

2 **Table 1**

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Parameter	Selection
GBD release	GBD 2023
Data source	GBD 2023 Results Tool
Visualization source	GBD Compare
Cause	Colorectal cancer (Cause ID: B.1.6)
Cancer definition in ICD-10 code.	C18: Malignant neoplasm of colon C19: Malignant neoplasm of rectosigmoid junction C20: Malignant neoplasm of rectum C21: Malignant neoplasm of anus and anal canal
Measures and Measure IDs	Incidence (Measure ID: 6), Deaths (Measure ID: 1),
Metric	Rate
Unit	Cases/deaths per 100,000 population per year
Sex	Male, Female, Both sexes
Age groups	Age-standardized
Years	From 2013 to 2023
Data extraction date	November 10th, 2025

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5 Geographic Coverage Table: GBD location hierarchy with levels.

6 **Table 2**

GBD Level	Region
0	Global
1	Sub-Saharan Africa
2	South Asia
2	North America and Middle East
2	Andean Latin America
2	Caribbean
2	Central Asia
2	Central Europe
2	Central Latin America

GBD Level	Region
2	East Asia
2	Eastern Europe
2	High-income Asia Pacific
2	High-income North America
2	Oceania
2	Southeast Asia
2	Southern Latin America
2	Tropical Latin America
2	Western Europe
2	Australasia

7 Joinpoint Regression Analysis:

8 **Table 3**

Regions	Outcome	Joinpoints (n)	Joinpoint Year	APC Segment 1 (CI)	APC Segment 2 (CI)
Global	ASIR	1	2020	-0.39 (-2.40, 0.29)	1.74 (-0.08, 4.13)
Global	ASMR	1	2020	-0.89 (-2.81, 0.81)	0.90 (-0.80, 3.09)
Andean Latin America	ASIR	1	2016	0.39 (-5.54, 3.89)	5.35* (4.14, 10.12)
Andean Latin America	ASMR	1	2016	-0.45 (-5.06, 2.45)	3.72* (2.71, 7.55)
Caribbean	ASIR	0	-	1.43* (0.91, 1.99)	-
Caribbean	ASMR	0	-	0.94* (0.53, 1.36)	-
Central Latin America	ASIR	1	2019	2.31* (1.99, 2.95)	0.68 (-0.44, 1.29)
Central Latin America	ASMR	1	2019	1.84* (1.54, 2.27)	-0.12 (-0.98, 0.40)
East Asia	ASIR	0	-	1.45* (0.64, 2.29)	-
East Asia	ASMR	0	-	-0.40 (-1.25, 0.48)	-
High-Income Asia Pacific	ASIR	1	2021	-0.63* (-0.93, -0.42)	2.66* (1.11, 3.59)
High-Income Asia Pacific	ASMR	1	2021	-0.97* (-1.19, -0.80)	2.39* (1.25, 3.04)

Regions	Outcome	Joinpoints (n)	Joinpoint Year	APC Segment 1 (CI)	APC Segment 2 (CI)
High-Income North America	ASIR	1	2019	-1.47* (-2.54, -1.04)	0.64 (-0.23, 2.52)
High-Income North America	ASMR	1	2019	-1.45* (-2.58, -1.09)	-0.33 (-1.00, 1.00)
Oceania	ASIR	1	2020	0.74* (0.04, 1.18)	4.19* (2.66, 6.54)
Oceania	ASMR	1	2020	0.46 (-1.50, 1.05)	3.36* (1.42, 6.06)
South Asia	ASIR	0	-	3.03* (2.58, 3.49)	-
South Asia	ASMR	0	-	3.03* (2.58, 3.49)	-
Southeast Asia	ASIR	1	2018	0.89 (-0.88, 1.58)	2.60* (1.89, 4.48)
Southeast Asia	ASMR	1	2019	0.32 (-0.96, 0.74)	1.82* (1.04, 3.61)
Southern Latin America	ASIR	1	2020	-0.45 (-2.48, 0.23)	3.16* (0.88, 6.86)
Southern Latin America	ASMR	1	2020	-1.53* (-2.99, -0.10)	1.62 (-0.22, 4.73)
Sub-Saharan Africa	ASIR	1	2020	1.03* (0.86, 1.18)	5.15* (4.68, 5.63)
Sub-Saharan Africa	ASMR	1	2020	0.72* (0.48, 0.95)	4.43* (3.43, 5.14)
Tropical Latin America	ASIR	1	2021	1.35* (0.63, 1.60)	3.53* (1.80, 4.50)
Tropical Latin America	ASMR	1	2021	0.51 (-0.67, 0.89)	2.59* (0.70, 3.74)
Western Europe	ASIR	1	2021	-1.02* (-1.45, -0.80)	1.85* (0.13, 2.73)
Western Europe	ASMR	1	2021	-1.56* (-1.88, -1.37)	1.22 (-0.23, 1.99)
North Africa and Middle East	ASIR	0	-	2.05* (1.89, 2.21)	-
North Africa and Middle East	ASMR	0	-	0.74* (0.54, 0.93)	-
Australasia	ASIR	1	2020	-2.33* (-3.12, -2.02)	-0.46 (-1.57, 1.18)

