Trends on the incidence of early-onset colorectal cancer in the United States: an age-period-cohort analysis

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Abstract

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Early-onset colorectal cancer (EO-CRC) has increased over recent decades, even as incidence among older adults has declined, and the drivers of this divergence remain poorly understood. We conducted an age–period–cohort analysis of EO-CRC among adults aged 20–54 years using population-based cancer registry data from the United States for the period 2000–2022. Cases were identified by ICD-O topography codes C18–C20, and age-specific incidence rates per 100,000 person-years were stratified by sex, race and ethnicity, county-level income, and tumor location. APC effects were estimated using log-linear Poisson regression, with the Intrinsic Estimator as a complementary approach. In considering different dimensions in the APC analysis, the age effect was nonlinear, accelerating notably past age 40 years. Period effects were modest across most demographic and tumor location subgroups, with IRRs ranging from 0.98 to 1.04 (95% CIs: 0.95–1.12) during 2015–2019 and between 0.91 and 1.12 (95% CIs: 0.76–1.20) during 2020–2022. Cohort effects reflected a pattern of rising risk across successive birth cohorts: the 1994 and 1999 cohorts showed the largest increases relative to the 1965 cohort, with IRRs from 1.3 to 2.1 (95% CI: 1.18–2.70). These increases were most pronounced

for rectal cancers (IRR: 1.77–1.82; 95% CI: 1.60–2.06). The disproportionate and subsite-specific nature of the cohort effect in rectal cancer may offer an important signal regarding the specific nature of exposures contributing to the growing burden of EO- CRC.

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I. Introduction

The incidence of early-onset colorectal cancer (EO-CRC) is rising at a concerning rate in the United States. Between 2013 and 2022, overall CRC incidence decreased by 0.9% annually, driven by reduction among adults aged 65 years and older (−2.5% per year), at a time when incidence increased by 3% annually among adults aged 20–49 years[1]; although EO-CRC is frequently defined as CRC diagnosed before age 50, incidence rates of CRC among adults aged 50-54 similarly increased by approximately 1.4% per year between 1992 and 2018[2].

Several factors likely contribute to rising EO-CRC rates: increasing obesity, sedentary behavior, changing environmental exposures, and persistent racial and ethnic disparities[3,4]. However, these established risk factors probably do not fully explain the pace or pattern of the observed increase in EO-CRC. It remains unclear whether recent trends reflect genuine generational shifts in risk, forces tied to a specific period in time, exposure to particular risk factors or a combination of these factors. Interpreting these trends accurately requires situating them within broader real-world changes in factors such as clinical practice, healthcare complexity, patient experiences, and recent changes in screening recommendations, including lowering the recommended screening age for average-risk adults from 50 to 45 years. Without this context, trends may be misinterpreted.

Age-Period-Cohort (APC) analysis provides an epidemiologic framework for examining secular trends in cancer incidence and for understanding how the likelihood of the event depends on the age, period (i.e., calendar time), and cohort (i.e., birth cohort)[5]. Although APC models cannot identify specific causal exposures, they can examine generational patterns consistent with underlying changes in lifestyle and environment. In this context, APC analysis facilitates evaluation of whether rising EO-CRC incidence reflects fundamental shifts in disease etiology driven by generational change or the emergence of novel population-level risk factors. A more granular understanding of these trends will facilitate hypothesis generation around early-life, structural, and biological determinants of EO-CRC, while informing future targeted prevention strategies for populations at greatest risk.

Existing APC analyses of EO-CRC have largely focused on overall incidence trends by sex and country[3,6–9], without examining how age, period, and cohort effects differ across racial and ethnic groups, socioeconomic context, or tumor location. Most published studies have also pooled colon and rectal cancers together, which may hide biologically meaningful differences by anatomical site. Meanwhile, disparities in EO-CRC incidence, stage at diagnosis, and survival across racial, ethnic, and socioeconomic groups are well documented[4,10,11], yet it remains unknown whether these disparities are reflected in the birth cohort component of risk. Specifically, it is unknown whether successive birth cohorts carry systematically different EO-CRC risk depending on race or ethnicity.

To address these existing gaps, we assessed differences in age, period, and cohort effects on EO-CRC incidence in the US from 2000-2022 by demographic factors (sex, race and ethnicity, county-level income in relation to the federal poverty level), and by tumor location (proximal colon, distal colon, rectum), using data from the Surveillance, Epidemiology, and End Results (SEER) cancer registry network.

II. Methods

Study Population and Data Source

This study utilized population-based cancer registry data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, covering the period 2000–2022 in the US. Incidence and delay-adjusted data was obtained from 21 registries (SEER 21), representing approximately 46% of the US population[12]. Analyses were conducted using aggregated data.

Eligible cases had a primary EO-CRC diagnosis between 2000 and 2022, a recorded age at diagnosis, and complete covariates (sex, race and ethnicity, county-level median household income, anatomic tumor subsite or location). Only individuals diagnosed between ages 20 and 54 years were included in the final analysis. Adults aged 50–54 years have exhibited incidence trends similar to those observed among younger adults and may represent a transitional group between early-onset and later-onset colorectal cancer. Including this age group in the present analysis of EO-CRC incidence patterns thus allows us to better capture existing patterns and to incorporate data from cases diagnosed shortly after the age of routine screening eligibility (wherein most diagnosed cancers likely arose before that eligibility threshold).

