Table S1. Summary of the revised literature on exogenous risk factors in early-onset colorectal cancer. OR—odds ratio; RR—relative risk; eoCRC—early-onset colorectal cancer; BMI—body mass index; NS—statistically not significant; Uv—univariate analysis; Mv—multivariate analysis.

Authors, ref.	Type of study, Country	Population (N)	eoCRC Cases (N)	Controls (N)	Age range/Mean Age ± SD	Sex	Exogenous risk factors analyzed	ORs/HRs/RRs (± 95% CI) for eoCRC (unless otherwise specified)	Notes
Imperiale *et al.* 2008 [37]	Retrospective case–control study (multicenter), USA	74	20 ACRN (11 eoCRCs)	54 age-matched	28-49	M/F	●Dietary factors (1998 Block food frequency survey [84]) ●Alcohol (not further specified) ●Smoking (not further specified) ●Regular exercise (not further specified) ●Weight at 21y ●Waist circumference at 21 y ●Lightest weight since 21y ●Smallest waist circumference since 21y	OR *for ACRN* [Regular exercise] = 0.39 (0.12–1.34); NS Pvalue * [lightest weight since 21y] = **0.049** No differences between case and controls in: (i) any of the 28 preselected dietary factors of the Block food frequency survey; (ii) alcohol use; (iii) cigarette smoking; (iv) weight at 21y (lbs.),	Advanced colorectal neoplasia (ACRN) defined as: adenocarcinoma or polyp with high-grade dysplasia of villous histology or tubular adenoma ≥1cm. * Adjusted for differences in gender.

								waist circumference at 21 y (in.), smallest waist circumference since 21y.	
Rosato *et al.* 2013 [29]	Case-control study (multicenter), Italy, Switzerland	1690	329	1361 age-matched	19-45	M/F	●Alcohol intake (drinks/week) ●Diet (tertile of intake) ●BMI at 30y (kg/m2), ●Occupational physical activity at 30-39y (mainly sitting, mainly standing, intermediate, heavy, strenuous) ●Leisure time physical activity at 30-39y (h/week)	MvA OR [Alcohol intake ≥14 drinks/w] = **1.56** (1.12–2.16); Ptrend = **0.009** MvA OR [BMI ≥ 25] = 0.91 (0.48–1.73); NS MvA OR [physical activity STRENUOUS] = 1.28 (0.56–2.89); NS MvA OR [Leisure time activity >7h/w] = 0.86 (0.45–1.63); NS MvB OR [Processed meat HIGH tertile] = **1.56** (1.11–2.20); Ptrend = **0.008**	MvA: age, sex, center, study, year of interview, education, family history of CRC, alcohol intake. MvB: as MvA + energy intake.

								MvB OR [Vegetables HIGH tertile] = **0.4** (0.28–0.56); Ptrend **<0.001** MvB OR [Citrus fruit HIGH tertile] = **0.61** (0.45–0.84); Ptrend = **0.002** MvB OR [Red meat HIGH tertile] = 1.07 (0.79–1.47); NS Mv B OR [Bread and cereals HIGH tertile] = 1.12 (0.76–1.64); NS Mv B OR [Fruit HIGH tertile] = 0.75 (0.54–1.02); NS	
Khan *et al.* 2015 [58]	Case-control study (single-institution), Pakistan	222	74	148 age and sex-matched	41.47 ± 15.54	M/F	●Dietary factors (no/yes) ●Smoking (no/yes)	Uv OR [Rice and powder] = **0.24** (0.14-0.44) ** Mv OR [Rice and powder]	Uv: univariable unadjusted OR. ** significant at 1%.

		●Alcohol (no/yes)	= 0.31 (0.10-1.00); NS Uv OR [Vegetarian] = **0.11** (0.06-0.20) ** Mv OR [Vegetarian] = 0.06 (0.02-0.22); NS Uv OR [Refined foods] = **0.01** (0.00-0.04) ** Uv OR [High fat diet] = **1.98** (1.13-3.49) * Mv OR [High fat diet] = 1.64 (0.58-4.62); NS Uv OR [Smoking] = **2.12** (1.08-4.17) * Mv OR [Smoking] = 1.27 (0.24-6.85); NS Uv OR [Alcohol intake] =**3.90** (2.00-7.58) ** Mv OR [Alcohol intake]	* significant at 5%. Mv OR: adjusted for all independent variables (not listed).