Regions	Outcome	Joinpoints (n)	Joinpoint Year	APC Segment 1 (CI)	APC Segment 2 (CI)
Australasia	ASMR	1	2020	-2.65* (-3.45, -2.36)	-1.02 (-2.02, 0.55)
Central Asia	ASIR	1	2020	0.48* (0.08, 0.10)	-3.33* (-5.22, -2.06)
Central Asia	ASMR	1	2020	-0.22 (-0.61, 0.32)	-3.67* (-5.52, -2.38)
Central Europe	ASIR	0	-	-0.48* (-0.62, -0.33)	-
Central Europe	ASMR	1	2019	-0.56 (-0.79, 0.17)	-1.44* (-2.34, -1.02)
Eastern Europe	ASIR	1	2019	0.26 (-0.28, 2.66)	-1.39* (-4.02, -0.45)
Eastern Europe	ASMR	0	-	-1.40* (-1.80, -1.00)	-

Summary table for Joinpoint regression of ASIR and ASMR from 2013 to 2023
Number of joinpoints for each region, location of joinpoints (year of trend change where applicable), and APC values with 95% CIs represented.

APC = annual percent change
CI = 95% confidence interval from Joinpoint regression.

***Indicates that APC is significantly different from zero at the $\alpha = 0.05$ level**

Most regions experienced a deflection in the analyzed rates between 2019 and 2021, such as Global, High-Income Asia Pacific, Western Europe, High-Income North America, Sub-Saharan Africa, and Oceania. Several regions demonstrated a downward trend in Segment 1 and an upward or stabilizing trend in Segment 2. High-Income Asia Pacific and Western Europe showed a decline in ASIR and then showed an increase post-2021. High-Income North America showed a decline in ASIR and ASMR up to 2019 after which both rates stabilized.

For Andean Latin America, ASIR (AAPC = +5.35%) and ASMR (+3.72) increased substantially after 2016. Similarly, Sub-Saharan Africa demonstrated an increase in both ASIR (+1.03% to 5.15%) and ASMR (+0.72% to +4.43%) after 2020. Oceania (+4.19%) and Tropical Latin America (+3.53%) both showed an increase in ASIR. These regions all experienced increasing burden of CRC.

Other regions showed no change in burden with 0 joinpoints detected in the past decade. South Asia, North Africa and Middle East, and Caribbean demonstrated statistically significant increases in ASIR. Central Europe demonstrated a continuous decrease in ASIR (-0.48%) and Eastern Europe demonstrated a continuous decrease in ASMR (-1.40%).

Some regions experienced a decline in burden with Central Asia demonstrating a decrease for both ASIR (-3.33%) and ASMR (-3.67%) after 2020. Similarly, Australasia demonstrated a decline for ASIR (-2.33%) and ASMR (-2.65%).