Data extraction was performed using SEER*Stat, and all analysis were conducted using R language (version 4.4). Because the study used de-identified, secondary data, no direct participant contact occurred and, therefore, institutional review board approval and individual consent were not required. Data management procedures included verification of site classification, evaluation of data completeness, and consistency checks to ensure analytic accuracy.

Variables and Measures

The primary exposure of interest was birth cohort, defined by year of birth and categorized into five-year cohort groups. The primary outcome was the incidence of EO-CRC, defined as the number of newly diagnosed cases of CRC diagnosed before age 54, identified using International Classification of Diseases for Oncology (ICD-O) topography codes C18–C20. Only invasive malignancies were included, and cancers of the appendix were excluded.

Age was grouped into six categories (20-24, 25-29, 30-34, 35-39, 40-44, 45-49, and 50-54), and calendar period into five intervals (2000–2004, 2005–2009, 2010–2014, 2015–2019, 2020–2022). Birth cohort was estimated as the difference between the period midpoint and the age-group midpoint (Cohort = Period − Age), producing cohort values at 5-year intervals ranging from 1950 to 1995, with additional single-year estimates arising from the terminal period stratum (2020–2022).

Covariates included were sex, race and ethnicity, income, and tumor location. Sex was defined as sex recorded in SEER records and was categorized as male or female. Race and ethnicity were classified based on SEER definitions: White, Black, Non-Hispanic Asian/Pacific Islander, Non-Hispanic American Indian/Alaska Native (AIAN), and Hispanic (any race). Due to changes in SEER race and ethnicity coding over time, White and Black categories include individuals of both Hispanic and non-Hispanic origins. Income status was derived from a Federal Poverty Level (FPL) variable constructed for this study. Federal Poverty Level was defined as an area-level measure of county-level socioeconomic status using median household income from SEER, linked to each case by year of diagnosis and county of residence. We constructed a proxy measure of FPL using annual US Department of Health and Human Services poverty guidelines for a four-person household (2000–2022). For each year, the 400% FPL threshold was calculated by

multiplying the corresponding 100% FPL value by four. SEER county-level income categories were converted to numeric ranges, and each case was classified by comparing the upper bound of its county income category to the year-specific 400% FPL threshold. Categories with an upper bound below or equal to the threshold were classified as ≤FPL, and those with an upper bound greater than to the threshold were classified as >FPL. This variable represents an area-level proxy of socioeconomic context rather than an individual-level measure of income or poverty. Individuals residing in counties classified as <400% FPL were considered to be in lower socioeconomic contexts, whereas those in ≥400% FPL were considered to be in higher socioeconomic contexts. The FPL variable was dichotomized at 400% of the FPL, a commonly used and U.S. policy-relevant threshold that determines eligibility for health insurance subsidies and tax credits. Finer income categories were not used, as they would have added strata without meaningfully improving interpretability or yielding stable estimates across the APC models. Tumor location was classified according to the anatomical subsite of the primary tumor using ICD-O-3 topography code: proximal colon (C18.0, C18.2-C18.5), distal colon (C18.6 – C18.7), rectum (C19.9, C20.9) and others/unspecified colon locations (C18.8, overlapping lesion of colon; C18.9, colon not otherwise specified).

Age-specific incidence rates per 100,000 person-years were calculated for each age group of interest. The 2010–2014 diagnosis period and the 1965 birth cohort served as reference group, corresponding to the median period and birth cohort in the study, respectively. Median categories were selected as the referent rather than boundary categories, consistent with commonly used APC modeling practices, to improve the stability and interpretability of APC estimates and reduce edge effects at the extremes of the observation window.

Statistical Analysis

In APC models, age effects represent chronological age–related biological processes and social dimensions of aging that are internal to individuals, capturing life-course developmental changes that influence cancer risk.[13,14] Period effects represent influences that operate at specific points in calendar time and affect all age groups simultaneously, encompassing a broad range of historical and environmental forces, including changes in diagnostic practices, screening guidelines and public health interventions.[13,14] Cohort effects describe differences in disease incidence across groups defined by year of birth and reflect the shared experiences of individuals who move through life together, providing insight into social change by capturing the cumulative influence of early-life and lifelong exposures that shape distinct risk trajectories across generations.[13,14]

APC effects were assessed using log-linear Poisson regression models implemented in the Epi package in R language. Nested models (age, age–drift, age–period, age–cohort, and full APC) were compared using likelihood ratio tests and goodness-of-fit statistics. From these models, net drift (the overall annual percent change in incidence across periods and cohorts) and local drift (age-specific annual percent changes over time) were estimated to characterize temporal trends.

In cases where the full APC model provided the best fit, we additionally estimated APC models using the Intrinsic Estimator (IE). The IE models were implemented using a custom R function, based on extensions of the IE approach described and provided by Yang et al. (2004)[15]. Both the conventional APC parameterization and the IE approach were fitted, and results were compared to assess whether estimated temporal patterns were robust to the choice of identifying assumption.

To quantify relative differences in EO-CRC incidence across diagnostic periods and birth cohorts, we calculated incidence rate ratios (IRR, Rate Ratio) from both the conventional APC model and the IE. In each model, estimated period and cohort effects were expressed relative to the reference period or cohort, with IRRs above 1 indicating higher incidence and values below 1 indicating lower incidence relative to that reference.

