45	0.08	0.03	0.17	0.26	0.05	0.04	0.63	0.36	0.13
Heptadecenoic C17:1	-0.52	0.21	0.19	0.44	0.74	0.15	0.11	0.15	0.25	0.27
Oleic acid C18:1	-0.53	0.04	0.04	0.13	0.22	0.17	0.07	0.64	0.40	0.18
Gadoleic acid C20:1	-0.36	0.04	0.10	-0.06	0.55	0.18	0.08	0.43	0.23	0.03
Erucic acid C22:1	-0.59	0.28	0.10	0.47	0.44	0.08	0.06	0.07	0.24	0.18
Polyunsaturated fatty acids										
Hexadecadienoic C16:2	-0.42	0.04	0.04	0.15	0.22	0.07	0.03	0.54	0.61	0.08
Linoleic acid C18:2	-0.54	0.08	0.18	0.04	0.23	0.58	0.24	0.29	0.31	0.14
Alpha Linolenic acid C18:3	-0.59	0.10	0.20	0.13	0.31	0.54	0.24	0.40	0.30	0.09
Eicosadienoic acid C20:2	-0.29	-0.05	-0.05	-0.07	0.07	-0.01	-0.01	0.75	0.21	0.09
Eicosatrienoic acid C20:3	-0.25	0.14	0.17	0.08	0.59	0.11	0.09	0.06	0.21	0.06
Arachidonic acid C20:4	-0.51	0.11	0.14	0.11	0.56	0.17	0.08	0.33	0.38	0.54
Timnodonic acid C20:5	-0.37	0.13	0.18	0.03	0.85	0.17	0.14	0.21	0.23	0.05
Docosatrienoic acid C22:3	-0.39	0.22	0.22	0.11	0.81	0.17	0.17	0.13	0.28	0.08
Docosatetraenoic acid C22:4	-0.45	0.15	0.17	0.15	0.61	0.18	0.11	0.13	0.21	0.66
Docosapentaenoic acid C22:5	-0.37	0.14	0.17	0.04	0.87	0.16	0.15	0.17	0.22	0.05
Docosahexaenoic acid C22:6	-0.33	0.11	0.16	0.02	0.82	0.15	0.14	0.16	0.19	0.04

*: All *p* value <0.001

Total fatty acids (TFA): SFA + MUFA + PUFA; Total *n*-6 PUFA: LA + AA; Total *n*-3 PUFA: EPA + DHA + ALA + DPA; *n*-3 HUFA: EPA + DHA + DPA; Marine-derived PUFA: EPA + DHA.

Supplementary Table 5. Meta-analysis of the association between types of dietary fatty acid intakes (highest vs lowest intake) and the risk of CRC among men and women by cancer sites