Table 4

<u>Regions</u>	<u>Male ASIR (UI)</u>	<u>Female ASIR (UI)</u>	<u>Male:Female Ratio</u>	<u>Male ASMR (UI)</u>	<u>Female ASMR (UI)</u>	<u>Male:Female Ratio</u>
Global	31.40 (27.70, 34.82)	20.07 (16.74, 22.90)	1.56	14.97 (13.70, 16.26)	9.95 (8.69, 11.36)	1.50
Andean Latin America	22.22 (18.15, 26.58)	21.24 (17.43, 25.68)	1.05	11.22 (9.51, 12.79)	10.88 (9.48, 12.59)	1.03
Caribbean	34.80 (29.73, 40.07)	29.47 (24.56, 33.78)	1.18	16.44 (14.80, 18.16)	15.14 (13.55, 16.99)	1.09
Central Latin America	16.38 (14.74, 18.16)	14.53 (12.76, 16.50)	1.13	10.15 (9.45, 10.92)	8.61 (7.97, 9.21)	1.18
East Asia	36.42 (29.83, 44.82)	18.62 (14.36, 25.31)	1.96	15.48 (13.51, 18.00)	8.32 (6.75, 11.15)	1.86
High-income Asia Pacific	64.88 (58.69, 70.95)	35.32 (29.63, 39.87)	1.84	20.93 (19.00, 22.31)	12.19 (9.84, 13.80)	1.72
High-income North America	44.97 (38.69, 50.82)	32.47 (27.20, 37.86)	1.38	15.15 (13.82, 16.58)	10.95 (9.52, 12.23)	1.38
Oceania	12.75 (8.12, 18.74)	7.77 (5.52, 10.56)	1.64	10.60 (6.70, 15.46)	6.34 (4.51, 8.70)	1.67
South Asia	7.00 (5.13, 9.36)	6.85 (5.17, 8.99)	1.02	5.67 (4.20, 7.67)	5.39 (4.11, 7.16)	1.05
Southeast Asia	23.90 (18.10, 29.78)	14.37 (10.94, 18.22)	1.66	16.26 (12.58, 20.48)	9.59 (7.57, 12.30)	1.7
Southern Latin America	38.01 (33.75, 42.65)	25.49 (21.93, 29.10)	1.49	23.91 (21.79, 26.08)	15.88 (14.33, 17.30)	1.51
Sub-Saharan Africa	12.61 (8.99, 17.26)	9.07 (6.42, 12.46)	1.39	11.23 (7.92, 15.35)	7.74 (5.56, 10.65)	1.45
Tropical Latin America	22.04 (19.82, 24.66)	17.11 (15.11, 19.32)	1.29	14.24 (13.25, 15.16)	10.86 (9.85, 11.67)	1.31
Western Europe	52.78 (47.05, 58.69)	34.45 (29.15, 39.01)	1.53	19.74 (17.90, 21.39)	12.31 (10.69, 13.59)	1.6
North Africa and Middle East	18.90 (15.49, 22.59)	14.85 (11.56, 18.67)	1.27	11.68 (9.65, 13.97)	9.02 (7.34, 11.17)	1.3
Australasia	47.47 (42.13, 52.81)	35.98 (30.73, 40.59)	1.32	15.58 (13.95, 17.24)	11.76 (10.02, 13.26)	1.33
Central Asia	13.24 (11.93, 14.48)	8.60 (7.58, 9.59)	1.54	9.76 (9.02, 10.41)	6.19 (5.62, 6.86)	1.58

Central Europe	47.66 (44.20, 51.49)	25.18 (22.43, 28.02)	1.89	30.24 (28.69, 31.47)	15.39 (14.18, 16.42)	1.97
Eastern Europe	40.78 (36.39, 46.00)	24.06 (20.64, 27.66)	1.69	23.34 (21.51, 25.24)	13.54 (12.12, 15.01)	1.72

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UI = 95% uncertainty interval reported by GBD 2023

35 Across all 19 regions, males demonstrated higher ASIRs and ASMRs. The global male-to-female
36 ASIR ratio was 1.56 (31.40 vs 20.07) and 1.50 for ASMR (14.97 vs 9.95). The widest gaps for
37 ASIR were for East Asia (male:female ratio: 1.96), followed by Central Europe (1.89), and High-
38 Income Asia Pacific (1.84). The widest gaps for ASMR were for Central Europe (1.97), followed
39 by East Asia (1.86), and Eastern Europe (1.72). The lowest sex disparity was observed in South
40 Asia with ASIR male-to-female ratio (1.02) and ASMR male-to-female ratio (1.05). Similarly,
41 Andean Latin America showed low sex disparity with ASIR male-to-female ratio (1.05) and
42 ASMR male-to-female ratio (1.03). The highest male ASIR burden was observed for High-
43 income Asia Pacific with 64.88 new cases per 100,000. The highest male burden for ASMR was
44 observed in Central Europe with 30.24 deaths per 100,000. The highest female burden for ASIR
45 was observed for Australasia with 35.98 per 100,000. Southern Latin America reported the
46 highest female burden for ASMR 15.88 per 100,000.