								=2.97 (0.35-24.93); NS	
Kim *et al.* 2016 [26]	Retrospective cohort study (Kangbuk Samsung Health Study) (multicenter), South Korea	70428	564 ACRN (25 eoCRC)	396 late-onset ACRN (29 late-onset CRC)	18-49	M/F	●Smoking (never -former/current), ●Obesity (BMI ≥ 25 (kg/m^2)	Mv OR *for ACRN* [Current smoking] = **1.37** (1.15-1.63); Pvalue **<0.001** Mv OR *for ACRN* [BMI obese] = **1.23** (1.03-1.47); Pvalue = **0.021**	Advanced colorectal neoplasms (ACRN) defined as: adenoma ≥1cm, adenoma with any component of villous histology, high-grade dysplasia, or invasive cancer. Mv: adjusted for age, sex, smoking, alcohol, obesity (BMI ≥ 25 kg/m2), triglyceride ≥150 mg/dl, HDL-C <40 mg/dl for men and <50 mg/dl for women, LDL-C, DM, hypertension, insulin, regular exercise, CRC family history, CEA.

Nguyen et al. 2018 [28]	Prospective cohort study (The Nurses' Health Study II) (multicenter), USA	89278	118	NA	41-47	F	●Sedentary TV viewing time (h/week)	Mv RR [7.1-14 h/w] =1.12 (0.72-1.75) Mv RR [>14 h/w] =1.69 (1.07-2.67) Ptrend = 0.03 Mv RR for eo-rectal cancer [>14 h/w] =2.44 (1.03-5.78); Ptrend = 0.04	Mv: adjusted for height, family history of CRC, diabetes, screening lower endoscopy within past 10y, lower endoscopy due to other indications within past 10y, smoking, alcohol intake, regular aspirin, NSAID, race, multivitamin, menopausal status, menopausal hormone use, dietary intake (total calories, red meat, fiber, folate, calcium), physical activities, BMI
Glover *et al.* 2019 [84]	Retrospective analysis of a commercial data-	8873080	1680	8871400 NoCRC	20-39	M/F	● BMI (kg/m^2) ●Alcohol (not further specified)	Mv OR [smoking] = **2.675** (2.406–2.974); **P < 0.001**	eoCRC = 20-39y individuals with CRC

	base (Explorys Inc., Cleveland, OH), USA						● Smoking (not further specified)	Mv OR [obesity] = **1.819** (1.618–2.044); **P < 0.001** Mv OR [Alcohol] = 0.908 (0.658–1.254); P = 0.56	NoCRC = 20-39y individuals without CRC Exclusion criteria: Crohn's disease, ulcerative Colitis, and family history of colorectal cancer (including patients with familial colorectal cancer syndromes).
Kim *et al.* 2019 [27]	Retrospective cross-sectional study (Kangbuk Samsung Health Study) (multicenter), South Korea	72356	622 ACRN (14 eoCRC) 20-29y group: 1 eoCRC 30-39 y group: 13 eoCRC	NA	20-39	M/F	●Smoking (never/current or former) ●Alcohol intake (≥20 g/d) ●Obesity (BMI ≥ 25 (kg/m^2) ●Regular exercise (moderate or vigorous for ≥3 times/week) ●Abdominal obesity	Mv OR *for ACRN* [20-29 y] [Current or former Smoker] = 0.88 (0.49–2.06); NS Mv OR *for ACRN* [30-39 y] [Current or former Smoker] = **1.30** (1.05–1.61); P = **0.015** Mv OR *for ACRN* [20-29 y] [Alcohol	Advanced colorectal neoplasms (ACRN) defined as: adenoma ≥1cm, adenoma with any component of villous histology, high-grade dysplasia, or invasive cancer. Mv: adjusted for age, sex,