Fatty acids	# of studies	RR (95% CI)	Test for heterogeneity		Test for publication bias		
			p ^a	I ² (%)	p for Egger ^b	p for Begg ^c	
Major fatty acids							
TFA							
Colon	11	1.04 (0.89-1.21)	0.03	48.8	0.95	0.37	
Rectum	6	1.01 (0.86-1.18)	0.91	0.0	0.66	1.0	
SFA							
Colon	10	0.98 (0.85-1.14)	0.28	16.8	0.44	0.44	
Rectum	5	0.95 (0.74-1.20)	0.54	0.0	0.62	0.81	
MUFA							
Colon	10	0.96 (0.84-1.10)	0.32	12.9	0.08	0.12	
Rectum	5	1.02 (0.79-1.32)	0.27	22.8	0.62	1.0	
PUFA							
Colon	6	1.06 (0.86-1.29)	0.16	35.1	0.78	1.0	
Rectum	4	0.90 (0.57-1.44)	0.02	68.5	0.69	0.73	
Total n-6PUFA							
Colon	6	1.01 (0.89-1.14)	0.70	0.0	0.14	0.08	
Rectum	6	1.14 (0.88-1.48)	0.11	42.0	0.61	0.76	
Total n-3PUFA							
Colon	5	0.89 (0.72-1.08)	0.30	17.4	0.90	1.0	
Rectum	4	1.25 (0.98-1.86)	0.92	0.0	0.08	0.09	
n-3HUFA							
Colon	6	0.97 (0.84-1.13)	0.03	52.4	0.46	1.0	
Rectum	6	0.95 (0.84-1.08)	0.71	0.0	0.11	0.23	
Marine-derived PUFA							
Colon	2	0.97 (0.80-1.19)	0.49	0.0	0.69	1.0	
Rectum	1	0.90 (0.64-1.24)	-	-	-	-	
Type of fatty acids							
LA (C18:2)							
Colon	7	1.06 (0.92-1.22)	0.55	0.0	0.20	0.37	
Rectum	5	1.42 (1.11-1.81)	0.32	14.1	0.43	0.46	
AA (C20:4)							
Colon	3	0.92 (0.85-1.12)	0.54	0.0	0.81	1.0	
Rectum	3	0.81 (0.63-1.04)	0.89	0.0	0.05	0.3	
ALA (C18:3)							
Colon	8	0.99 (0.89-1.11)	0.95	0.0	0.58	1.0	
Rectum	8	1.06 (0.87-1.30)	0.21	26.6	0.18	0.25	
EPA (C20:5)							
Colon	5	0.88 (0.78-0.99)	0.34	12.0	0.64	0.45	
Rectum	5	0.88 (0.77-1.01)	0.65	0.0	0.78	1.0	

DHA (C22:6)						
Colon	5	0.90 (0.78-1.03)	0.27	22.2	0.98	1.0
Rectum	3	0.87 (0.76-1.00)	0.65	0.0	0.64	0.45
DPA (C22:5)						
Colon	4	0.87 (0.76-0.99)	0.31	16.3	0.92	0.46
Rectum	2	0.90 (0.78-1.03)	0.55	0.0	0.004	0.09

a: p value for heterogeneity

b: p of Egger, p value of Egger rank correlation method for testing publication bias

c: p of Begg, p value of Begg rank correlation method for testing publication bias

d: p value for effect modification by gender (only women, only men, and men & women)

Total fatty acids (TFA): SFA + MUFA + PUFA; Total *n*-6 PUFA: LA + AA; Total *n*-3 PUFA: EPA + DHA + ALA + DPA or EPA + DHA + ALA; *n*-3 HUFA: EPA + DHA + DPA; Marine-derived PUFA: EPA + DHA.

Supplementary Table 6. Meta-analysis of the association between types of dietary fatty acid intakes (highest vs lowest intake) and the risk of CRC among men and women by geographic region