Results

Age Effect

A consistent age pattern was observed across all subgroups: incidence rose gradually through early adulthood, accelerated around age 35, and steepened further after age 40, with the highest rates observed in the 50-54 year group. This pattern was uniform across all subgroups (Figure 1), reflecting the underlying role of age in shaping CRC incidence.

Period Effect

Period effects were modest relative to age and cohort effects. Across most subgroups, IRRs comparing period-specific incidence rates to rates in the 2010-2014 period remained close to 1.0, followed by a gradual increase in more recent years (Figure 1). By 2020–2022, IRRs exceeded 1.0, indicating a modest recent upturn in incidence.

Subgroup-specific deviations from this general pattern were noted. Relative to the 2010-2014 period, among Black individuals, the IRR rose in the early 2000s and remained above 1.0 through the late 2010s before declining, peaking in 2005-2009 (IRR: 1.04; 95% CI: 1.02, 1.05). Rates among Asian/Pacific Islander individuals showed a generally declining trend through 2020, followed by a sharp increase, with an IRR of 1.19 (95% CI: 0.93, 1.54) in 2020–2022, though the wide confidence interval warrants caution. Among individuals residing in higher-income counties (>400% FPL), period effects rose in the late 2000s and stayed above 1.0,

peaking in 2015–2019 (IRR: 1.12; 95% CI: 1.00, 1.25), before a marked decline in 2020-2022 (IRR: 0.70; 95% CI: 0.57, 0.86).

By anatomic subsite, rectal cancer showed a steady decline in period effects through the late 2010s, followed by a pronounced increase in 2020-2022 (IRR: 1.12; 95% CI: 1.05, 1.19) compared to 2010-2014 period.

Cohort Effect

Across all subgroups, IRRs comparing incidence birth cohorts to the 1965 birth cohort increased progressively across successive birth cohorts, with the upward trend becoming most evident among those born around the late 1960s to early 1970s (Figure 1). Earlier cohorts (born 1950–1960) had IRRs below 1.0 relative to the 1965 reference cohort. The 1975 cohort marked a turning point, with IRRs exceeding 1.0 in most subgroups, and values continued to rise steadily through the 1980s and 1990s birth cohorts. A slight decline was observed in the most recent cohorts (1995 and 2000) in some subgroups, though estimates there carried wider uncertainty and should be interpreted cautiously.

When stratified by sex, relative to the 1965 birth cohort, IRRs rose steadily across all birth cohorts, peaking at 1.55 (95% CI: 1.45, 1.66) for the 1994 cohort in males and 1.57 (95% CI: 1.39, 1.77) for the 1999 cohort in females. By race and ethnicity, all groups showed a monotonically increasing pattern beginning with the 1975 cohort and continuing through the late 1990s, with the exception of Black individuals, whose rate ratios began rising somewhat later, with birth cohorts born around the early 1980s. Peak IRRs comparing incidence rates to the 1965 birth cohort of the same racial / ethnic group were: 1.50 (95% CI: 1.40, 1.61) for the 1994 cohort among White individuals; 1.57 (95% CI: 1.22, 2.05) in the 1999 cohort among Black individuals; 1.79 (95% CI: 1.52, 2.10) in the 1994 cohort among Hispanic individuals; 1.88 (95% CI: 1.19, 2.99) in the 1999 cohort among Asian / Pacific Islander individuals; and

2.55 (95% CI: 1.03, 6.29) in the 1979 cohort among AIAN individuals, though the latter estimate is highly imprecise and should be interpreted with caution.

When stratified by income, the IRR comparing incidence to that in the 1965 birth cohort peaked at 1.37 (95% CI: 1.18–1.58) for the 1999 cohort among those in lower income counties (≤FPL), and peaked at 2.09 (95% CI: 1.61, 2.71) for the 1998 cohort among those in higher income areas (>FPL). By anatomic subsite, when compared to rates for the 1965 birth cohort, rectal cancer rates exhibited the largest cohort-driven increase, peaking at 1.83 (95% CI: 1.68, 1.99) for the 1985 cohort, followed by distal colon at 1.65 (95% CI: 1.50, 1.80) for the 1994 cohort, and proximal colon at 1.17 (95% CI: 1.08, 1.25) for the 1989 cohort.

The 1994 and 1999 birth cohorts showed the largest increases in EO-CRC incidence across most demographic groups and tumor subsites, with IRRs generally ranging from 1.3 to 2.1 relative to the 1965 cohort across sex, race and ethnicity, income, and anatomic subsite. Cohort-related increases were most pronounced among residents of higher-income counties (IRR: 2.04–2.09; 95% CI: 1.61, 2.72), Hispanic individuals (IRR: 1.67–1.79; 95% CI: 1.26, 2.23), Asian/Pacific Islander individuals (IRR: 1.35–1.89; 95% CI: 1.04, 2.99), and rectal cancer cases (IRR: 1.77–1.82; 95% CI: 1.60, 2.06). Observations for proximal colon cancer diverged from this pattern, with IRRs near 1.0 in the most recent birth cohorts.

Additional descriptive analyses of EO-CRC incidence trends by age group, period of diagnosis, and birth cohort across all subgroups are provided in the Supplementary Results.