				(waist circumference > 90 cm for men and > 80 for women)	intake ≥ 20g/d] = 1.42 (0.78–3.27); NS Mv OR *for ACRN* [30-39 y] [Alcohol intake ≥ 20g/d] = **1.34** (1.10–1.63); P = **0.004** Mv OR *for ACRN* [20-29 y] [Regular exercise] = 0.66 (0.23–1.87); NS Mv OR *for ACRN* [30-39 y] [Regular exercise] = 0.98 (0.75–1.28); NS Mv OR *for ACRN* [20-29 y] [BMI obese] = **2.46** (1.24–4.87); P = **0.01** Mv OR *for ACRN* [30-39 y] [BMI obese] = **1.33** (1.11–1.61); P = **0.003** Mv OR *for ACRN* [20-29	smoking, alcohol, obesity (BMI ≥ 25 kg/m2), NSAID use, regular exercise.

								y] [Abdominal obesity] = **2.26** (1.12–4.54); P = **0.023** Mv OR *for ACRN* [30-39 y] [Abdominal obesity] = **1.28** (1.05–1.57); P = **0.014**	
Liu *et al.* 2019 [31]	Prospective cohort study (The Nurses' Health Study II) (multicenter), USA	85256	114	NA	41-47	F	●BMI (kg/m²) at 18y ●Current BMI ●Weight change since 18y	MvA RR [current BMI 25-29.9] = **1.37** (0.81-2.30) MvA RR [current BMI ≥ 30] = **1.93** (1.15-3.25) Ptrend = **0.01** MvB RR [BMI at 18y ≥ 23] = 1.63 (1.01-2.61); NS MvC RR [weight change GAIN 20-39.9 kg] = **1.65** (0.96-2.81) MvC RR [weight	MvA: adjusted for height, history of diabetes, smoking pack-years, alcohol intake, regular aspirin, NSAID, multivitamin, menopausal status, menopausal hormone use, dietary intake (total calories, red meat, fiber, folate, calcium), physical activities.

								change GAIN ≥40 kg] = **2.15** (1.01-4.55) Ptrend = **0.007**	MvB: as MvA + family history of CRC, screening lower endoscopy within past 10y, lower endoscopy due to other indications within past 10y, weight change since 18y. MvC: as MvA + family history of CRC, screening lower endoscopy within past 10y, lower endoscopy due to other indications within past 10y,BMI at 18y.
Syed et al. 2019 [70]	Population-based cohort analysis (Explorys database 2012-2016), USA	68860	5710	11800420 age-matched controls	25-49	M/F	●BMI (kg/m2) ●Smoking (yes/no) ●Alcohol intake (yes/no)	Mv OR [BMI ≥ 30] = 2.88 (2.74-3.04) Mv OR [smoking] = 2.46 (2.33-2.59) Ptrend < 0.001	Mv: male gender, Caucasian and African-American race, abdominal pain, rectal pain, altered

								Mv OR [alcohol use] = 1.71 (1.62-1.80)	bowel function, rectal bleeding, weight loss, family history of cancer, GI malignancy, polyps, smoking, alcohol use, colitis, obesity, hypertension, hyperlipidaemia, polyps.
Breau & Ellis 2020 [80]	Meta-analysis of 6 epidemiologic studies	NA	NA	NA	< 50	M/F	● Cigarette smoking (current smoker if consuming cigarettes on a regular basis) ● Alcohol ● Obesity (BMI of 25 kg/m^2 or greater)	pooled OR [smoking and advanced yCRAC] = 1.56 (1.23-1.98) pooled OR [alcohol and advanced yCRAC] = 1.46 (95% CI 1.27-1.69) pooled OR [obesity and advanced yCRAC] = 1.26 (1.04-1.54).	yCRAC = young-onset colorectal adenomas and cancer, in adults less than 50 years).

Chen et al. 2020 [105]	Nested case-control study (IBM MarketScan Commercial Database 2006–2015), USA	113 million	4673	40832 frequency-matched controls	18-50	M/F	●Metabolic syndrome co-morbidity	Mv OR [Metabolic syndrome] = 1.25 (1.09 to 1.43); Ptrend < **0.001**	Mv: age, sex, duration of insurance enrolment and region, health insurance plan, residence and the following factors between 91 days and 2 years prior to the index dates: outpatient visits, Charlson Comorbidity Index without diabetes, IBD, family history of GI neoplasm, screening colonoscopy, other colonoscopies, faecal occult blood test and regular Rx NSAIDs use.
Gausman *et al.* 2020 [30]	Retrospective case-control study (single-institution),	4193	269	2802 late-onset CRC 1122 age-	18-49	M/F	●BMI (kg/m^2) ●Smoking (yes/no)	Mv OR *eoCRC vs age-matched controls* [BMI overweight]	Exclusion criteria: personal history of hereditary CRC syn-

