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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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eMethods

Data source

We used the up-to-date Cancer Incidence in Five Continents Plus (*CI5plus*), a compendium series of high-quality population-based cancer registry data, which has collected data from the same catchment areas over the series and consistently used the International Classification of Diseases for Oncology (ICD-O) system to classify cancer sites (topography) and histology (morphology).[1,2] The Human Development Index 2022 was retrieved from the United Nations Development Programmem,[3] and was categorized into very low (<0.550), low (0.550-0.699), high (0.700-0.799), or very high (⩾0.800).

Available diagnosis years in the CI5plus ranged from 1943-2003 to 2015-2017 across registries. Data with national coverage were available for 27 countries/territories, while the remaining 23 relied on one or more subnational PBCRs (**eTable1** for PBCR details) with population coverage ranging from 0.6% in China to 74.5% in Canada. Of note, data from all 6 non-very-high human development index countries (India, Philippines, Uganda, China, Colombia, Ecuador) relied on subnational PBCR, with population coverage varying from 0.6% in China to 11.5% in Ecuador. The population coverage of the CI5plus for all countries/territories combined in the study is approximately 10% (24% excluding India and China). For 13 countries with multiple subnational registries, case and population numbers were aggregated only for the calendar years common to all subnational registries and used as proxies for the cancer burden of the country. We checked for any missing data by year of diagnosis and age group to ensure continuity for eligibility in trend analysis.

Early-onset cancers are usually defined as cancers that occur from ages 18 to 49 years.[4] In our analysis, however, we used cancers that occur in ages 25-49 years because CRC (ICD-10, C18-20) is rare before age 25. We used the age of 75 as a cut-off for late-onset CRC to improve comparability across countries with differing life expectancy, which varied from 62.1 years in Uganda to 84.2 years in Japan (eTable1). Case and population numbers were extracted from each registry by year of diagnosis, sex, and 5-year age group.

Joinpoint regression

We employed Joinpoint regression to quantify and visualize cancer incidence trends. Joinpoint regression uses a segmented line regression model to fit a series of joined straight lines on a logarithmic scale, which is a useful simplification of reality and offers more interpretable results, often with respect to changes in the prevalence of risk factors as well as cancer control policies and interventions. The method was developed by the US National Cancer Institute (Joinpont 1.0) in 1998 and has since evolved to enhance both accuracy and computational efficiency over time and become one of the most widely used tools to characterize cancer trends.[5] We used the latest version Joinpoint 5.2.0. which is available at https://surveillance.cancer.gov/joinpoint/.

In the regression model, year of diagnosis was the independent variable, whereas the logarithm of age-standardized incidence rate (ASR) was the dependent variable. The direct method and the Segi-Doll World standard population were used for age standardization.[6,7] Country/territory names, age at diagnosis (25-49 vs 50-74 years) and/or sex were included as by-variables to obtain stratified results. The ordinary least squares fitting of a Joinpoint regression model was first performed, assuming constant variance and uncorrelated errors. When the errors are heteroscedastic and/or correlated according to the variance structure, Joinpoint performs weighted least squares analysis with the variance-covariance matrix (option set for Standard Error (Provided)).

To find the number of Joinpoints and the best possible fit of the regression model, we used a setting that uses the Grid Search method[8] and the permutation test (4499 permutations and 0.05 level of overall significance level (maximum over-fitting probability)).[9] We set minimum number of Joinpoints at 0 and maximum number of Joinpoints at 2, requiring at least seven data points to consider a Joinpoint and, on average, at least two data points between consecutive Joinpoints.[10] The decision to set the maximum number of Joinpoints at 2 was made to produce more interpretable and parsimonious results (i.e., fewer joinpoints will be detected, especially if slope changes are small), while also minimizing the noises from data, particularly for countries with smaller sample sizes.[11]

Annual percent change (APC) for each identified segment was calculated, assuming a constant percentage change in ASR every year linearly on a log scale. If we denote b_i as the slope coefficient for the i^{th} segment, then: $APC_i = \{exp(b_i) - 1\} \times 100$. As a summary measure, we also calculated average annual percent change (AAPC) over a pre-fixed interval (the latest 10 years [10-year AAPC], the entire study range), which is computed as a weighted average of the APCs from the Joinpoint model, with the weights equal to the length of the APC interval. AAPCs for the latest 5-years (5-year AAPCs) were calculated without constraints on the maximum number of Joinpoints to improve sensitivity in detecting even small shifts in slopes for the most recent time period, while using the weighted BIC (Bayesian Information Criterion) method for computational efficiency.

We used parametric method (vs empirical quantile) to calculate the confidence intervals for APC and AAPCs, assuming the true AAPC is based on the normal distribution, and the APC confidence interval is based on a *t* distribution. AAPCs between two groups (young vs older adults; men vs women) were compared by using the following approximate 100(1-α)% confidence interval with the estimated difference of $AAPC^{(1)}$ - $AAPC^{(2)}$,[12] where

$$AAPC^{(1)} = \left\{exp\left(\sum \tilde{w}_i^{(1)} b_i^{(1)}\right) - 1\right\} \times 100 = \left\{exp\left(\hat{\varphi}^{(1)}\right) - 1\right\} \times 100$$

$$AAPC^{(2)} = \left\{exp\left(\sum \tilde{w}_i^{(2)} b_i^{(2)}\right) - 1\right\} \times 100 = \left\{exp\left(\hat{\varphi}^{(2)}\right) - 1\right\} \times 100$$

An approximate 100(1-α)% confidence interval for $\varphi^{(1)} - \varphi^{(2)}$ is $(d_{L(\alpha)}, d_{U(\alpha)})$, where

$$d_{L(\alpha)} = \hat{\varphi}^{(1)} - \hat{\varphi}^{(2)} - z_{1-\alpha/2}\sqrt{\widehat{Var}\left(\hat{\varphi}^{(1)}\right) + \widehat{Var}\left(\hat{\varphi}^{(2)}\right)}$$

$$d_{U(\alpha)} = \hat{\varphi}^{(1)} - \hat{\varphi}^{(2)} + z_{1-\alpha/2}\sqrt{\widehat{Var}\left(\hat{\varphi}^{(1)}\right) + \widehat{Var}\left(\hat{\varphi}^{(2)}\right)}$$

Then, using a Taylor series expansion, an approximate 100(1-α)% confidence interval for the difference between the two true average annual percent change rates were obtained as

$$\tilde{d}_{L(\alpha)} = AAPC^{(1)} - AAPC^{(2)} - z_{1-\alpha/2}100\sqrt{e^{2\hat{\varphi}^{(1)}}\widehat{Var}\left(\hat{\varphi}^{(1)}\right) + e^{2\hat{\varphi}^{(2)}}\widehat{Var}\left(\hat{\varphi}^{(2)}\right)}$$

$$\tilde{d}_{U(\alpha)} = AAPC^{(1)} - AAPC^{(2)} + z_{1-\alpha/2}100\sqrt{e^{2\hat{\varphi}^{(1)}}\widehat{Var}\left(\hat{\varphi}^{(1)}\right) + e^{2\hat{\varphi}^{(2)}}\widehat{Var}\left(\hat{\varphi}^{(2)}\right)}$$

The null hypothesis is that APC, AAPC, or difference in AAPCs is zero at a significance level of α (0.05). If the confidence interval contains zero, then there is no evidence to reject the null hypothesis that the true APC, AAPC, or difference in AAPCs is zero. Otherwise, we reject the null hypothesis in favour of the alternative hypothesis that the true APC, AAPC, or difference in AAPCs is different from zero. For difference in AAPCs, the Z- statistics were used to calculate p-values, assuming a normal assumption. All tests of statistical significance were two-sided.

To visually inspect the model fitting, the observed ASRs were overlaid with modelled estimates. All graphical presentations were performed with R-4.4.1 or Origin 2024b.

eTable 1. Characteristics of countries/territories and coverage and quality metrics of population-based cancer registry data

Country or territories	Human Development Index, 2022 (Tier) *	Life expectance in 2017 †	Population size in 2017 ‡	Population-based cancer registry					
				Registries	National or Sub-national	Coverage (%)	Diagnosis year available	Death Certificate Only (%) ¶	Morphologically verified (%) #
Africa									
Uganda	0.53 (Low)	62.1	42,863,000	Kyadondo	Subnational	7.1	1993-2017	0.2	58.4
Asia									
Bahrain	0.88 (Very high)	79.7	1,493,000	Bahraini	Subnational	46.5	1998-2017	-	100
China	0.77 (High)	77.2	1,409,517,000	Shanghai City, Jiashan County, Zhongshan City, Nangang District, Harbin City	Subnational	0.6	2002-2017	0.2	91.9
India	0.63 (Medium)	70.5	1,339,180,000	Mumbai, Chennai, Barshi, Dindigul Ambilikkai	Subnational	1.5	2003-2017	4.5	85.8
Israel	0.92 (Very high)	82.7	8,322,000	Israel	National	100	1963-2017	1.2	98.0
Japan	0.93 (Very high)	84.2	127,484,000	Miyagi Prefecture, Osaka	Subnational	8.8	1978-2015	1.5	96.6
Kuwait	0.83 (Very high)	79.8	4,137,000	Kuwaiti	Subnational	32.8	1998-2017	2.2	97.8
Philippines	0.7 (Medium)	71.5	104,918,000	Manila	Subnational	6.3	1983-2017	3.9	84.3
Qatar	0.86 (Very high)	80.7	2,639,000	Qatari	Subnational	11.1	2003-2017	-	100.0
Republic of Korea	0.93 (Very high)	83.3	50,982,000	Republic of Korea	National	100	1999-2017	0.6	97.7
Thailand	0.8 (Very high)	78.4	69,038,000	Chiang Mai, Khon Kaen, Songkhla, Lampang	Subnational	7.7	1993-2017	0.6	94.1
Türkiye	0.84 (Very high)	77.1	80,745,000	Izmir, Antalya	Subnational	8.1	1998-2017	0.4	97.3
Europe									
Austria	0.92 (Very high)	81.6	8,735,000	Austria	National	100	1998-2017	3.3	89.4
Belarus	0.81 (Very high)	74.5	9,468,000	Belarus	National	100	1983-2017	1.3	97.4
Croatia	0.86 (Very high)	78.1	4,189,000	Croatia	National	100	1988-2017	1.6	86.5
Cyprus	0.9 (Very high)	81.3	1,180,000	Cyprus	Subnational	71.5	1998-2017	2.1	97.3
Czechia	0.89 (Very high)	79.0	10,618,000	Czechia	National	100	1983-2017	0.3	97.9
Denmark	0.95 (Very high)	81.1	5,734,000	Denmark	National	100	1943-2017	0.1	99.2
Estonia	0.89 (Very high)	78.0	1,310,000	Estonia	National	100	1983-2017	0.5	95.5
Finland	0.94 (Very high)	81.5	5,523,000	Finland	National	100	2008-2017	0.2	97.9
France	0.9 (Very high)	82.5	64,980,000	Calvados, Doubs, Haut-Rhin, Isère, Somme, Hérault, Loire-Atlantique, Manche, Vendée	Subnational	11.8	1998-2017	-	99.1
Germany	0.94 (Very high)	80.9	82,114,000	Hamburg, Bremen, Schleswig-Holstein, Saarland	Subnational	7.8	2003-2017	2.7	89.4
Iceland	0.96 (Very high)	82.5	335,000	Iceland	National	100	1955-2017	0	98.9
Ireland	0.95 (Very high)	81.9	4,762,000	Ireland	National	100	1994-2017	0.1	99.4
Italy	0.9 (Very high)	82.7	59,360,000	Trento, Syracuse, Palermo, South Tyrol	Subnational	4.5	2003-2017	1	95.4
Latvia	0.86 (Very high)	74.8	1,950,000	Latvia	National	100	1983-2017	1.3	93.9