III. Discussion

This study examined age, period, and cohort effects on EO-CRC incidence in the US from 2000 to 2022, combining descriptive trend analysis with formal APC modeling. Across nearly all demographic groups and anatomic subsites, incidence rose over the study period with broadly similar temporal patterns. Age, period, and cohort effects were consistent across most subgroups, yet meaningful variation was observed within strata, highlighting the complexity of interpreting temporal trends in EO-CRC. Our findings of rising EO-CRC incidence are consistent with a growing body of evidence documenting this trend in the US and globally [3,16,17].

Age was the dominant driver of EO-CRC incidence across every subgroup examined where incidence rates accelerated sharply after 35 and steepened further after 40. This pattern aligns with the well-established biology of colorectal carcinogenesis and was remarkably consistent regardless of sex, race/ethnicity, income, or tumor location. Our findings show the steepest increases in individuals aged 40–49, with a steady rise also observed among those aged 30–39, particularly in the most recent diagnostic period (2015–2022). Similar findings were reported by Aldhaleei et al., whose APC analysis showed an exponential age effect with the greatest increase in incidence rates among those aged 40–44 from 1990 to 2021[3]. Comparable age gradients have been documented in prior analyses of SEER data and international registries[16,18].

The rise in incidence observed among individuals under 50 reflects a meaningful shift in the overall age distribution of CRC, a disease historically concentrated in older adults, who continue to bear the highest rates despite a recent decline. This shift is more consistent with a birth cohort hypothesis where the rising incidence is attributed to changing generational exposures and lifestyle factors rather than genetic characteristics[19].

Period effects were modest relative to age and cohort effects, with IRRs remaining close to 1.0 throughout most of the study period. The transient decline observed from the mid-2000s to approximately 2010–2012, followed by a more recent upward shift particularly after 2015–2017, likely reflects multiple overlapping forces. First, this pattern may reflect factors operating simultaneously across age groups, including changes in healthcare utilization, the growing availability of less invasive and more affordable diagnostic tests, and a gradual shift in clinician awareness that CRC is no longer exclusively a disease of older adults. Second, in 2018 the American Cancer Society recommended that average-risk adults begin CRC screening at age 45 rather than 50, which may partly explain the accelerating incidence among those aged 45–49[20]. Third, the sharp increase observed in 2020–2022 may partially reflect short-term disruptions in preventive services and delayed diagnoses during the COVID-19 pandemic, followed by a rebound in diagnostic activity as care resumed.

Subgroup-specific deviations in period effects, notably the sharper period increase for rectal cancer and the differences by county-level income, are unlikely to reflect screening or diagnostic influences. EO-CRC is predominantly diagnosed after symptom onset; for adults under 45, no screening recommendations existed before 2018, and the period shifts observed between 2005 and 2017 predate any major policy change or awareness campaign that might have differentially affected detection in younger populations. These patterns more likely reflect distinct variation in diagnostic access across groups or cohort-related influences that the APC framework might not fully isolate: because age, period, and cohort are linearly dependent, what appears as a period deviation may partly capture generational exposure differences that the model cannot cleanly attribute to either dimension.

Cohort effects were consistent across sex, race/ethnicity, income, and tumor location, with IRRs increasing progressively among individuals born after 1965–1970 and peak values observed in cohorts born in the late 1970s to late 1990s. This pattern is well-established in the literature[3,6,21]. Downham et al. reported similar findings, showing that EO-CRC incidence has increased across successive birth cohorts since 1960, with individuals born in the 1990s facing at least a four-fold higher risk than those born in the 1960s, with sharper increases at younger ages[6].

The consistency of cohort effects we observed across sex, race/ethnicity, income, and tumor location strongly suggests that the rise in EO-CRC is not confined to any single demographic or clinical subgroup but instead reflects broadly shared generational exposures. This cross-cutting pattern also implies that the primary drivers of rising incidence may be less related to upstream social determinants of health and more attributable to downstream exposures shared across population groups, alongside other environmental factors.

The observed cohort effect is consistent with an accumulation of overlapping risk factors experienced across early life, including obesity and metabolic dysfunction[22], westernized dietary patterns[23], gut dysbiosis[24], and exposure to novel carcinogenic compounds in agricultural, occupational, and food industry contexts[23]. Dietary patterns characterized by high consumption of sugar-sweetened beverages, processed and red meats, refined grains, high-fat dairy, and ultra-processed foods, alongside low fiber intake, have been significantly associated with EO-CRC risk[25]. While plausible biological mechanisms linking these exposures to colorectal carcinogenesis have been proposed, including inflammatory pathways, insulin resistance, and microbiome disruption, the relative contribution of each pathway and their interactions are not yet fully understood.

Because period-related forces in EO-CRC, such as changes in screening and clinical practices, are comparatively limited for the under-50 population, it is plausible that some cohort-driven variation is reflected in the period effect through the calendar year of diagnosis rather than through true period-specific exposures. These findings underscore the importance of cautious interpretation and highlight that both mechanisms likely contribute, with their relative importance varying across population subgroups and the broader epidemiologic context.

Several limitations merit acknowledgment. The use of aggregated SEER data in this analysis means that individual-level risk factor information cannot be linked to cancer records, which limits the ability to directly assess how changing exposures contribute to observed trends. Socioeconomic status is measured at the area level rather than the individual level, which likely obscures some of the true variation in incidence across income groups and reduces the heterogeneity that would be visible with individual-level data. The income-based findings should be interpreted accordingly.