Fatty acids	# of studies	RR (95% CI)	Test for heterogeneity		Test for publication bias		
			p ^a	I ² (%)	p for Egger ^b	p for Begg ^c	
Major fatty acids							
TFA							
U.S.A	9	1.03 (0.91-1.17)	0.07	42.2	0.77	0.53	
Europe/Australia	4	0.94 (0.78-1.14)	0.91	0.0	0.20	0.46	
Asia	4	1.01 (0.83-1.23)	0.04	51.9	0.83	0.39	
SFA							
U.S.A	7	1.00 (0.83-1.21)	0.25	22.2	0.99	0.90	
Europe/Australia	7	1.00 (0.87-1.15)	0.66	0.0	0.56	0.39	
Asia	4	0.96 (0.82-1.12)	0.22	25.8	0.47	0.71	
MUFA							
U.S.A	5	1.06 (0.81-1.39)	0.06	52.8	0.02	0.02	
Europe/Australia	5	1.08 (0.89-1.29)	0.33	13.3	0.46	1.0	
Asia	4	1.01 (0.87-1.17)	0.23	25.4	0.37	0.27	
PUFA							
U.S.A	1	0.74 (0.49-1.12)	0.43	-			
Europe/Australia	5	1.16 (0.98-1.36)	0.22	0.0	0.58	0.45	
Asia	4	1.00 (0.86-1.18)	0.18	26.0	0.33	0.54	
Total n-6PUFA							
U.S.A	5	1.01 (0.85-1.20)	0.03	59.9	0.39	0.45	
Europe/Australia	4	1.17 (0.94-1.45)	0.16	41.7	0.82	1.0	
Asia	4	0.98 (0.87-1.10)	0.82	0.0	0.04	1.0	
Total n-3PUFA							
U.S.A	5	0.92 (0.77-1.11)	0.04	57.7	0.82	1.0	
Europe/Australia	4	1.11 (0.88-1.40)	0.12	48.5	0.50	0.73	
Asia	4	1.02 (0.90-1.15)	0.58	0.0	0.67	0.37	
n-3HUFA							
U.S.A	2	1.04 (0.92-1.17)	0.89	0.0	-	1.0	
Europe/Australia	1	0.86 (0.78-1.10)	-	-			
Asia	3	0.94 (0.87-1.01)	0.68	0.0	0.81	0.13	
Marine-derived PUFA							
U.S.A	3	0.96 (0.86-1.08)	0.92	0.0	0.43	0.31	
Europe/Australia	1	1.20 (0.78-1.85)	-	-	-	-	
Asia	3	1.10 (0.91-1.33)	0.07	49.5	0.58	0.76	
Type of fatty acids							
LA (C18:2)							
U.S.A	3	1.00 (0.71-1.43)	0.21	36.7	0.70	1.0	
Europe/Australia	5	1.25 (1.09-1.45)	0.72	0.0	0.70	1.0	
Asia	2	1.19 (0.97-1.46)	0.98	0.0	-	1.0	
AA (C20:4)							
U.S.A	1	0.90 (0.59-1.37)	-	-	-	-	
Europe/Australia	2	0.93 (0.66-1.31)	0.14	54.3	-	1.0	

Asia	2	0.90 (0.75-1.08)	0.76	0.0	-	1.0
ALA (C18:3)						
U.S.A	3	1.02 (0.85-1.23)	0.09	54.4	0.73	0.73
Europe/Australia	5	1.07 (0.94-1.23)	0.73	0.0	0.63	0.71
Asia	3	1.06 (0.90-1.25)	0.87	0.0	0.32	1.0
EPA (C20:5)						
U.S.A	2	0.87 (0.68-1.12)	0.61	0.0	-	1.0
Europe/Australia	4	0.91 (0.81-1.01)	0.32	13.7	0.14	0.31
Asia	2	0.85 (0.69-1.04)	0.35	10.5	0.38	0.46
DHA (C22:6)						
U.S.A	2	0.93 (0.73-1.20)	0.37	0.0	-	1.0
Europe/Australia	4	0.89 (0.81-0.97)	0.71	0.0	0.22	0.09
Asia	2	0.89 (0.71-1.11)	0.31	16.0	0.91	0.46
DPA (C22:5)						
U.S.A	0					
Europe/Australia	3	0.85 (0.78-0.94)	0.43	0.0	0.01	0.30
Asia	2	0.94 (0.73-1.21)	0.24	27.7	0.94	0.81