Lithuania	0.88 (Very high)	75.4	2,890,000	Lithuania	National	100	1988-2017	11.2	85.7
Malta	0.92 (Very high)	83.6	431,000	Malta	National	100	1993-2017	1.5	90.9
Norway	0.96 (Very high)	82.6	5,305,000	Norway	National	100	1953-2017	0.4	99.5
Poland	0.88 (Very high)	77.7	38,171,000	Kielce cancer registry	Subnational	3.2	1999-2017	-	98.4
Slovenia	0.92 (Very high)	81.1	2,080,000	Slovenia	National	100	1983-2017	-	99.8
Spain	0.91 (Very high)	83.0	46,354,000	Tarragona, Granada, Murcia, Navarra, Basque Country, Girona, Canary Islands	Subnational	18.2	1993-2016	0.6	98.8
Sweden	0.95 (Very high)	82.4	9,911,000	Sweden	National	100	1960-2017	0	100
Switzerland	0.96 (Very high)	83.4	8,476,000	Geneva, Vaud, Valais, Ticino, Graubünden and Glarus	Subnational	26.2	1998-2017	1.4	98.1
The Netherlands	0.94 (Very high)	81.7	17,036,000	The Netherlands	National	100	1989-2017	-	99.7
UK, England	0.93 (Very high)	81.2	55,619,430	England	National	100	1971-2017	0.3	97.6
UK, Northern Ireland**	0.93 (Very high)	81.2	1,870,834	Northern Ireland	National	100	1993-2017	0.5	98.1
UK, Scotland**	0.93 (Very high)	81.2	5,424,800	Scotland	National	100	1978-2017	0.1	98.0
UK, Wales**	0.93 (Very high)	81.2	3,125,165	Wales	National	100	2003-2017	0.4	97.2
Latin America and the Caribbean									
Argentina	0.84 (Very high)	76.8	44,271,000	Mendoza	Subnational	4.2	2003-2017	2.3	97.0
Chile	0.86 (Very high)	80.4	18,055,000	Valdivia	Subnational	2.2	1998-2017	3.7	92.6
Colombia	0.75 (High)	76.6	49,066,000	Cali, Bucaramanga, Manizales, Pasto	Subnational	9.1	2003-2017	1.5	91.1
Costa Rica	0.81 (Very high)	79.4	4,906,000	Costa Rica	National	100	1982-2016	1.5	77.7
Ecuador	0.74 (High)	77.0	16,625,000	Quito	Subnational	11.5	1985-2017	1.9	97.3
France, Martinique	Not applicable	82.3	385,000	Martinique	National	-	1993-2017	-	
USA, Puerto Rico	Not applicable	79.3	3,663,000	Puerto Rico	National	100	2003-2017	1.3	96.2
North America									
Canada	0.94 (Very high)	82.0	36,624,000	Canada cancer registry (Excl Nova Scotia, Northwest Territories, Nunavut, Quebec and Yukon)	Subnational	74.5	1978-2017	0.7	98.1
USA	0.92 (Very high)	78.8	324,459,000	SEER 9 (San Francisco-Oakland and Los Angeles Cancer Registries (California), Connecticut Tumor Registry, Atlanta Tumor Registry (Georgia), Hawaii Tumor Registry, State Health Registry of Iowa, Detroit Cancer Registry (Michigan), New Mexico Tumor Registry, Utah Cancer Registry, Seattle-Puget Sound Tumor Registry (Washington State))	Subnational (45 states and Washington DC)	9.3	1978-2017	0.7	98.1
Oceania									
Australia	0.95 (Very high)	83.0	24,451,000	Australia	National	100.0	1993-2017	0.5	97.8
New Zealand	0.94 (Very high)	82.2	4,706,000	New Zealand	National	100.0	1983-2017	0.3	98.9

* United Nations Development Programme. Human Development Index (HDI). Available from https://hdr.undp.org/data-center/human-development-index#/indicies/HDI. Accessed August 26, 2024.

† Life expectancy: United Nations, Department of Economic and Social Affairs, Population Division (2022). World Population Prospects 2022: Online Edition.

‡ Population size: United Nations (2017). World Population Prospects - Data Booklet, 2017 Revision. Available from: https://population.un.org/wpp/Publications/Files/WPP2017_DataBooklet.pdf. Accessed August 21, 2024/

¶ The percentage of cases in incidence based on information only from the death certificate (DCO).

The percentage of morphologically verified (MV) cases.

** UK, Wales, Scotland, Northern Ireland Populations: Office for National Statistics - UK (2017). Estimates of the population for the UK, England, Wales, Scoland, and Northern Ireland. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland. Accessed August 21, 2024

For more information on the Cancer Incidence in Five Continents Plus, refer to https://ci5.iarc.fr/ci5plus/.

eTable 2. Trends in incidence rate of colorectal cancer from Joinpoint models (annual percent change [APC], average annual percent change [AAPC]) in ages 25-49 years in 50 countries or territories

	Trend 1			Trend 2			Trend 3			AAPC (95% CI)					
	Year	APC (95% CI)	p	Year	APC (95% CI)	p	Year	APC (95% CI)	p	5-year	p	10-year	p	Entire period	P
Argentina	2003-2017	2.92 (0.80 to 5.10)	0.0107							2.92 (0.80 to 5.10)	0.0107	2.92 (0.80 to 5.10)	0.0107	2.92 (0.80 to 5.10)	0.0107
Australia	1993-2005	0.15 (-0.51 to 0.81)	0.6491	2005-2017	3.01 (2.43 to 3.58)	<0.0001				3.01 (2.43 to 3.58)	<0.0001	3.01 (2.43 to 3.58)	<0.0001	1.57 (1.15 to 1.98)	<0.0001
Austria	1998-2012	-1.02 (-1.94 to -0.09)	0.0343	2012-2015	8.64 (-10.05 to 31.21)	0.3579	2015-2017	-12.16 (-28.14 to 7.38)	0.1850	-0.12 (-0.82 to 0.60)	0.7354	-0.57 (-7.25 to 6.58)	0.8711	-0.81 (-4.07 to 2.57)	0.6343
Bahrain	1998-2017	-0.27 (-2.63 to 2.15)	0.8154							-0.27 (-2.63 to 2.15)	0.8154	-0.27 (-2.63 to 2.15)	0.8154	-0.27 (-2.63 to 2.15)	0.8154
Belarus	1983-2015	0.58 (0.35 to 0.81)	<0.0001	2015-2017	13.13 (-1.81 to 30.34)	0.0855				6.67 (-0.34 to 14.17)	0.0627	3.24 (0.17 to 6.41)	0.0387	1.28 (0.45 to 2.12)	0.0026
Canada	1978-1996	-1.19 (-1.52 to -0.85)	<0.0001	1996-2006	1.09 (0.28 to 1.91)	0.0100	2006-2017	2.83 (2.29 to 3.37)	<0.0001	2.83 (2.29 to 3.37)	<0.0001	2.83 (2.29 to 3.37)	<0.0001	0.52 (0.23 to 0.81)	0.0005
Chile	1998-2017	3.96 (1.26 to 6.74)	0.0062							3.96 (1.26 to 6.74)	0.0062	3.96 (1.26 to 6.74)	0.0062	3.96 (1.26 to 6.74)	0.0062
China	2002-2010	-2.88 (-4.19 to -1.55)	0.0011	2010-2013	9.36 (-4.42 to 25.12)	0.1640	2013-2017	-1.1 (-5.28 to 3.26)	0.5697	-1.10 (-5.28 to 3.26)	0.5697	1.86 (-2.29 to 6.18)	0.3858	-0.07 (-2.60 to 2.53)	0.9590
Colombia	2003-2006	11.83 (-0.32 to 25.47)	0.0556	2006-2017	0.14 (-1.12 to 1.40)	0.8137				0.14 (-1.12 to 1.40)	0.8137	0.14 (-1.12 to 1.40)	0.8137	2.53 (0.17 to 4.96)	0.0358
Costa Rica	1982-2016	1.49 (1.02 to 1.97)	<0.0001							1.49 (1.02 to 1.97)	<0.0001	1.49 (1.02 to 1.97)	<0.0001	1.49 (1.02 to 1.97)	<0.0001
Croatia	1988-2017	1.38 (0.69 to 2.08)	0.0003							0.01 (-1.04 to 1.07)	0.9881	1.38 (0.69 to 2.08)	0.0003	1.38 (0.69 to 2.08)	0.0003
Cyprus	1998-2017	1.23 (-0.53 to 3.02)	0.1611							-1.76 (-4.85 to 1.42)	0.2529	1.23 (-0.53 to 3.02)	0.1611	1.23 (-0.53 to 3.02)	0.1611
Czechia	1983-1995	1.08 (0.21 to 1.96)	0.0165	1995-2013	-1.30 (-1.79 to -0.80)	<0.0001	2013-2017	2.68 (-1.98 to 7.55)	0.2526	2.68 (-1.98 to 7.55)	0.2526	0.45 (-1.53 to 2.47)	0.6568	0.00 (-0.65 to 0.65)	0.9965
Denmark	1943-1979	-0.17 (-0.43 to 0.09)	0.1887	1979-1998	-1.22 (-1.95 to -0.49)	0.0014	1998-2017	1.67 (1.03 to 2.31)	<0.0001	1.72 (1.12 to 2.32)	<0.0001	1.67 (1.03 to 2.31)	<0.0001	0.03 (-0.25 to 0.30)	0.8562
Ecuador	1985-2017	2.10(1.29 to 2.91)	<0.0001							2.10 (1.29 to 2.91)	<0.0001	2.10 (1.29 to 2.91)	<0.0001	2.10 (1.29 to 2.91)	<0.0001
Estonia	1983-2017	0.54 (-0.11 to 1.19)	0.1008							0.54 (-0.11 to 1.19)	0.1008	0.54 (-0.11 to 1.19)	0.1008	0.54 (-0.11 to 1.19)	0.1008
Finland	1953-1969	2.73 (1.02 to 4.46)	0.0021	1969-2017	0.89 (0.65 to 1.13)	<0.0001				0.89 (0.65 to 1.13)	<0.0001	0.89 (0.65 to 1.13)	<0.0001	1.34 (0.89 to 1.80)	<0.0001
France	1998-2008	-1.14 (-2.15 to -0.13)	0.0301	2008-2017	2.09 (0.88 to 3.32)	0.0022				2.09 (0.88 to 3.32)	0.0022	2.09 (0.88 to 3.32)	0.0022	0.38 (-0.34 to 1.10)	0.3062
France, Martinique	1993-2017	1.74 (0.13 to 3.37)	0.0357							1.74 (0.13 to 3.37)	0.0357	1.74 (0.13 to 3.37)	0.0357	1.74 (0.13 to 3.37)	0.0357
Germany	2003-2017	1.99 (1.23 to 2.75)	0.0001							-1.51 (-7.52 to 4.89)	0.6358	1.99 (1.23 to 2.75)	0.0001	1.99 (1.23 to 2.75)	0.0001
Iceland	1955-2013	0.99 (0.40 to 1.59)	0.0014	2013-2017	15.82 (-3.28 to 38.70)	0.1083				15.82 (-3.28 to 38.70)	0.1083	7.33 (-0.77 to 16.1)	0.0773	1.89 (0.61 to 3.18)	0.0036
India	2003-2017	1.26 (-0.03 to 2.57)	0.0554							1.26 (-0.03 to 2.57)	0.0554	1.26 (-0.03 to 2.57)	0.0554	1.26 (-0.03 to 2.57)	0.0554
Ireland	1994-2017	0.62 (0.07 to 1.18)	0.0296							0.62 (0.07 to 1.18)	0.0296	0.62 (0.07 to 1.18)	0.0296	0.62 (0.07 to 1.18)	0.0296
Israel	1963-1995	1.53 (1.11 to 1.96)	<0.0001	1995-2017	0.46 (0.03 to 0.89)	0.0387				0.46 (0.02 to 0.89)	0.0387	0.46 (0.02 to 0.89)	0.0387	1.09 (0.79 to 1.39)	<0.0001
Italy	2003-2017	0.41 (-0.71 to 1.53)	0.4476							0.41 (-0.71 to 1.53)	0.4476	0.41 (-0.71 to 1.53)	0.4476	0.41 (-0.71 to 1.53)	0.4476
Japan	1978-1991	3.33 (2.48 to 4.18)	<0.0001	1991-2009	-0.46 (-0.97 to 0.06)	0.0800	2009-2015	4.69 (2.24 to 7.19)	0.0004	4.80 (2.57 to 7.08)	0.0001	2.94 (1.39 to 4.52)	0.0002	1.68 (1.16 to 2.21)	<0.0001
Kuwait	1998-2017	0.49 (-1.61 to 2.62)	0.6346							0.49 (-1.61 to 2.62)	0.6346	0.49 (-1.61 to 2.62)	0.6346	0.49 (-1.61 to 2.62)	0.6346
Latvia	1983-2017	-0.06 (-0.59 to 0.48)	0.8325							-0.06 (-0.59 to 0.48)	0.8325	-0.06 (-0.59 to 0.48)	0.8325	-0.06 (-0.59 to 0.48)	0.8325
Lithuania	1988-2017	0.01	0.9763							0.01	0.9763	0.01	0.9763	0.01	0.9763