	USA			matched controls				= 0.98 (0.95-1.00); NS Mv OR *eoCRC vs loCRC* [BMI overweight] = **0.98** (0.95-0.99); P = **0.04**	drome (documentation of Lynch syndrome, familial adenomatous polyposis or MUTYH-associated poliposis, or pathogenic germline mutations in the mismatch repair or EpCAM genes. BMI overweight: 25-29.9 kg/m^2
Holowatyj *et al.* 2020 [96]	Population-based cohort Study (Centers for Disease Control and Prevention and National Institutes of Health/National Cancer Institute's Surveillance, Epidemiology, and End Results Program),	28790	28790	NA	15-49	F	●BMI (kg/m^2) ●Physical inactivity (no leisure-time physical activity) ●Smoking (daily or ≥ 100 cigarettes over lifetime)	Correlation (p) with geographical hotspot of mortality [physical inactivity] = **0.21;** Ptrend **< 0.01** Correlation (p) with geographical hotspot of mortality [current BMI ≥ 30] = **-0.07;** Ptrend **< 0.01** Correlation	Mv: diagnosis age, race/ethnicity, country of CRC diagnosis, marital status, American Joint Committee on Cancer clinical stage, tumor site, histopathologic subtype, cancer sequence, sur-

	USA							(p) with geographical hotspot of mortality [smoking] = **0.09;** Ptrend **< 0.01**	gery, chemotherapy, and radiation therapy.
Hussan *et al.* 2020 [104]	Cohort study (Surveillance, Epidemiology, and End Results database), USA	1272243	10178 (Obese)	NA	20-49	M/F	●BMI (kg/m^2) at CRC resection	Average annual percentage change (2002-2013) eoCRC diagnosis [BMI ≥ 30] = **+15.3%;** Ptrend = 0.047	Patient-level variables: age, gender, median household income quartile by zip code, health insurance status.
Krigel *et al.* 2020 [118]	Retrospective study (monocenter), USA	4333	363 any CRN, of which 48 ACRN (of which 26 eoCRCs)	3970	18-49	M/F	● Smoking status (no, yes, unknown)	Mv OR [smoking yes] = 2.17 (0.97-4.85; P = 0.059 Mv OR [smoking unknown] = **3.11** (1.57-6.14); P = **0.001**	ACRN = advanced colorectal neoplasia: advanced adenomas or adenocarcinoma. Exclusion criteria: personal history of CRN, inflammatory bowel diseases, those undergoing colonscopy for screening

									only or without a known indication.
Low *et al.* 2020 [32]	Retrospective case-control study (Veterans Health Administration), (multicenter), USA	68067	651	67416 Age-matched normal Colonoscopy Controls	18-49	M/F	●Smoking (never/former/ current) ●BMI (underweight /normal/overweight/obese/ unknow) ●Aspirin use (no/yes)	Mv OR [Former smoker] = **0.82** (0.60-1.12) * Mv OR [Current smoker] = **1.10** (0.89-1.35) * Mv OR [BMI underweight] = **1.87** (0.86-4.04) * Mv OR [BMI overweight] = **0.69** (0.55-0.87) * Mv OR [BMI obese] = **0.69** (0.55-0.86) * Mv OR [aspirine use] = **0.66** (0.52-0.84) *	* P < 0.05.
Sanford *et al.* 2020 [103]	Cross-sectional household survey (National Health Interview Survey – self reported diagnosis), USA	321975	239	NA	18-49	M/F	●BMI (kg/m^2) ●Smoking (non smoking / current or former smoker)	Mv OR [BMI ≥ 30, self-reported EOCRC] = **1.39** (1.00–1.92); P = 0.049; Mv OR [Age (< vs. ≥50 years) *BMI	Mv: BMI, age, sex, race, ethnicity, insurance status and smoking.