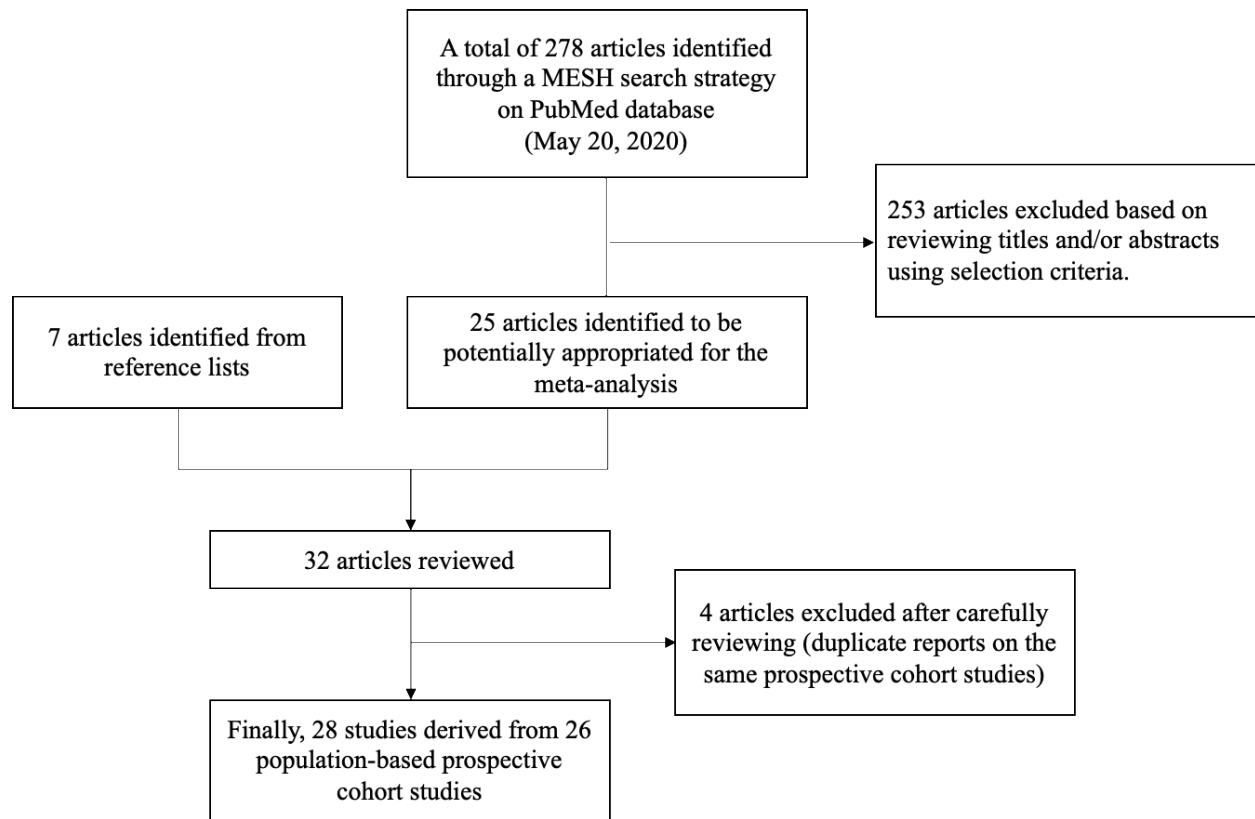
^a: *p* value for heterogeneity

^b: *p* of Egger, *p* value of Egger rank correlation method for testing publication bias

^c: *p* of Begg, *p* value of Begg rank correlation method for testing publication bias