		(-0.53 to 0.55)								(-0.53 to 0.55)		(-0.53 to 0.55)		(-0.53 to 0.55)	
Malta	1993-2017	-0.39 (-1.79 to 1.04)	0.5778							5.18 (-1.37 to 12.17)	0.1168	-0.39 (-1.79 to 1.04)	0.5778	-0.39 (-1.79 to 1.04)	0.5778
New Zealand	1983-1992	-6.00 (-7.97 to -3.98)	<0.0001	1992-2007	-0.23 (-1.27 to 0.82)	0.6530	2007-2017	3.97 (2.44 to 5.52)	<0.0001	3.89 (2.50 to 5.29)	<0.0001	3.97 (2.44 to 5.52)	<0.0001	-0.59 (-1.40 to 0.21)	0.1494
Norway	1953-1979	2.73 (2.11 to 3.34)	<0.0001	1979-2007	0.18 (-0.25 to 0.61)	0.4069	2007-2017	3.52 (1.94 to 5.13)	<0.0001	3.52 (1.94 to 5.13)	<0.0001	3.52 (1.94 to 5.13)	<0.0001	1.73 (1.34 to 2.12)	<0.0001
Philippines	1983-2006	1.79 (0.84 to 2.76)	0.0006	2006-2017	-1.88 (-3.92 to 0.21)	0.0753				-1.88 (-3.92 to 0.21)	0.0753	-1.88 (-3.92 to 0.21)	0.0753	0.59 (-0.30 to 1.49)	0.1957
Poland	1999-2017	-0.16 (-1.56 to 1.26)	0.8129							-0.16 (-1.56 to 1.26)	0.8129	-0.16 (-1.56 to 1.26)	0.8129	-0.16 (-1.56 to 1.26)	0.8129
Qatar	2003-2010	8.44 (-3.22 to 21.51)	0.1358	2010-2013	-29.62 (-70.99 to 70.73)	0.3798	2013-2017	31.31 (4.86 to 64.43)	0.0242	31.31 (4.86 to 64.43)	0.0242	2.22 (-21.13 to 32.49)	0.8681	4.40 (-12.16 to 24.09)	0.6250
Republic of Korea	1999-2012	4.51 (4.07 to 4.96)	<0.0001	2012-2015	-7.92 (-14.37 to -0.98)	0.0296	2015-2017	1.52 (-5.79 to 9.40)	0.6653	-3.31 (-7.70 to 1.28)	0.1548	-0.45 (-3.03 to 2.19)	0.7352	2.00 (0.65 to 3.37)	0.0036
Slovenia	1983-2017	0.64 (0.30 to 0.99)	0.0005							0.64 (0.30 to 0.99)	0.0005	0.64 (0.30 to 0.99)	0.0005	0.64 (0.30 to 0.99)	0.0005
Spain	1993-2016	-0.17 (-0.56 to 0.23)	0.3852							-0.17 (-0.56 to 0.23)	0.3852	-0.17 (-0.56 to 0.23)	0.3852	-0.17 (-0.56 to 0.23)	0.3852
Sweden	1960-1971	0.39 (-0.85 to 1.65)	0.5290	1971-1997	-1.16 (-1.52 to -0.79)	<0.0001	1997-2017	2.32 (1.85 to 2.79)	<0.0001	2.64 (1.99 to 3.30)	<0.0001	2.32 (1.85 to 2.79)	<0.0001	0.35 (0.02 to 0.68)	0.0363
Switzerland	1998-2017	0.83 (-0.42 to 2.09)	0.1826							0.83 (-0.42 to 2.09)	0.1826	0.83 (-0.42 to 2.09)	0.1826	0.83 (-0.42 to 2.09)	0.1826
Thailand	1993-2017	2.76 (2.17 to 3.36)	<0.0001							2.76 (2.17 to 3.36)	<0.0001	2.76 (2.17 to 3.36)	<0.0001	2.76 (2.17 to 3.36)	<0.0001
The Netherlands	1989-1997	-0.70 (-1.61 to 0.23)	0.1321	1997-2017	1.77 (1.56 to 1.99)	<0.0001				1.77 (1.56 to 1.99)	<0.0001	1.77 (1.56 to 1.99)	<0.0001	1.06 (0.77 to 1.35)	<0.0001
Türkiye	1998-2017	2.15 (1.57 to 2.74)	<0.0001							2.15 (1.57 to 2.74)	<0.0001	2.15 (1.57 to 2.74)	<0.0001	2.15 (1.57 to 2.74)	<0.0001
Uganda	1993-2017	0.22 (-1.84 to 2.34)	0.8265							0.22 (-1.84 to 2.34)	0.8265	0.22 (-1.84 to 2.34)	0.8265	0.22 (-1.84 to 2.34)	0.8265
UK, England	1971-2003	-0.45 (-0.60 to -0.29)	<0.0001	2003-2017	3.59 (3.12 to 4.06)	<0.0001				3.59 (3.12 to 4.06)	<0.0001	3.59 (3.12 to 4.06)	<0.0001	0.77 (0.59 to 0.94)	<0.0001
UK, Northern Ireland	1993-2017	0.54 (-0.41 to 1.49)	0.2528							0.54 (-0.41 to 1.49)	0.2528	0.54 (-0.41 to 1.49)	0.2528	0.54 (-0.41 to 1.49)	0.2528
UK, Scotland	1978-2017	0.64 (0.39 to 0.88)	<0.0001							1.75 (0.61 to 2.89)	0.0035	0.64 (0.39 to 0.88)	<0.0001	0.64 (0.39 to 0.88)	<0.0001
UK, Wales	2003-2017	1.55 (-0.16 to 3.28)	0.0723							1.55 (-0.16 to 3.28)	0.0723	1.55 (-0.16 to 3.28)	0.0723	1.55 (-0.16 to 3.28)	0.0723
USA	1978-1994	-0.51 (-1.03 to 0.01)	0.0531	1994-2017	2.13 (1.90 to 2.36)	<0.0001				2.13 (1.90 to 2.36)	<0.0001	2.13 (1.90 to 2.36)	<0.0001	1.04 (0.79 to 1.28)	<0.0001
USA, Puerto Rico	2003-2017	3.81 (2.68 to 4.96)	<0.0001							3.81 (2.68 to 4.96)	<0.0001	3.81 (2.68 to 4.96)	<0.0001	3.81 (2.68 to 4.96)	<0.0001

NOTE APC for each identified segment was calculated, assuming a constant percentage change in age-standardized incidence rate every year linearly on a log scale. The 10-year AAPC and AAPC for the entire period were based on permutation methods with allowing maximum number of Joinpoints of 2, whereas the 5-year AAPC were based on the weighted BIC (Bayesian Information Criterion) method without constraints on the maximum number of Joinpoint. Parametric method was used to calculate the confidence intervals for APC and AAPCs. For more information, refer to eMethods.

eTable 3. Trends in incidence rate of colorectal cancer from Joinpoint models (annual percent change [APC], average annual percent change [AAPC]) in ages 50-74 years in 50 countries or territories