Estimates for some population groups were based on small and, therefore, unstable numbers. In particular, estimates for the AIAN population were unstable throughout the analysis. Further, Hispanic ethnicity within White and Black racial categories was not examined separately due to insufficient case counts for Non-Hispanic White and Non-Hispanic Black subgroups, which may mask relevant within-group variation.

In addition, given the nature of the data source, there is limited or no information on several key potential confounders, effect modifiers, and other relevant exposures, a constraint inherent to population-based cancer surveillance data. SEER registries are not geographically or socio-demographically uniform across the country; they are disproportionately located in urban and metropolitan areas and intentionally oversample racial and ethnic minority populations, while several states and regions are not included[26,27]. These structural differences may limit the generalizability of observed age, period, and cohort trends in EO-CRC to populations residing in non-SEER regions or more rural settings.

Finally, the identification problem inherent to APC modeling means that period and cohort effects cannot be cleanly separated without imposing additional assumptions. APC models are useful tools for decomposing incidence trends, but they cannot establish causality. The results presented here are intended to inform hypothesis generation about the drivers of EO-CRC incidence, not to confirm them.

Despite these limitations, this study has several strengths worth noting. This study draws on population-based cancer registry data, providing broad coverage across demographic groups and an extended observation window from 2000 to 2022. APC modeling, while not without limitations, is well-established in demography and epidemiology literature and offers a principled framework for decomposing temporal trends under explicit assumptions. Importantly, this study examines cohort effects across multiple demographic characteristics and