								(< vs. ≥30)] = **0.67** (0.47-0.94); P = 0.02 Mv OR [smoking, self-reported EOCRC] = **1.51** (1.10–2.08); P = 0.01	
Zheng *et al.* 2020 [33]	Prospective cohort study (The Nurses' Health Study II) (multicenter), USA	29474	375 early-onset high-risk adenoma (eoHRA)	NA	41-47	F	●Western dietary pattern (quartile or quintile of consumption) ●Prudent dietary pattern (quintile of consumption)	Mv OR *for eoHRA* [Western diet HIGHEST quintile] = **1.67** (1.18-2.37); Ptrend = **0.01** Mv OR *for eoHRA* [Prudent diet HIGHEST quintile] = **0.69** (0.48-0.98); Ptrend = **0.03** Mv OR *for advanced adenomas of distal colon and rectum* [Western diet HIGHEST quartile] = **1.65** (1.14-2.38); Ptrend = **0.01**	High-risk adenomas (HRA) defined as any of the following: ≥1 cm in size, tubulovillous/villous histology, high-grade displasia, presence of ≥3 adenomas. Advanced adenomas defined considering only size and histology. Mv: adjusted for age, total caloric intake, time period of endoscopy, n.

							Mv OR *for advanced adenomas of distal colon and rectum* [Prudent diet HIGHEST quartile] = **0.68** (0.47-0.99); Ptrend = **0.04**	of reported endoscopies, time in years since the most recent endoscopy, reason for the current endoscopy, height, BMI, family history of CRC, menopausal status, menopausal hormone use, type 2 diabetes, smoking pack-years, physical activity, multivitamin, regular use of aspirin and NSAID
Agazzi *et al.* 2021 [117]	Retrospective observational study (single-center), Italy	1778	223 (196 adenomas, 27 eoCRCs)	1555 Age-matched Colonoscopy Controls	18-49	M/F	● Smoking (no/previous/current)	Mv OR [current smoking] = 1.10 (0.65-1.86); P = 0.724 Mv OR [previous smoking] = 0.89 (0.50-1.58);P = 0.693	Exclusion criteria: patients with Lynch syndrome or other familial polyposis syndromes. Multivariable logistic regression was per-

									formed pooling together cases of adenoma and eoCRC, considering age as a continuous variable
Archambault *et al.* 2021 [57]	Data from 13 population-based studies (Colon Cancer Family Registry, the Colorectal Transdisciplinary study, and the Genetics and Epidemiology of Colorectal Cancer Consortium)	7816	3767	4049 Age-matched	< 50	M/F	● Smoking (pack-years of smoking among current and former smokers) ● Sedentary lifestyle (yes if moderate/vigorous physical activity, leisure time, and undifferentiated activities for < 1 hour/week) ● Alcohol (<1 g/day - nondrinker, 1-28 g/day, > 28 g/day). ● Dietary factors: fruit, vegetable, red meat, processed meat	Mv OR [Pack-years of smoking] = 0.96 (0.92-1.01); P = 0.12 Mv OR [Sedentary lifestyle] = 1.13 (0.88-1.44); P = 0.34 Mv OR [Alcohol use, 0 g/d] = **1.23** (1.08-1.39); **P = 0.001** Mv OR [Alcohol use, >28 g/d] = **1.25** (1.04-1.50); **P = 0.02** Mv OR [Lower fruit intake, servings/dd] = 1.01 (0.96-1.07); P = 0.69	All self-reported variables were ascertained at the reference time for each study, defined as patient selection or blood collection for cohort studies and 1-2 years prior to selection for case-control studies, to ensure exposures were assessed before cancer diagnoses. For studies assessing height and BMI via direct measurement, variables

							(servings/day); total dietary fiber intake (g/day).	Mv OR [Lower vegetable intake, servings/dd] = 1.00 (0.94-1.06); P = 0.98 Mv OR [Greater red meat intake, servings/dd] = **1.10** (1.04-1.16); **P <.001** Mv OR [Greater processed meat intake, servings/dd] = 1.03 (0.95-1.12); P = 0.43 Mv OR [Lower total fiber intake, g/dd] = 1.11 (1.00-1.23); P = 0.06	were captured at the reference time of each respective study.
Chang *et al.* 2021 [59]	Retrospective case-control study (Ontario Cancer Registry), Canada	428	175	253 age and sex-matched	20-49	M/F	● BMI (kg/m^2) 2 years before diagnosis (obese ≥ 30.0 kg/m2) ● BMI at 20years	Mv OR [BMI obese, 2y before] = 0.59 (0.34–1.01); *p*trend = 0.06 Mv OR [BMI obese, at 20y] = 0.43	Information on tumor microsatellite instability (MSI) status was obtained from pathology reports of