	Trend 1			Trend 2			Trend 3			AAPC (95% CI)					
	Year	APC (95% CI)	P	Year	APC (95% CI)	P	Year	APC (95% CI)	P	5-year	P	10-year	P	Entire period	P
Argentina	2003-2017	0.33 (-0.79 to 1.46)	0.5418							-3.87 (-10.09 to 2.78)	0.2475	0.33 (-0.79 to 1.46)	0.5418	0.33 (-0.79 to 1.46)	0.5418
Australia	1993-2007	-0.37 (-0.69 to -0.05)	0.0254	2007-2017	-2.62 (-3.09 to -2.15)	<0.0001				-2.62 (-3.09 to -2.15)	<0.0001	-2.62 (-3.09 to -2.15)	<0.0001	-1.31 (-1.57 to -1.06)	<0.0001
Austria	1998-2005	-1.07 (-2.02 to -0.11)	0.0309	2005-2017	-2.71 (-3.14 to -2.28)	<0.0001				-2.71 (-3.14 to -2.28)	<0.0001	-2.71 (-3.14 to -2.28)	<0.0001	-2.11 (-2.51 to -1.7)	<0.0001
Bahrain	1998-2017	3.36 (2.29 to 4.45)	<0.0001							3.36 (2.29 to 4.45)	<0.0001	3.36 (2.29 to 4.45)	<0.0001	3.36 (2.29 to 4.45)	<0.0001
Belarus	1983-1988	4.09 (1.78 to 6.45)	0.0010	1988-2017	1.95 (1.83 to 2.06)	<0.0001				1.95 (1.83 to 2.06)	<0.0001	1.95 (1.83 to 2.06)	<0.0001	2.26 (1.92 to 2.60)	<0.0001
Canada	1978-2005	-0.08 (-0.21 to 0.06)	0.2762	2005-2015	-1.00 (-1.58 to -0.42)	0.0015	2015-2017	-5.28(-11.00 to 0.80)	0.0854	-1.74 (-2.36 to -1.13)	<0.0001	-1.97 (-3.34 to -0.58)	0.0055	-0.59 (-0.94 to -0.24)	0.0011
Chile	1998-2017	1.55 (0.13 to 2.99)	0.0338							1.55 (0.13 to 2.99)	0.0338	1.55 (0.13 to 2.99)	0.0338	1.55 (0.13 to 2.99)	0.0338
China	2002-2017	0.92 (0.58 to 1.25)	<0.0001							0.92 (0.58 to 1.25)	<0.0001	0.92 (0.58 to 1.25)	<0.0001	0.92 (0.58 to 1.25)	<0.0001
Colombia	2003-2017	0.68 (-0.03 to 1.39)	0.0582							0.68 (-0.03 to 1.39)	0.0582	0.68 (-0.03 to 1.39)	0.0582	0.68 (-0.03 to 1.39)	0.0582
Costa Rica	1982-2016	2.38 (2.02 to 2.74)	<0.0001							2.38 (2.02 to 2.74)	<0.0001	2.38 (2.02 to 2.74)	<0.0001	2.38 (2.02 to 2.74)	<0.0001
Croatia	1988-1999	5.44 (3.82 to 7.08)	<0.0001	1999-2017	0.80 (0.22 to 1.37)	0.0083				0.80 (0.22 to 1.37)	0.0083	0.80 (0.22 to 1.37)	0.0083	2.53 (1.87 to 3.20)	<0.0001
Cyprus	1998-2007	3.98 (1.32 to 6.71)	0.0058	2007-2017	-1.16 (-2.91 to 0.62)	0.1850				-1.16 (-2.91 to 0.62)	0.1850	-1.16 (-2.91 to 0.62)	0.1850	1.24 (-0.19 to 2.69)	0.0886
Czechia	1983-2000	2.41 (2.14 to 2.69)	<0.0001	2000-2014	-1.22 (-1.56 to -0.88)	<0.0001	2014-2017	-5.85 (-9.01 to -2.57)	0.0012	-4.71 (-7.02 to -2.34)	0.0001	-2.79 (-3.86 to -1.70)	<0.0001	0.16 (-0.19 to 0.50)	0.3767
Denmark	1943-1954	-1.06 (-2.13 to 0.01)	0.0531	1954-2012	0.54 (0.47 to 0.61)	<0.0001	2012-2017	3.91 (1.76 to 6.12)	0.0005	1.33 (-3.27 to 6.15)	0.5770	2.40 (1.24 to 3.58)	<0.0001	0.52 (0.31 to 0.74)	<0.0001
Ecuador	1985-2017	1.76 (1.14 to 2.38)	<0.0001							1.76 (1.14 to 2.38)	<0.0001	1.76 (1.14 to 2.38)	<0.0001	1.76 (1.14 to 2.38)	<0.0001
Estonia	1983-2017	1.09 (0.85 to 1.33)	<0.0001							1.09 (0.85 to 1.33)	<0.0001	1.09 (0.85 to 1.33)	<0.0001	1.09 (0.85 to 1.33)	<0.0001
Finland	1953-1963	3.64 (2.38 to 4.92)	<0.0001	1963-1997	1.47 (1.33 to 1.61)	<0.0001	1997-2017	0.61 (0.4 to 0.83)	<0.0001	0.59 (0.37 to 0.82)	<0.0001	0.61 (0.40 to 0.83)	<0.0001	1.54 (1.32 to 1.75)	<0.0001
France	1998-2017	-0.11 (-0.60 to 0.39)	0.6542							-0.11 (-0.60 to 0.39)	0.6542	-0.11 (-0.60 to 0.39)	0.6542	-0.11 (-0.60 to 0.39)	0.6542
France, Martinique	1993-2017	3.85 (2.80 to 4.90)	<0.0001							3.85 (2.80 to 4.90)	<0.0001	3.85 (2.80 to 4.90)	<0.0001	3.85 (2.80 to 4.90)	<0.0001
Germany	2003-2017	-1.69 (-2.05 to -1.33)	<0.0001							-1.43 (-1.92 to -0.94)	0.0001	-1.69 (-2.05 to -1.33)	<0.0001	-1.69 (-2.05 to -1.33)	<0.0001
Iceland	1955-1964	7.45 (0.29 to 15.11)	0.0413	1964-2017	0.88 (0.61 to 1.15)	<0.0001				0.88 (0.61 to 1.15)	<0.0001	0.88 (0.61 to 1.15)	<0.0001	1.81 (0.79 to 2.84)	0.0005
India	2003-2017	2.59 (2.04 to 3.15)	<0.0001							2.01 (1.20 to 2.82)	0.0002	2.59 (2.04 to 3.15)	<0.0001	2.59 (2.04 to 3.15)	<0.0001
Ireland	1994-2015	-0.20 (-0.46 to 0.06)	0.1166	2015-2017	-6.55 (-14.74 to 2.43)	0.1387				-3.43 (-7.49 to 0.81)	0.1116	-1.65 (-3.52 to 0.26)	0.0894	-0.77 (-1.54 to 0.01)	0.0516
Israel	1963-1981	3.85 (3.09 to 4.62)	<0.0001	1981-2005	1.16 (0.85 to 1.47)	<0.0001	2005-2017	-4.01 (-4.64 to -3.38)	<0.0001	-4.30 (-5.04 to -3.54)	<0.0001	-4.01 (-4.64 to -3.38)	<0.0001	0.87 (0.56 to 1.18)	<0.0001
Italy	2003-2009	1.91 (0.00 to 3.86)	0.0505	2009-2017	-3.12 (-4.28 to -1.95)	0.0002				-3.12 (-4.28 to -1.95)	0.0002	-2.58 (-3.51 to -1.63)	<0.0001	-1.00 (-1.92 to -0.06)	0.0362
Japan	1978-1994	5.00 (4.59 to 5.41)	<0.0001	1994-2002	-0.92 (-1.82 to -0.02)	0.0451	2002-2015	2.03 (1.71 to 2.35)	<0.0001	2.03 (1.71 to 2.35)	<0.0001	2.03 (1.71 to 2.35)	<0.0001	2.65 (2.37 to 2.93)	<0.0001