anatomic subsites simultaneously, a combination that, to our knowledge, has not been previously reported in the APC EO-CRC literature. That cross-stratified perspective strengthens the case for a genuine cohort-driven component to rising EO-CRC incidence and adds specificity to theories about the potential etiologic exposures behind this epidemiologic shift. The analysis also integrates APC modeling with descriptive statistics and contextual information, which together provide a more complete picture of EO-CRC trends than any single approach could offer on its own.

In conclusion, taken together, our findings point in a consistent direction: the rise in EO-CRC is plausible to be primarily a cohort phenomenon, driven by exposures that have shifted across generations rather than by discrete period-specific events. The fact that cohort trajectories run roughly parallel across demographic groups, despite differences in absolute incidence, is difficult to explain through group-specific social or clinical factors alone. A shared environmental etiology, operating broadly across the population and from early in life, is the more parsimonious explanation. The disproportionate increase in incidence and the notorious consistent increasing cohort effect in rectal and distal colon cancers may be a signal about the specific nature of those exposures. Identifying what these exposures are, and when in the life course they matter most remains the central unanswered question in EO-CRC research.

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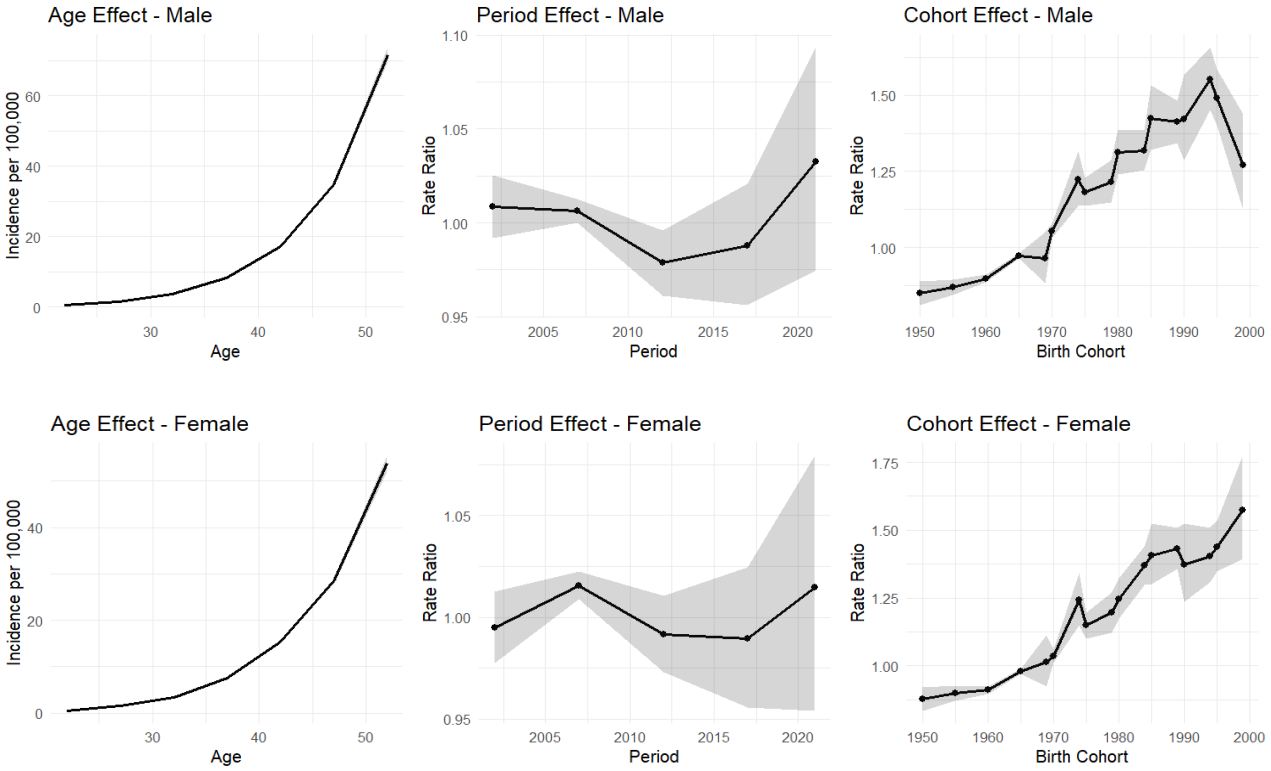
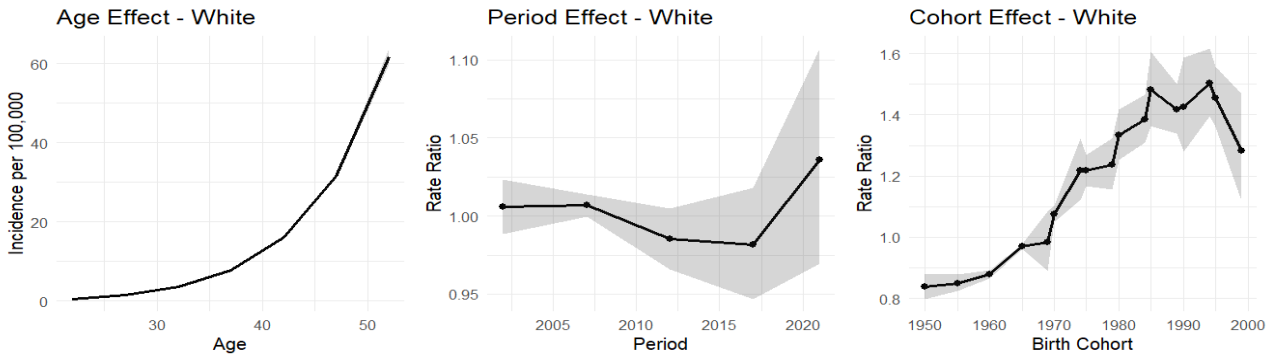
Figures