	● Smoking status (never, ever) ● Pack-year smoking (<3.5 / 3.5-9.9 / ≥10) ● Alcohol (<once per month / 1-3 times per month / 1-6 times per week / daily) ●Physical activity (active: ≥ 24 units; somewhat active: 14–23 units; insufficiently active: < 14 units) ●Sedentary time (<5h per day / 5-10h per day / ≥ 10h per day) ●Diet (daily or weekly frequency of consumption of fruits, vegetables, high-fiber /wholegrain	(0.20–0.90); *p*trend = 0.06 Mv OR [ever smoking] = 1.07 (0.68–1.67) Mv OR [smoking, first tertile of pack-years] = 1.94 (1.04–3.60) Mv OR [smoking, third tertile of pack-years] = 0.79 (0.40–1.57) Mv OR [sedentary time, ≥ 10 h/day] = **1.93** (1.02–3.65); ***p*trend = 0.049** Mv OR [physical activity, insufficiently active] = 1.46 (0.90–2.38) Mv OR [daily alcohol consumption] =	eoCRCs: 89% MSI-low, 11% MSI-high. Dietary habits and other lifestyle factors were referred to the time period "2 years ago". Mv: Adjusted for age, sex, family history of CRC, regular aspirin/NSAID use, smoking, physical activity, BMI, alcohol, red/processed meat intake, total fruit and vegetable intake, high-fiber food intake, calcium supplement use. ●Ever smoked: ≥

	foods, red meat, processed meat, sugary desserts, fast food, canned food, processed snacks) ●Westernized dietary pattern (quartile) ●Drinks (sugary drinks, coffee/ tea, water, sugar substitutes)	1.07 (0.49–2.32) Mv OR [sugary drinks, ≥ 7/week] = **2.99** (1.57–5.68); ***p*trend = 0.002** Mv OR [sugary desserts, (3-6 times/week] = 2.28 (1.28–4.04) Mv OR [Total fruits and vegetables, ≥ 6 servings/day] = 0.58 (0.30-1.13);*p*trend= 0.11 Mv OR [red meat, ≥ 5 servings/week] = 1.06 (0.56-1.98) Mv OR [processed meat, ≥ 3 servings/week] = 1.23 (0.62-2.42) Mv OR [sugary dessert, ≥ 7	100 cigarettes before 2 years ago. ●Pack-year: calculated by multiplying the number of packs of cigarettes smoked per day (1 pack = 20 cigarettes) by the number of years smoked ●Physical activity: adapted from the Godin-Shephard Leisure-Time Physical Activity Questionnaire: number of times engaged in strenuous or moderate exercise for > 15 min during a typical 7-day week. Weekly frequency (times per

			times/week] = 1.45 (0.86–2.47) Mv OR [fast food, ≥ 2 times/week] = 1.84 (0.98–3.46); *p*trend=0.07 Mv OR [canned food, ≥ 3 times/week] = 1.70 (0.95–3.05); *p*trend=0.09 Mv OR [coffee or tea, ≥ 3 cups/day] = 1.68 (0.85–3.30) Mv OR [Artificial sweeteners, ≥ 7 times/week] = 1.66 (0.89–3.13) Mv OR [Western diet, quartile 4] = **1.92** (1.01–3.66); ***p*trend = 0.047**	week) of strenuous and moderate exercise was multiplied by 9 and 5, respectively, and summed across activity types to calculate the composite score (active: ≥ 24 units; somewhat active: 14–23 units; insufficiently active: < 14 units) ●Sedentary time (number of hours spent sitting on a typical day at work, school, home, in a car/bus/train, and during leisure time, averaged over weekdays and weekend

								NB: p value for linear trend calculated by treating the ordinal variable or the median value of each category (where applicable) as a continuous variable in the model, shown only when ptrend is < 0.10 for at least one of the age- and sex- adjusted and multivariable-adjusted ORs	days) supplement use
Himbert *et al*. 2021 [113]	Prospective cohort study (ColoCare Study) (multicenter), USA and Germany	2193	459 eoCRCs	1734 loCRCs	60 ± 13	M/F	●BMI (underweight ≤18.5 kg/m2; normal weight >18.5 to <25 kg/m2; overweight ≥25 kg/m2 to <30 kg/m2; obese ≥30 kg/m2).	Mv OR [BMI overweight] = 0.56 (0.41-0.76) Mv OR [BMI obese] = 0.66 (0.48-0.90) Mv OR [Never smoker] = 1.55 (1.21–1.98)	MV: adjusted for sex, race, tumor site and stage, BMI, smoking, and study site.