Kuwait	1998-2017	1.65 (0.34 to 2.98)	0.0162							1.65 (0.34 to 2.98)	0.0162	1.65 (0.34 to 2.98)	0.0162	1.65 (0.34 to 2.98)	0.0162
Latvia	1983-1999	2.37 (1.65 to 3.09)	<0.0001	1999-2017	0.53 (0.02 to 1.05)	0.0438				0.53 (0.02 to 1.05)	0.0438	0.53 (0.02 to 1.05)	0.0438	1.39 (0.97 to 1.81)	<0.0001
Lithuania	1988-1995	4.82 (2.82 to 6.86)	<0.0001	1995-2011	1.15 (0.63 to 1.66)	0.0001	2011-2017	-1.89 (-3.86 to 0.11)	0.0631	-1.89 (-3.86 to 0.11)	0.0631	-0.89 (-2.15 to 0.39)	0.1730	1.38 (0.72 to 2.04)	<0.0001
Malta	1993-2017	0.61 (-0.05 to 1.28)	0.0673							-5.54 (-16.35 to 6.66)	0.3578	0.61 (-0.05 to 1.28)	0.0673	0.61 (-0.05 to 1.28)	0.0673
New Zealand	1983-1998	0.72 (0.28 to 1.16)	0.0022	1998-2017	-2.39 (-2.67 to -2.12)	<0.0001				-2.39 (-2.67 to -2.12)	<0.0001	-2.39 (-2.67 to -2.12)	<0.0001	-1.03 (-1.27 to -0.80)	<0.0001
Norway	1953-1983	2.95 (2.76 to 3.14)	<0.0001	1983-1997	1.57 (1.10 to 2.05)	<0.0001	1997-2017	0.20 (-0.01 to 0.41)	0.0580	0.22 (0.05 to 0.39)	0.0107	0.20 (-0.01 to 0.41)	0.0580	1.78 (1.63 to 1.93)	<0.0001
Philippines	1983-2006	1.86 (1.27 to 2.46)	<0.0001	2006-2010	-5.97 (-14.96 to 3.96)	0.2191	2010-2017	1.60 (-0.84 to 4.10)	0.1902	1.60 (-0.84 to 4.10)	0.1902	-0.13 (-2.88 to 2.70)	0.9268	0.86 (-0.43 to 2.16)	0.1927
Poland	1999-2017	0.39 (-0.29 to 1.08)	0.2415							0.39 (-0.29 to 1.08)	0.2415	0.39 (-0.29 to 1.08)	0.2415	0.39 (-0.29 to 1.08)	0.2415
Qatar	2003-2017	0.55 (-0.96 to 2.08)	0.4511							0.55 (-0.96 to 2.08)	0.4511	0.55 (-0.96 to 2.08)	0.4511	0.55 (-0.96 to 2.08)	0.4511
Republic of Korea	1999-2006	7.67 (6.23 to 9.13)	<0.0001	2006-2011	2.77 (0.38 to 5.21)	0.0266	2011-2017	-5.20 (-6.32 to -4.07)	<0.0001	-4.05 (-5.79 to -2.27)	<0.0001	-2.62 (-3.58 to -1.65)	<0.0001	1.87 (1.03 to 2.71)	<0.0001
Slovenia	1983-2010	2.51 (2.15 to 2.87)	<0.0001	2010-2017	-5.99 (-7.97 to -3.96)	<0.0001				-5.99 (-7.97 to -3.96)	<0.0001	-4.16 (-5.68 to -2.62)	<0.0001	0.70 (0.20 to 1.20)	0.0064
Spain	1993-2013	2.40 (2.20 to 2.60)	<0.0001	2013-2016	-4.43 (-7.21 to -1.57)	0.0045				-2.77 (-4.76 to -0.73)	0.0080	0.07 (-0.85 to 1.01)	0.8797	1.48 (1.08 to 1.88)	<0.0001
Sweden	1960-1987	0.80 (0.66 to 0.94)	<0.0001	1987-2017	0.34 (0.24 to 0.45)	<0.0001				-0.13 (-0.65 to 0.39)	0.6100	0.34 (0.24 to 0.45)	<0.0001	0.56 (0.48 to 0.64)	<0.0001
Switzerland	1998-2017	-0.71 (-1.17 to -0.25)	0.0047							-0.71 (-1.17 to -0.25)	0.0047	-0.71 (-1.17 to -0.25)	0.0047	-0.71 (-1.17 to -0.25)	0.0047
Thailand	1993-2017	3.77 (3.40 to 4.15)	<0.0001							3.77 (3.40 to 4.15)	<0.0001	3.77 (3.40 to 4.15)	<0.0001	3.77 (3.40 to 4.15)	<0.0001
The Netherlands	1989-2012	1.26 (1.17 to 1.34)	<0.0001	2012-2015	6.73 (3.50 to 10.07)	0.0002	2015-2017	-6.49 (-9.12 to -3.78)	0.0001	0.56 (-1.23 to 2.38)	0.5451	1.24 (0.10 to 2.40)	0.0330	1.25 (0.88 to 1.63)	<0.0001
Türkiye	1998-2003	8.66 (3.78 to 13.77)	0.0016	2003-2017	1.83 (1.18 to 2.49)	<0.0001				1.58 (0.91 to 2.26)	0.0002	1.83 (1.18 to 2.49)	<0.0001	3.58 (2.35 to 4.83)	<0.0001
Uganda	1993-2017	2.37 (1.19 to 3.56)	0.0004							2.37 (1.19 to 3.56)	0.0004	2.37 (1.19 to 3.56)	0.0004	2.37 (1.19 to 3.56)	0.0004
UK, England	1971-1992	0.92 (0.74 to 1.10)	<0.0001	1992-2011	0.39 (0.18 to 0.60)	0.0005	2011-2017	-1.28 (-2.27 to -0.27)	0.0146	-1.63 (-2.13 to -1.12)	<0.0001	-0.72 (-1.38 to -0.07)	0.0308	0.41 (0.24 to 0.59)	<0.0001
UK, Northern Ireland	1993-2012	0.30 (-0.15 to 0.75)	0.1817	2012-2017	-4.02 (-7.04 to -0.90)	0.0145				-4.02 (-7.04 to -0.90)	0.0145	-2.12 (-3.75 to -0.47)	0.0123	-0.62 (-1.32 to 0.09)	0.0882
UK, Scotland	1978-2010	0.77 (0.57 to 0.98)	<0.0001	2010-2017	-3.12 (-4.84 to -1.37)	0.0010				-1.33 (-4.85 to 2.32)	0.4692	-2.27 (-3.57 to -0.94)	0.0008	0.06 (-0.29 to 0.41)	0.7269
UK, Wales	2003-2009	2.64 (1.08 to 4.21)	0.0035	2009-2017	-1.86 (-2.78 to -0.94)	0.0012				-1.86 (-2.78 to -0.94)	0.0012	-1.37 (-2.11 to -0.63)	0.0003	0.04 (-0.70 to 0.79)	0.9138
USA	1978-2002	-0.75 (-0.93 to -0.58)	<0.0001	2002-2012	-3.05 (-3.77 to -2.31)	<0.0001	2012-2017	-0.23 (-1.98 to 1.56)	0.7948	-0.17 (-1.26 to 0.93)	0.7529	-1.49 (-2.47 to -0.50)	0.0033	-1.28 (-1.58 to -0.98)	<0.0001
USA, Puerto Rico	2003-2009	-0.75 (-2.16 to 0.67)	0.2505	2009-2015	2.09 (0.31 to 3.90)	0.0272	2015-2017	-7.50 (-14.74 to 0.36)	0.0583	-2.82 (-6.13 to 0.60)	0.1047	-0.44 (-2.21 to 1.37)	0.6336	-0.55 (-1.79 to 0.71)	0.3904

NOTE APC for each identified segment was calculated, assuming a constant percentage change in age-standardized incidence rate every year linearly on a log scale. The 10-year AAPC and AAPC for the entire period were based on permutation methods with allowing maximum number of Joinpoints of 2, whereas the 5-year AAPC were based on the weighted BIC (Bayesian Information Criterion) method without constraints on the maximum number of Joinpoint. Parametric method was used to calculate the confidence intervals for APC and AAPCs. For more information, refer to eMethods.

eTable 4 Difference in the 10-year average annual percent change (AAPC) in colorectal cancer incidence rates between young (25-49 years) and older (50-74 years) adults in 50 countries and territories

	Age, 25-49 years	Age, 50-74 years	Difference (95% CI)	p
Argentina	2.92 (0.80 to 5.10)	0.33 (-0.80 to 1.46)	2.60 (1.56 to 5.08)	<0.0001
Australia	3.01 (2.43 to 3.58)	-2.62 (-3.09 to -2.15)	5.62 (5.30 to 47.58)	<0.0001
Austria	-0.57 (-7.25 to 6.58)	-2.71 (-3.14 to -2.28)	2.13 (-0.88 to 5.12)	0.1666
Bahrain	-0.27 (-2.63 to 2.15)	3.36 (2.29 to 4.45)	3.63 (-4.77 to -2.58)	<0.0001
Belarus	3.24 (0.17 to 6.41)	1.95 (1.83 to 2.06)	1.30 (-0.04 to 2.62)	0.0533
Canada	2.83 (2.29 to 3.37)	-1.97 (-3.34 to -0.59)	4.80 (4.15 to 43.49)	<0.0001
Chile	3.96 (1.26 to 6.74)	1.55 (0.13 to 2.99)	2.41 (1.10 to 4.57)	0.0003
China	1.86 (-2.29 to 6.18)	0.92 (0.58 to 1.26)	0.94 (-0.88 to 2.75)	0.3086
Colombia	0.14 (-1.12 to 1.40)	0.68 (-0.03 to 1.39)	0.54 (-1.17 to 0.02)	0.0903
Costa Rica	1.49 (1.02 to 1.97)	2.38 (2.02 to 2.74)	0.89 (-1.15 to -0.68)	<0.0001
Croatia	1.39 (0.69 to 2.09)	0.80 (0.22 to 1.37)	0.59 (0.20 to 1.01)	0.0029
Cyprus	1.23 (-0.53 to 3.02)	-1.16 (-2.91 to 0.63)	2.39 (1.30 to 5.33)	<0.0001
Czechia	0.45 (-1.53 to 2.47)	-2.79 (-3.86 to -1.70)	3.24 (2.25 to 7.90)	<0.0001
Denmark	1.67 (1.03 to 2.31)	2.40 (1.24 to 3.58)	0.73 (-1.31 to -0.43)	0.0112
Ecuador	2.10 (1.29 to 2.91)	1.76 (1.14 to 2.38)	0.34 (-0.10 to 0.76)	0.1247
Estonia	0.54 (-0.11 to 1.19)	1.09 (0.85 to 1.33)	0.55 (-0.85 to -0.26)	0.0004
Finland	0.89 (0.65 to 1.13)	0.61 (0.40 to 0.83)	0.27 (0.13 to 0.42)	0.0001
France	2.09 (0.88 to 3.32)	-0.11 (-0.60 to 0.39)	2.20 (1.63 to 3.41)	<0.0001
France, Martinique	1.74 (0.13 to 3.37)	3.85 (2.80 to 4.90)	3.68 (3.32 to 8.09)	<0.0001
Germany	1.99 (1.23 to 2.75)	-1.69 (-2.05 to -1.33)	6.45 (2.93 to 10.51)	0.0002
Iceland	7.33 (-0.77 to 16.10)	0.88 (0.61 to 1.15)	1.33 (-1.94 to -0.77)	<0.0001
India	1.26 (-0.03 to 2.57)	2.59 (2.05 to 3.15)	2.27 (1.41 to 5.69)	<0.0001
Ireland	0.62 (0.07 to 1.18)	-1.65 (-3.52 to 0.26)	4.47 (4.13 to 22.20)	<0.0001
Israel	0.46 (0.03 to 0.89)	-4.01 (-4.64 to -3.38)	2.98 (2.34 to 7.36)	<0.0001
Italy	0.41 (-0.71 to 1.53)	-2.58 (-3.51 to -1.63)	0.91 (0.23 to 1.60)	0.0080
Japan	2.94 (1.39 to 4.52)	2.03 (1.71 to 2.35)	1.17 (-2.25 to -0.25)	0.0329
Kuwait	0.49 (-1.61 to 2.62)	1.65 (0.34 to 2.98)	0.59 (-0.91 to -0.34)	0.0004
Latvia	-0.06 (-0.59 to 0.48)	0.53 (0.02 to 1.05)	0.90 (0.29 to 1.68)	0.0037
Lithuania	0.01 (-0.53 to 0.55)	-0.89 (-2.15 to 0.39)	1.00 (-1.68 to -0.38)	0.0039
Malta	-0.39 (-1.79 to 1.04)	0.61 (-0.05 to 1.28)	2.11 (-2.94 to -1.40)	<0.0001
New Zealand	3.97 (2.44 to 5.52)	-2.40 (-2.67 to -2.12)	6.36 (5.70 to 42.38)	<0.0001
Norway	3.52 (1.94 to 5.13)	0.20 (-0.01 to 0.41)	3.32 (2.63 to 4.75)	<0.0001
Philippines	-1.88 (-3.92 to 0.21)	-0.13 (-2.88 to 2.70)	1.75 (-3.26 to -0.83)	0.0241
Poland	-0.16 (-1.56 to 1.26)	0.39 (-0.29 to 1.08)	0.55 (-1.23 to 0.07)	0.1112
Qatar	2.22 (-21.13 to 32.49)	0.55 (-0.96 to 2.08)	4.25 (3.33 to 26.07)	<0.0001
Republic of Korea	-0.45 (-3.03 to 2.19)	-2.62 (-3.58 to -1.65)	1.68 (-9.71 to 12.97)	0.7709
Slovenia	0.65 (0.31 to 0.99)	-4.16 (-5.68 to -2.62)	2.16 (0.95 to 3.75)	0.0005
Spain	-0.17 (-0.56 to 0.23)	0.07 (-0.85 to 1.01)	4.81 (4.11 to 47.01)	<0.0001
Sweden	2.32 (1.85 to 2.79)	0.34 (0.24 to 0.45)	0.24 (-0.68 to 0.03)	0.2817
Switzerland	0.83 (-0.42 to 2.09)	-0.71 (-1.17 to -0.25)	1.97 (1.77 to 2.30)	<0.0001
Thailand	2.76 (2.17 to 3.36)	3.77 (3.40 to 4.15)	1.54 (0.96 to 2.29)	<0.0001
The Netherlands	1.77 (1.56 to 1.99)	1.25 (0.10 to 2.40)	1.01 (-1.31 to -0.75)	<0.0001
Türkiye	2.15 (1.57 to 2.74)	1.83 (1.18 to 2.49)	0.53 (0.02 to 1.04)	0.0390