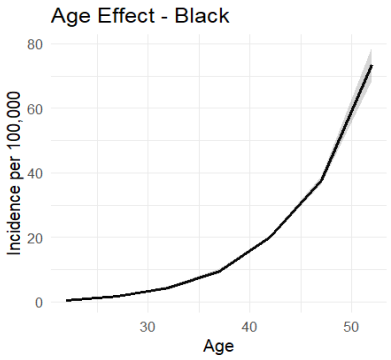
Figure 1. Age–period–cohort effects on colorectal cancer incidence in the United States, 2000–2022, stratified by demographic factors (1A by sex, 1B by race / ethnicity, 1C by county-level income) and tumor location (1D). Period and cohort effect estimates are incidence rate ratio relative to 2010-2014 for period effect, and 1965 birth cohort for cohort effect. Shaded areas represent 95% confidence intervals.

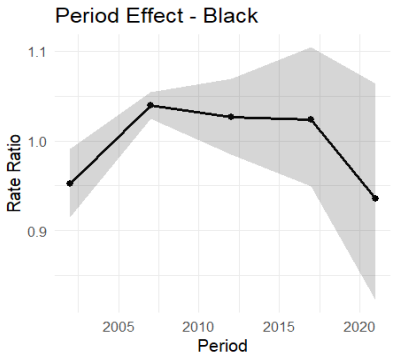
A) Sex

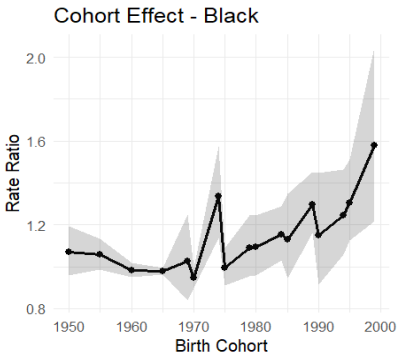


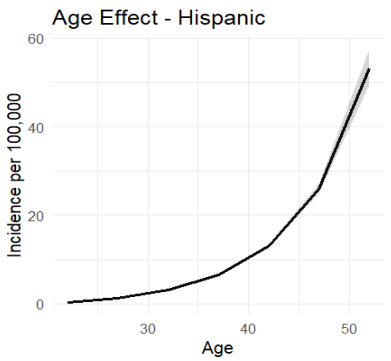
B) Race

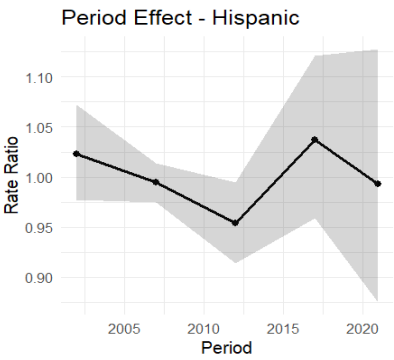


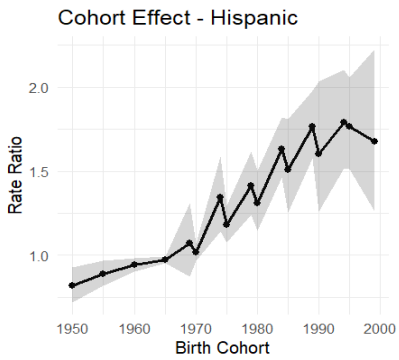

Age Effect - Black
Incidence per 100,000
0
20
40
60
80
30
40
50
Age

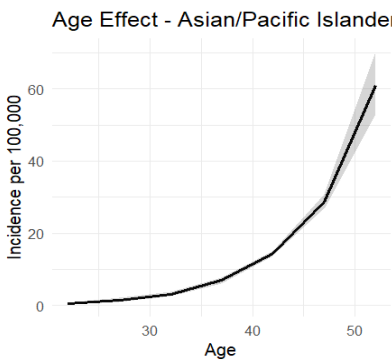

Period Effect - Black
Rate Ratio
0.9
1.0
1.1
2005
2010
2015
2020
Period

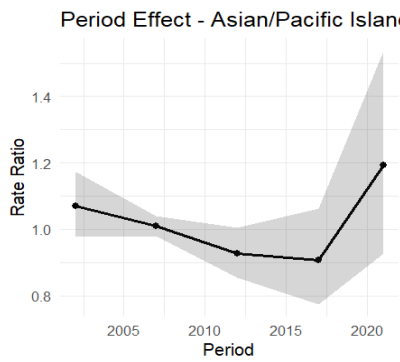

Cohort Effect - Black
Rate Ratio
0.8
1.2
1.6
2.0
1950
1960
1970
1980
1990
2000
Birth Cohort

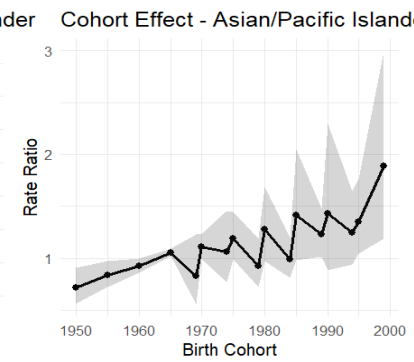

Age Effect - Hispanic
Incidence per 100,000
0
20
40
60
30
40
50
Age

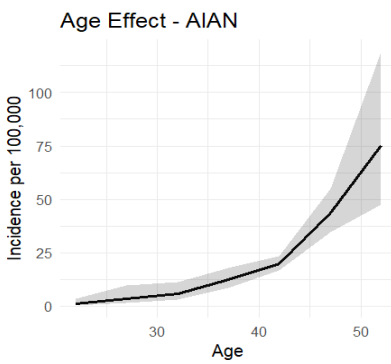

Period Effect - Hispanic
Rate Ratio
0.90
0.95
1.00
1.05
1.10
2005
2010
2015
2020
Period

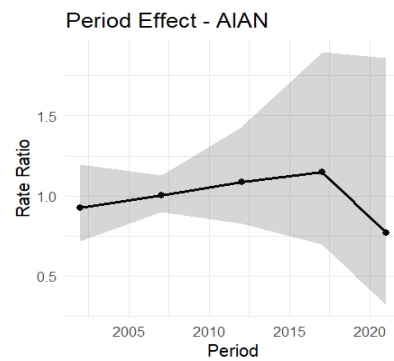

Cohort Effect - Hispanic
Rate Ratio
1.0
1.5
2.0
1950
1960
1970
1980
1990
2000
Birth Cohort

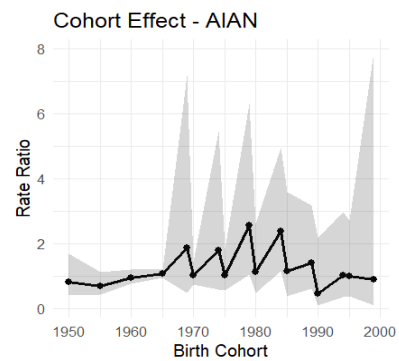

Age Effect - Asian/Pacific Islander
Incidence per 100,000
0
20
40
60
30
40
50
Age


Period Effect - Asian/Pacific Islander
Rate Ratio
0.8
1.0
1.2
1.4
2005
2010
2015
2020
Period