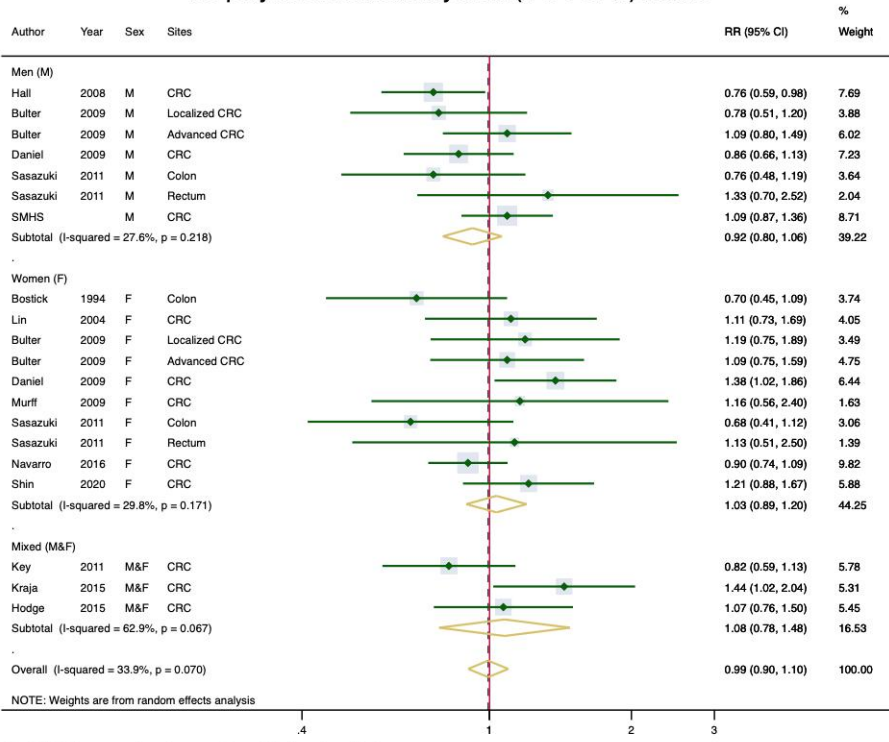
Total fatty acids (TFA): SFA + MUFA + PUFA; Total *n*-6 PUFA: LA + AA; Total *n*-3 PUFA: EPA + DHA + ALA + DPA or EPA + DHA + ALA; *n*-3 HUFA: EPA + DHA + DPA; Marine-derived PUFA: EPA + DHA.

Supplementary Figures



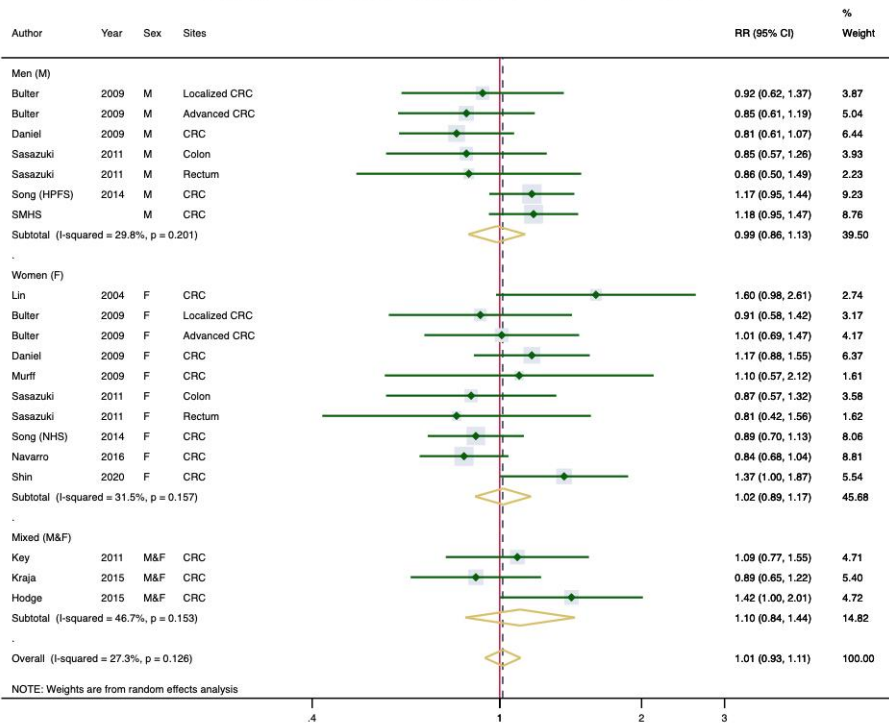
Supplementary Figure 1: Selection of studies for meta-analysis

n3 polyunsaturated fatty acid (n-3 PUFA) intake



Mixed (M&F): These prospective studies reported the result including males and females.

n6 polyunsaturated fatty acid (n-6 PUFA) intake



Mixed (M&F): These prospective studies reported the result including males and females.

Supplementary Figure 2: Meta-analysis of n-3 PUFA and n-6 PUFA intake and risk of CRC