Uganda	0.22 (-1.85 to 2.34)	2.37 (1.19 to 3.56)	0.32 (-0.05 to 0.69)	0.0894
UK, England	3.59 (3.12 to 4.06)	-0.72 (-1.38 to -0.07)	2.15 (-3.19 to -1.23)	<0.0001
UK, Northern Ireland	0.54 (-0.41 to 1.49)	-2.12 (-3.75 to -0.47)	4.31 (3.96 to 19.37)	<0.0001
UK, Scotland	0.64 (0.39 to 0.88)	-2.27 (-3.57 to -0.95)	2.66 (1.83 to 7.21)	<0.0001
UK, Wales	1.55 (-0.16 to 3.28)	-1.37 (-2.11 to -0.63)	2.9 (2.32 to 8.83)	<0.0001
USA	2.13 (1.90 to 2.360)	-1.49 (-2.47 to -0.50)	2.92 (2.11 to 5.70)	<0.0001
USA, Puerto Rico	3.81 (2.68 to 4.96)	-0.44 (-2.21 to 1.37)	3.62 (3.18 to 14.03)	<0.0001

eTable 5 Difference in the 10-year average annual percent change (AAPC) in colorectal cancer incidence rates between men and women by age group in 50 countries and territories

Country or Territory	20-49 years		Difference between sexes (95% CI)	p	50-74 years		Difference between sexes (95% CI)	p
	Men	Women			Men	Women		
Argentina	3.91 (1.65 to 6.21)	1.74 (-1.50 to 5.09)	2.16 (0.45 to 4.56)	0.0126	0.85 (-0.60 to 2.32)	-0.32 (-1.58 to 0.96)	1.16 (0.32 to 2.15)	0.0065
Australia	2.92 (2.16 to 3.68)	3.50 (2.37 to 4.65)	-0.58 (-1.17 to -0.22)	0.0475	-2.84 (-3.42 to -2.26)	-2.42 (-3.04 to -1.80)	-0.42 (-0.79 to -0.14)	0.0290
Austria	0.05 (-6.40 to 6.95)	-0.04 (-0.77 to 0.69)	0.09 (-2.82 to 2.99)	0.9495	-3.07 (-3.57 to -2.56)	-2.04 (-2.34 to -1.73)	-1.03 (-1.29 to -0.80)	<0.0001
Bahrain	-	1.07 (-2.10 to 4.35)	-	-	2.07 (0.42 to 3.74)	4.94 (3.01 to 6.91)	-2.88 (-3.96 to -2.15)	<0.0001
Belarus	4.46 (-0.67 to 9.85)	0.62 (0.35 to 0.90)	3.83 (1.60 to 6.10)	0.0006	2.1 (1.95 to 2.24)	1.79 (1.66 to 1.92)	0.31 (0.22 to 0.40)	<0.0001
Canada	2.51 (2.10 to 2.91)	2.73 (2.03 to 3.43)	-0.22 (-0.57 to 0.02)	0.2079	-1.88 (-2.40 to -1.36)	-1.07 (-1.39 to -0.75)	-0.81 (-1.07 to -0.57)	<0.0001
Chile	5.36 (1.88 to 8.96)	2.43 (-0.97 to 5.95)	2.93 (0.83 to 6.59)	0.0055	1.77 (-0.13 to 3.71)	1.18 (-0.44 to 2.82)	0.60 (-0.48 to 1.53)	0.2761
China	2.11 (-2.72 to 7.18)	2.31 (-0.10 to 4.77)	-0.20 (-2.56 to 1.93)	0.8703	1.72 (1.20 to 2.24)	-0.24 (-0.62 to 0.14)	1.96 (1.68 to 2.88)	<0.0001
Colombia	2.12 (0.16 to 4.13)	0.69 (-0.65 to 2.05)	1.43 (0.40 to 2.65)	0.0062	1.10 (0.29 to 1.93)	0.32 (-0.57 to 1.22)	0.78 (0.26 to 1.40)	0.0033
Costa Rica	-2.43 (-5.80 to 1.06)	1.76 (1.11 to 2.43)	-4.19 (-5.73 to -2.66)	<0.0001	1.50 (0.43 to 2.58)	2.15 (1.76 to 2.55)	-0.65 (-1.14 to -0.18)	0.0091
Croatia	1.24 (0.35 to 2.14)	0.53 (-0.66 to 1.73)	0.71 (0.07 to 1.38)	0.0296	0.72 (0.03 to 1.41)	0.61 (0.01 to 1.21)	0.11 (-0.28 to 0.47)	0.5764
Cyprus	1.05 (-1.41 to 3.56)	1.49 (-0.57 to 3.58)	-0.44 (-1.84 to 0.64)	0.5342	-1.05 (-5.72 to 3.86)	-2.61 (-4.74 to -0.43)	1.56 (-0.74 to 3.69)	0.1851
Czechia	0.85 (-1.73 to 3.49)	-0.18 (-0.41 to 0.05)	1.03 (-0.10 to 2.15)	0.0736	-3.20 (-4.90 to -1.46)	-2.60 (-3.96 to -1.22)	-0.60 (-1.57 to 0.18)	0.2336
Denmark	1.94 (0.46 to 3.44)	1.59 (0.91 to 2.28)	0.34 (-0.36 to 1.01)	0.3349	2.57 (1.39 to 3.76)	1.33 (-2.87 to 5.72)	1.24 (-0.68 to 2.29)	0.2040
Ecuador	3.53 (2.27 to 4.81)	0.89 (-0.10 to 1.89)	2.65 (1.96 to 5.72)	<0.0001	2.01 (1.22 to 2.82)	1.49 (0.78 to 2.21)	0.52 (0.06 to 0.99)	0.0255
Estonia	0.57 (-0.20 to 1.34)	0.47 (-0.36 to 1.31)	0.09 (-0.40 to 0.51)	0.7044	0.61 (0.06 to 1.16)	0.83 (0.53 to 1.13)	-0.22 (-0.49 to 0.03)	0.1116
Finland	1.09 (0.89 to 1.30)	1.10 (0.86 to 1.34)	-0.01 (-0.15 to 0.12)	0.9073	0.18 (-0.33 to 0.70)	0.85 (0.78 to 0.92)	-0.67 (-0.89 to -0.44)	<0.0001
France	-0.86 (-1.45 to -0.27)	2.69 (-3.32 to 9.08)	-3.55 (-6.21 to -3.29)	0.0081	-0.47 (-1.02 to 0.09)	0.34 (-0.14 to 0.82)	-0.81 (-1.13 to -0.56)	<0.0001
Germany	2.02 (0.86 to 3.19)	1.92 (0.66 to 3.19)	0.10 (-0.64 to 0.68)	0.7865	-1.76 (-2.20 to -1.32)	-1.64 (-2.24 to -1.03)	-0.12 (-0.45 to 0.13)	0.4614
Iceland	-	-	-	-	1.30 (0.97 to 1.62)	0.70 (0.39 to 1.00)	0.60 (0.41 to 0.84)	<0.0001
India	0.93 (-0.81 to 2.70)	1.82 (0.06 to 3.61)	-0.89 (-1.96 to -0.12)	0.1024	2.28 (1.43 to 3.14)	2.96 (2.02 to 3.90)	-0.67 (-1.21 to -0.28)	0.0144
Ireland	0.43 (-0.32 to 1.18)	0.81 (-0.06 to 1.68)	-0.38 (-0.88 to -0.02)	0.1335	-1.74 (-3.47 to 0.03)	-0.47 (-0.80 to -0.13)	-1.27 (-2.05 to -0.50)	0.0015
Israel	1.43 (0.78 to 2.10)	-0.23 (-1.28 to 0.83)	1.66 (1.12 to 3.11)	<0.0001	-4.72 (-5.59 to -3.84)	-3.41 (-4.03 to -2.78)	-1.31 (-1.79 to -0.92)	<0.0001
Italy	-0.43 (-2.04 to 1.20)	1.17 (-1.22 to 3.61)	-1.6 (-2.86 to -0.89)	0.0123	-3.19 (-4.28 to -2.08)	-2.56 (-5.32 to 0.29)	-0.63 (-1.96 to -0.11)	0.3580
Japan	2.99 (1.28 to 4.73)	2.58 (1.49 to 3.68)	0.41 (-0.46 to 1.20)	0.3504	1.88 (1.56 to 2.21)	2.30 (1.92 to 2.68)	-0.42 (-0.63 to -0.25)	0.0001
Kuwait	1.99 (-0.62 to 4.67)	-0.94 (-3.47 to 1.66)	2.93 (1.34 to 7.35)	0.0003	1.67 (-0.03 to 3.41)	1.65 (-0.08 to 3.41)	0.02 (-1.03 to 0.81)	0.9678
Latvia	0.27 (-0.34 to 0.88)	-0.34 (-1.12 to 0.44)	0.61 (0.18 to 1.09)	0.0058	0.77 (0.19 to 1.34)	0.07 (-0.82 to 0.96)	0.70 (0.24 to 1.25)	0.0028
Lithuania	0.21 (-0.38 to 0.81)	-0.15 (-0.88 to 0.59)	0.36 (-0.05 to 0.76)	0.0821	-0.81 (-2.11 to 0.51)	0.15 (-0.46 to 0.77)	-0.96 (-1.59 to -0.39)	0.0029
Malta	-0.08 (-2.38 to 2.28)	-0.88 (-2.99 to 1.28)	0.81 (-0.57 to 1.95)	0.2523	0.91 (0.10 to 1.72)	-0.04 (-0.92 to 0.85)	0.94 (0.42 to 1.63)	0.0004
Martinique	2.10 (-0.94 to 5.23)	1.43 (-0.30 to 3.18)	0.67 (-0.85 to 2.03)	0.3825	4.30 (3.06 to 5.55)	3.10 (1.64 to 4.58)	1.20 (0.38 to 2.24)	0.0036