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Table 5

<u>Regions</u>	<u>Joinpoint number (n)</u>	<u>Joinpoint Year</u>	<u>AAPC (CI)</u>	<u>P-value of AAPC</u>	<u>APC Segment 1 (CI)</u>	<u>APC Segment 2 (CI)</u>
Global	1	2020	0.25 (-0.22, 0.60)	0.25	-0.39 (-2.42, 0.29)	1.74 (-0.04, 4.14)
Andean Latin America	1	2016	3.83* (2.78, 5.06)	< 0.000001	0.41 (-5.73, 4.03)	5.34* (4.09, 10.21)
Caribbean	0	-	1.43* (0.90, 1.99)	< 0.000001	1.43* (0.90, 1.99)	-
Central Latin America	1	2019	1.66* (1.45, 1.88)	< 0.000001	2.32* (1.99, 2.97)	0.67 (-0.44, 1.29)
East Asia	0	-	1.49* (0.67, 2.34)	< 0.000001	1.49* (0.67, 2.34)	-
High-income	1	2021	0.02	0.88	-0.63* (-0.92, -0.42)	2.65* (1.10, 3.59)

Asia Pacific			(-0.20, 0.18)			
High-income North America	1	2019	-0.63* (-0.91, -0.40)	< 0.000001	-1.47* (-2.62, -1.02)	0.64 (-0.24, 2.54)
Oceania	1	2020	1.76* (1.40, 2.07)	< 0.000001	0.73 (-0.0048, 1.20)	4.20* (2.67, 6.54)
South Asia	0	-	3.04* (2.58, 3.51)	< 0.000001	3.04* (2.58, 3.51)	-
Southeast Asia	1	2018	1.74* (1.41, 2.07)	< 0.000001	0.89 (-0.94, 1.59)	2.60* (1.90, 4.44)
Southern Latin America	1	2020	0.62 (-0.03, 1.23)	0.06	-0.44 (-2.52, 0.25)	3.14* (0.89, 6.83)
Sub-Saharan Africa	1	2020	2.24* (2.13, 2.37)	< 0.000001	1.03* (0.85, 1.19)	5.15* (4.68, 5.62)
Tropical Latin America	1	2021	1.78* (1.48, 1.96)	< 0.000001	1.35* (0.62, 1.60)	3.53* (1.82, 4.49)
Western Europe	1	2021	-0.45* (-0.71, -0.29)	< 0.000001	-1.02* (-1.45, -0.80)	1.85* (0.15, 2.72)
North Africa and Middle East	0	-	2.05* (1.89, 2.21)	< 0.000001	2.05* (1.89, 2.21)	-
Australasia	1	2020	-1.78* (-2.06, -1.53)	< 0.000001	-2.34* (-3.13, -2.02)	-0.46 (-1.56, 1.16)
Central Asia	1	2020	-0.68* (-0.95, -0.39)	< 0.000001	0.48* (0.08, 1.00)	-3.33* (-5.20, -2.07)
Central	0	-	-0.48*	< 0.000001	-0.48* (-0.62,-0.33)	-

Europe			(-0.62,-0.33)			
Eastern Europe	1	2019	-0.40 (-0.85, 0.10)	0.11	0.26 (-0.30, 2.76)	-1.38* (-4.00, -0.44)

Table 5 incorporated standard errors derived from the GBD UIs to calculate the CIs for ASIR

UI = 95% uncertainty interval reported by GBD 2023
CI = 95% confidence interval derived from Joinpoint regression

We repeated the Joinpoint analysis using the calculated SEs in place of the assumed homoscedastic error. The table above presents the number of joinpoints and the year they were identified in. AAPC and 95% CIs, p-values, and APC estimates were included for every segment of each analyzed region. The secondary analysis showed no major variance from our original Joinpoint Regression analysis for ASIR.