							● Smoking (ever-smoker/never smoker)		
Hur *et al.* 2021 [65]	Prospective cohort study (The Nurses' Health Study II) (multicenter), USA	95464. Only 41272 reported adolescenceintake at age 13–18 years	109 eoCRCs	NA	41.5 ± 5.5	F	● Sugar-sweetened beverages (SSBs) during adulthood (validated food frequency questionnaires -FFQ- every 4 years ● SSBs intake during adolescence (FFQ in 1998)	Mv RR [≥2 servings of SSBs per day *in adulthood*] = **2.18** (1.10-4.35); Ptrend=**0.02** Mv RR [≥2 servings of SSBs per day *in adolescence*] = **3.41** (1.08-10.8); Ptrend=**0.01**	MV: adjusted for race, height, BMI, menopausal status and menopausal hormone use, family history of CRC, pack-years of smoking, physical activity, regular use of aspirin, regular use of non-steroidal anti-inflammatory drugs, current use of multivitamins, intake of alcohol, red and processed meat, dietary fibre, total folate and total calcium.

								pooled OR [BMI ≥ 25 kg/m² and CRC ≤55y] = 1.42 (1.19-1.68); I(2) = 0%, Phetero-geneity = 0.60 pooled OR [BMI ≥ 25 kg/m² and CRC <50y] = 1.38 (1.08-1.76) pooled OR [BMI ≥ 30 kg/m² and CRC ≤55y] = 1.88 (1.40-2.54); I(2) = 92%, Pheter-ogeneity < 0.01) pooled OR [BMI ≥ 30 kg/m² and CRC <50y] = 1.87 (1.31-2.68)	Exclusion criteria: studies only examined risk factors for advanced polyps or combined advanced polyps with CRC in the outcome definition.
Li *et al.* 2021 [107]	Meta-analy-sis of 4 epi-demiologic studies	NA	NA	NA	≤ 55	M/F	● BMI (kg/m²) (be-fore diagno-sis but not near diagno-sis)		
O'Sullivan *et al.* 2021 [83]	Meta-analy-sis of 14 epi-demiologic studies	NA	NA	NA	< 50	M/F	● BMI (kg/m²) ●Alcohol (high vs. non-drink-ers) ●Cigarette Smoking	Pooled RR [obesity] = 1.54 (1.01-2.35), I2 = 98.7% p=0.00 Pooled RR [alcohol] = 1.71 (1.62-	Exclusion criteria: studies only examined risk factors for advanced polyps or combined

								1.80); I2 = 0.0% p= 0.85 Pooled RR [smoking] = 1.35 (0.81-2.25), I2 = 99.4% p= 0.00	advanced polyps with CRC in the outcome definition.
Schumacher *et al.* 2021 [119]	Retrospective population-based case–control study (Kaiser Permanente Southern California), USA	6160	1032	5128 Age and sex-matched	15-49	M/F	● BMI (kg/m^2), ≥1 year prior to eoCRC diagnosis /index date ● Smoking (current/former/never)	Mv OR [obesity BMI ≥ 30] = **1.41** (1.15–1.74); **P <0.01** Mv OR [obesity BMI ≥ 30 and colon cancer] = **1.56** (1.17–2.07); **P <0.01** Mv OR [obesity BMI ≥ 30 and rectal cancer] = 1.19 (0.85–1.68); P = 0.31 Mv OR [current smoking] = 0.82 (0.62-1.07) Mv OR [former smoking] = 0.78 (0.63–0.97)	Exclusion criteria: history of inflammatory bowel disease. Mv adjusted for race/ethnicity, smoking, family history, neighborhood socioeconomic status, and health care utilization.