New Zealand	3.15 (2.11 to 4.20)	3.45 (0.90 to 6.07)	-0.30 (-1.49 to 0.21)	0.6110	-2.02 (-2.28 to -1.77)	-2.90 (-3.35 to -2.45)	0.88 (0.65 to 1.28)	<0.0001
Norway	2.22 (1.48 to 2.97)	3.99 (1.36 to 6.70)	-1.77 (-2.95 to -1.44)	0.0028	0.38 (0.19 to 0.56)	0.14 (-0.13 to 0.41)	0.23 (0.09 to 0.39)	0.0013
Philippines	-1.99 (-4.35 to 0.42)	0.55 (0.04 to 1.06)	-2.54 (-3.62 to -1.48)	<0.0001	0.19 (-0.34 to 0.72)	-1.38 (-5.82 to 3.27)	1.56 (-0.44 to 2.88)	0.1276
Poland	-0.21 (-2.20 to 1.81)	0.03 (-1.54 to 1.61)	-0.24 (-1.35 to 0.65)	0.6696	0.53 (-0.30 to 1.37)	0.03 (-0.71 to 0.77)	0.50 (0.02 to 0.99)	0.0398
Puerto Rico	4.28 (2.72 to 5.87)	3.38 (2.20 to 4.57)	0.91 (0.07 to 1.76)	0.0310	-0.99 (-3.10 to 1.17)	-0.10 (-3.77 to 3.70)	-0.89 (-2.76 to 0.05)	0.3518
Qatar	-	-	-	-	-1.33 (-5.42 to 2.93)	1.87 (-2.39 to 6.32)	-3.2 (-5.82 to -1.35)	0.0162
Republic of Korea	-1.57 (-2.64 to -0.50)	0.27 (-3.10 to 3.77)	-1.85 (-3.41 to -1.37)	0.0203	-2.77 (-3.74 to -1.80)	-2.7 (-3.75 to -1.64)	-0.07 (-0.71 to 0.41)	0.8195
Slovenia	0.59 (0.21 to 0.96)	0.73 (0.11 to 1.36)	-0.15 (-0.46 to 0.09)	0.3637	-4.61 (-6.36 to -2.82)	-3.85 (-5.76 to -1.91)	-0.75 (-1.91 to 0.05)	0.2142
Spain	-0.37 (-0.89 to 0.16)	0.06 (-0.44 to 0.57)	-0.43 (-0.75 to -0.18)	0.0082	-0.20 (-0.94 to 0.54)	0.40 (-1.03 to 1.86)	-0.60 (-1.31 to -0.24)	0.0934
Sweden	3.06 (2.15 to 3.98)	2.38 (1.47 to 3.29)	0.69 (0.13 to 1.27)	0.0136	-0.05 (-1.36 to 1.28)	0.29 (0.15 to 0.42)	-0.33 (-0.91 to 0.24)	0.2551
Switzerland	0.52 (-0.83 to 1.90)	1.07 (-0.70 to 2.87)	-0.55 (-1.52 to 0.07)	0.2646	-0.97 (-1.56 to -0.37)	-0.47 (-0.90 to -0.05)	-0.50 (-0.82 to -0.22)	0.0024
Thailand	3.07 (2.61 to 3.54)	2.37 (1.38 to 3.38)	0.70 (0.23 to 1.27)	0.0033	4.09 (3.61 to 4.58)	3.39 (2.72 to 4.05)	0.71 (0.36 to 1.15)	0.0001
The Netherlands	0.93 (-0.37 to 2.25)	1.47 (1.29 to 1.65)	-0.54 (-1.11 to 0.03)	0.0634	1.09 (-0.62 to 2.82)	1.33 (1.10 to 1.57)	-0.25 (-0.99 to 0.50)	0.5200
Türkiye	1.53 (0.88 to 2.19)	2.94 (1.76 to 4.12)	-1.41 (-1.98 to -1.11)	<0.0001	2.28 (1.60 to 2.96)	1.47 (0.83 to 2.12)	0.81 (0.41 to 1.32)	0.0001
Uganda	0.86 (-1.30 to 3.07)	-0.44 (-3.30 to 2.50)	1.31 (-0.27 to 2.65)	0.1045	3.75 (2.03 to 5.50)	1.13 (-0.03 to 2.30)	2.62 (1.73 to 5.55)	<0.0001
UK, England	2.97 (2.41 to 3.54)	5.00 (3.98 to 6.04)	-2.03 (-2.53 to -1.78)	<0.0001	-1.07 (-1.74 to -0.39)	0.15 (0.05 to 0.25)	-1.22 (-1.51 to -0.92)	<0.0001
UK, Northern Ireland	0.36 (-0.98 to 1.71)	0.68 (-0.28 to 1.66)	-0.32 (-1.04 to 0.28)	0.3750	-3.23 (-4.71 to -1.73)	-0.25 (-0.68 to 0.18)	-2.97 (-3.66 to -2.31)	<0.0001
UK, Scotland	0.47 (0.15 to 0.79)	0.78 (0.43 to 1.13)	-0.31 (-0.51 to -0.14)	0.0029	-2.61 (-4.12 to -1.09)	-1.17 (-2.72 to 0.40)	-1.44 (-2.40 to -0.77)	0.0033
UK, Wales	1.91 (-0.22 to 4.09)	1.15 (-0.74 to 3.07)	0.76 (-0.47 to 1.82)	0.2237	-1.81 (-3.18 to -0.41)	-0.89 (-2.02 to 0.25)	-0.91 (-1.70 to -0.30)	0.0232
USA	2.05 (1.81 to 2.29)	2.15 (1.80 to 2.50)	-0.10 (-0.28 to 0.05)	0.2709	-2.47 (-2.80 to -2.14)	-1.47 (-2.52 to -0.40)	-1.00 (-1.48 to -0.82)	0.0001

eTable 6. Risk factors for early-onset colorectal cancer (EOCRC) and colorectal adenoma (EOCRA) under age 50

Risk factor	Age at diagnosis	Design	Country	N for EOCRC	Reference	Relative Risk (95% CI)	
Risk factors: health conditions							
Obesity	<50	Meta-analysis[13]	US, Israel	7 studies[14-20] 24,006	BMI 18.5- <25 during adulthood/adolescence	≥30	Odds ratio=1.54 (1.01-2.35)
	<50	Cohort[21]	Korea	7,492	Persistent obesity*: no	Yes	Hazard ratio=1.09 (1.03-1.16)
					Persistent abdominal obesity†: no	Yes	Hazard ratio=1.18 (1.09-1.29)
	<50	Cohort[18]	US	114 F	Weight change since age 18	Each 5kg increase	Hazard ratio=1.09 (1.02-1.16) F
	36-45	Cohort[19]	Israel	698	BMI 5 to <85th percentiles at age 16-19	Overweight (85 to <95th)	Hazard ratio=1.35 (1.04-1.76)
						Obese (≥95th)	Hazard ratio=1.58 (1.02-2.44)
	<50	Cohort[18]	US	114F	BMI 18.5-<21 at age 18	21-<23	Hazard ratio=1.32 (0.80-2.16) F
						≥23	Hazard ratio=1.63 (1.01-2.61) F
Diabetes	<50	Cohort[22]	Sweden	141	No	Yes	Hazard ratio=1.90 (1.60-2.30)
	18-49	Case-control[23]	US	6,001	No	Yes	Odds ratio=1.24 (1.09-1.41)
Metabolic syndrome	<50	Case-control[24]	US	4,673	No	Yes	Odds ratio=1.25 (1.09-1.43)
Non-alcoholic fatty liver disease (NAFLD) ‡	20-49	Cohort[25]	Korea	7,910	No	Yes	Hazard ratio=1.14 (1.06-1.22)
Antibiotics	<50	Case-control[26]	Sweden	2,557	All oral antibiotics: no	Yes	Odds ratio=1.06 (0.96, 1.17)
					Broad spectrum	Yes	Odds ratio=1.13 (1.02, 1.26)
	<50	Case-control[27]	Sweden	1,905	No	Low (1-10 days), moderate (11-60 days), high (61-180 days), and very high (>180 days) use	No clear dose-response for proximal, distal, and rectal cancer
Birth via cesarean delivery	<50	Case-control[28]	Sweden	280 F 284 M	Vaginal delivery	Cesarean delivery	Odds ratio=1.62 (1.01-2.60) F Odds ratio=1.05 (0.64-1.72) M
Risk factors: lifestyle and behavioral							
Alcohol	<50	Case-control[29]	US, Canada, Australia, Europe	3,767	1-28 g/d	0g/d	Odds ratio=1.23 (1.08-1.39)
						>28 g/d	Odds ratio=1.25 (1.04-1.50)
	<50	Cohort[30]	Korea	8,314	0-<10 g/d	Moderate (10-<30 g/d for men and 10-<20 g/d for women)	Hazard ratio=1.09 (1.02-1.60)
						Heavy (≥30 g/d for men and ≥ 20g/d for women)	Hazard ratio=1.20 (1.11-1.29)
Sedentary behavior	<50	Cohort[31]	US	118 F	Sedentary TV viewing time: ≤7 h/wk	>14 h/wk	Hazard ratio=1.69 (1.07-2.67) F
Diet quality	<50	Cohort[32]	US	375 high risk EOCRA F	Western dietary pattern: Q1(lowest)	Q5 (highest)	Hazard ratio=1.67 (1.18-2.37) F
					Prudent dietary pattern: Q1		Hazard ratio=0.69 (0.48-0.98) F
					DASH: Q1		Hazard ratio=0.65 (0.45-0.93) F
					AMED: Q1		Hazard ratio=0.55 (0.38-0.79) F
					AHEI-2010: Q1		Hazard ratio=0.71 (0.51-1.01) F
Sugar-sweetened beverage (SSB)	<50	Cohort[33]	US	109 F	Adulthood <1 serving/wk	≥2 serving/d	Hazard ratio=2.18 (1.10-4.35) F
				35 F	Age 13-18	Per 1 serving/d	Hazard ratio=1.32 (1.00-1.75) F
Sulfur microbial diet	<50	Cohort[34]	US	EOCRA: 2,911 F	Sulfur microbial diet score: Q1 (lowest)	Q4 (highest)	Hazard ratio=1.31 (1.10-1.56) F
Red meat	<50	Case-control[29]	US, Canada, Australia, Europe	3,767	Red meat intake	Per 1 serving/d	Odds ratio=1.10 (1.04-1.16)
Risk factors: protective							

Vitamin D	<50	Cohort[35]	US	111[F]	Total vitamin D intake	Per 400 IU/d	Hazard ratio=0.46 (0.26-0.83) [F]
					Dietary vitamin D intake	Per 400 IU/d	Hazard ratio=0.34 (0.15-0.79) [F]
	<50	Cohort[36]	Korea	229	Serum 25-hydroxyvitamin D	Per 5 ng/ml	Hazard ratio=0.86 (0.77-0.97)
Aspirin	18-49	Case-control[17]	US veterans	651	All aspirin: no	Yes	Odds ratio=0.66 (0.52-0.84)
Nonsteroidal anti-inflammatory drug (NSAID)	<50	Case-control[29]	US, Canada, Australia, Europe	3,767	Regular use: yes	No	Odds ratio=1.43 (1.21-1.68)

Abbreviation: AHEI, Alternative Healthy Eating Index; AMED, Alternative Mediterranean Diet; BMI, body mass index; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; EOCRC, early-onset colorectal cancer (<age 50); EOCRA, early-onset colorectal adenoma (<age 50); NAFLD, non-alcoholic fatty liver disease; NSAID, nonsteroidal anti-inflammatory drug; RR, relative risk; SSB, sugar-sweetened beverages.