Table 6

<u>Regions</u>	<u>Joinpoint number (n)</u>	<u>Joinpoint Year</u>	<u>AAPC (CI)</u>	<u>P-value of AAPC</u>	<u>APC Segment 1 (CI)</u>	<u>APC Segment 2 (CI)</u>
Global	1	2020	-0.35* (-0.81, -0.06)	0.02	-0.88 (-2.57, 0.27)	0.92 (-0.82, 3.06)
Andean Latin America	1	2016	2.48* (1.69, 3.42)	< 0.000001	-0.50 (-5.01, 2.37)	3.78* (2.76, 7.60)
Caribbean	0	-	1.03* (0.60, 1.43)	< 0.000001	1.03* (0.60, 1.43)	-
Central Latin America	1	2019	1.08* (0.90, 1.26)	< 0.000001	1.82* (1.53, 2.25)	-0.02 (-0.99, 0.53)
East Asia	0	-	-0.49 (-1.51, 0.47)	0.29	-0.49 (-1.51, 0.47)	-
High-income Asia Pacific	1	2021	-0.31* (-0.51, -0.19)	< 0.000001	-0.97* (-1.20, -0.80)	2.36* (1.10, 3.04)

<u>Regions</u>	<u>Joinpoint number (n)</u>	<u>Joinpoint Year</u>	<u>AAPC (CI)</u>	<u>P-value of AAPC</u>	<u>APC Segment 1 (CI)</u>	<u>APC Segment 2 (CI)</u>
High-income North America	1	2019	-1.00* (-1.22, -0.80)	< 0.000001	-1.45* (-2.65, -1.07)	-0.33 (-0.99, 0.96)
Oceania	1	2020	1.33* (0.81, 1.69)	< 0.000001	0.48 (-1.42, 1.06)	3.33* (1.32, 6.07)
South Asia	0	-	2.25* (1.91, 2.59)	< 0.000001	2.25* (1.91, 2.59)	-
Southeast Asia	1	2018	0.92* (0.59, 1.24)	< 0.000001	0.31 (-0.97, 0.73)	1.84* (1.02, 3.68)
Southern Latin America	1	2020	-0.52* (-1.06, -0.01)	0.05	-1.58* (-2.77, -1.05)	1.99 (-0.09, 5.14)
Sub-Saharan Africa	1	2020	1.82* (1.66, 1.99)	< 0.000001	0.72* (0.48, 0.95)	4.43* (3.44, 5.15)
Tropical Latin America	1	2021	0.93* (0.52, 1.18)	< 0.000001	0.49 (-0.90, 1.03)	2.69* (0.61, 3.92)
Western Europe	1	2021	-1.01* (-1.26, -0.87)	< 0.000001	-1.56* (-1.89, -1.37)	1.23 (-0.37, 2.02)
North Africa and Middle East	0	-	0.73* (0.54, 0.94)	< 0.000001	0.73* (0.54, 0.94)	-
Australasia	1	2020	-2.17* (-2.45, -1.92)	< 0.000001	-2.64* (-3.44, -2.37)	-1.06 (-2.07, 0.64)
Central Asia	1	2020	-1.29* (-1.58, -0.97)	< 0.000001	-0.22 (-0.59, 0.34)	-3.74* (-5.77, -2.41)

<u>Regions</u>	<u>Joinpoint number (n)</u>	<u>Joinpoint Year</u>	<u>AAPC (CI)</u>	<u>P-value of AAPC</u>	<u>APC Segment 1 (CI)</u>	<u>APC Segment 2 (CI)</u>
Central Europe	1	2018	-0.89* (-1.15, -0.66)	< 0.000001	-0.47 (-0.81, 0.69)	-1.31* (-2.59, -0.95)
Eastern Europe	0	-	-1.39* (-1.77, -1.02)	< 0.000001	-1.39* (-1.77, -1.02)	-

Table 5 incorporated standard errors derived from the GBD UIs to calculate the CIs for ASMR

**UI = 95% uncertainty interval reported by GBD 2023
CI = 95% confidence interval derived from Joinpoint regression**

We repeated the Joinpoint analysis using the calculated SEs in place of the assumed homoscedastic error. The table above presents the number of joinpoints and the year they were identified in. AAPC and 95% CIs, p-values, and APC estimates were included for every segment of each analyzed region. The secondary analysis showed no major variance from our original Joinpoint Regression analysis for ASMR.