* BMI ≥ 25 kg/m^2 for both two 3-year apart screenings.

† Waist circumference ≥ 90 cm in men and ≥ 85 cm in women for both two 3-year apart screening.

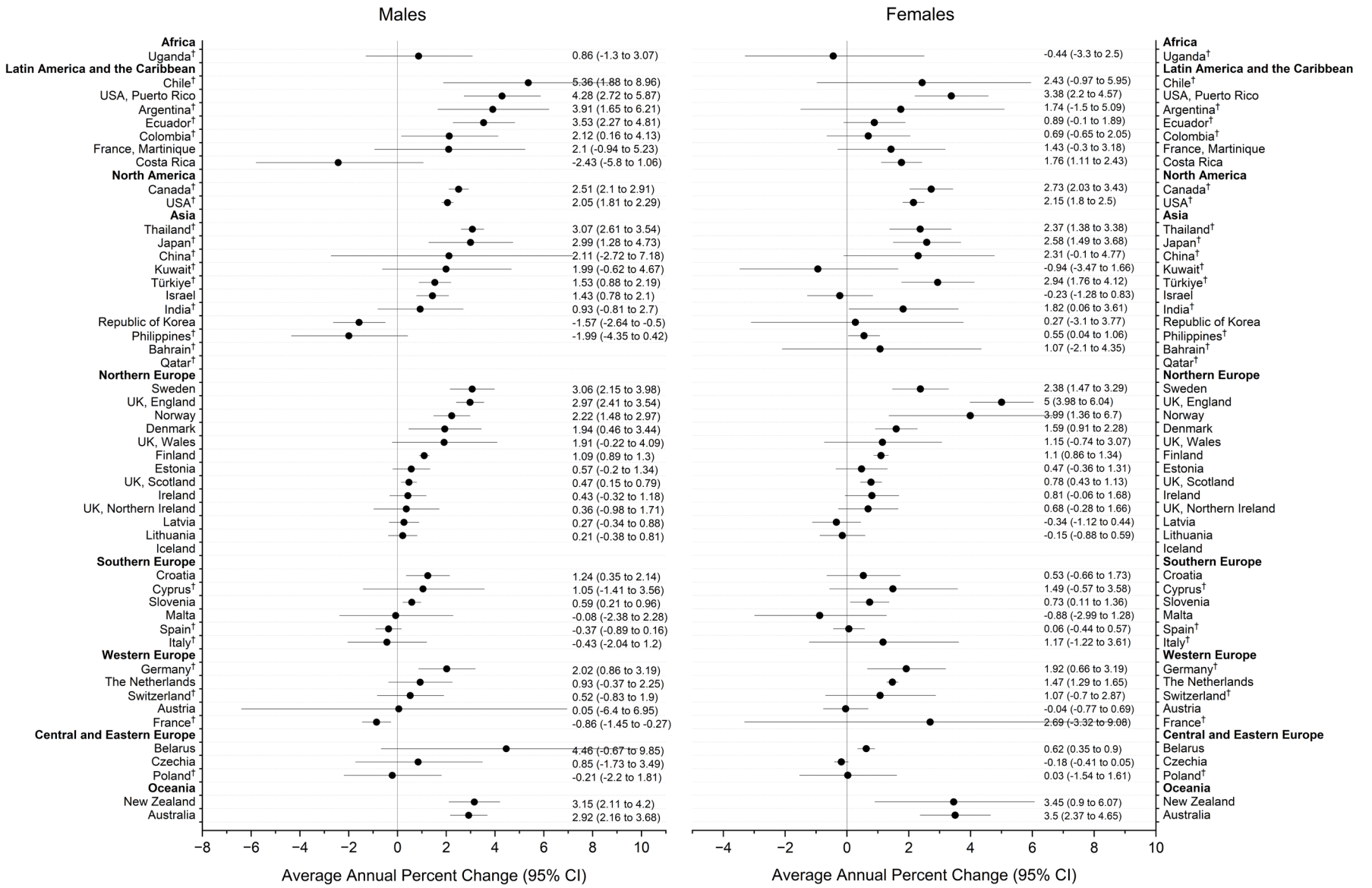
‡ NAFLD measured using a fatty liver index.

§ High-risk adenomas include adenomas ≥1 cm, tubulovillous or villous histology, high-grade dysplasia, or ≥3 adenomas.

F. Female

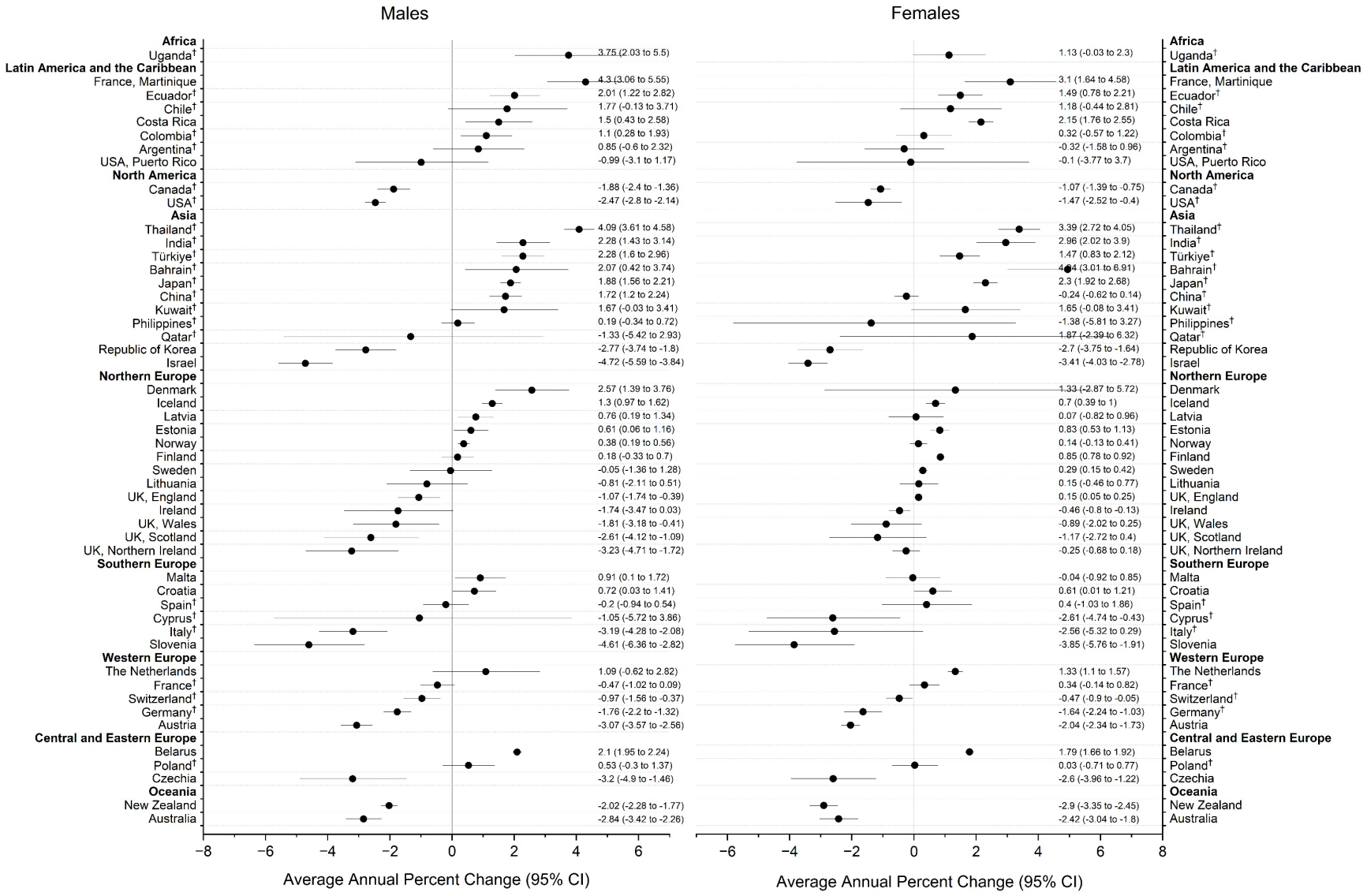
M. Male

eFigure 1. The 10-year average annual percent change (AAPC) and 95% confidence interval in colorectal cancer incidence rates in young (25-49 years) adults from 2008 to 2017* by sex



*Exceptions are Costa Rica and Spain (2005-2016) and Japan (2006-2015). †Sub-national data. Refer to Table 1 for population coverage and eTable 1 for details on population-based cancer registries. Dots represent the 10-year AAPC, and lines indicate the corresponding 95% confidence intervals (all p-values can be found in eTable 5).

eFigure 2. The 10-year average annual percent change (AAPC) and 95% confidence interval in colorectal cancer incidence rates in older (50-74 years) adults from 2008 to 2017* by sex



*Exceptions are Costa Rica and Spain (2005-2016) and Japan (2006-2015). †Sub-national data. Refer to Table 1 for population coverage and eTable 1 for details on population-based cancer registries.

Dots represent the 10-year AAPC, and lines indicate the corresponding 95% confidence intervals (all p-values can be found in eTable 5).

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