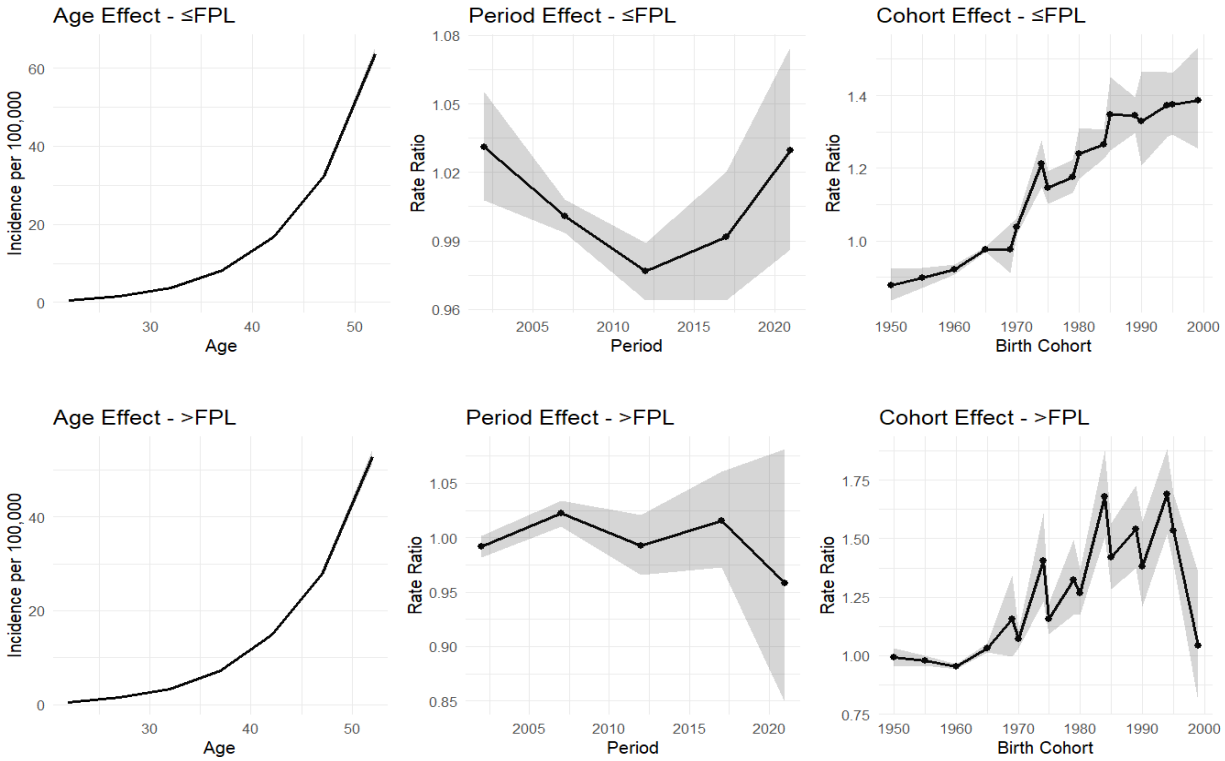

Cohort Effect - Asian/Pacific Islande
Rate Ratio
1
2
3
1950
1960
1970
1980
1990
2000
Birth Cohort


Age Effect - AIAN
Incidence per 100,000
0
25
50
75
100
30
40
50
Age

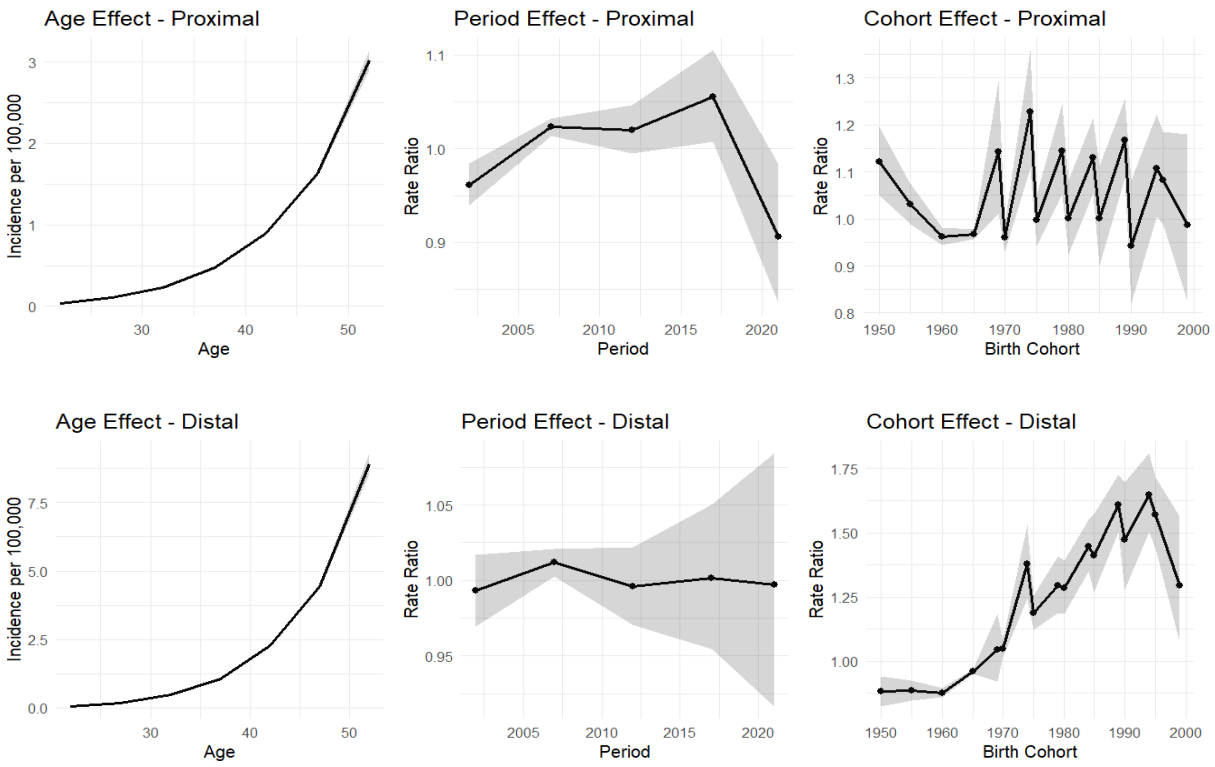

Period Effect - AIAN
Rate Ratio
0.5
1.0
1.5
2005
2010
2015
2020
Period

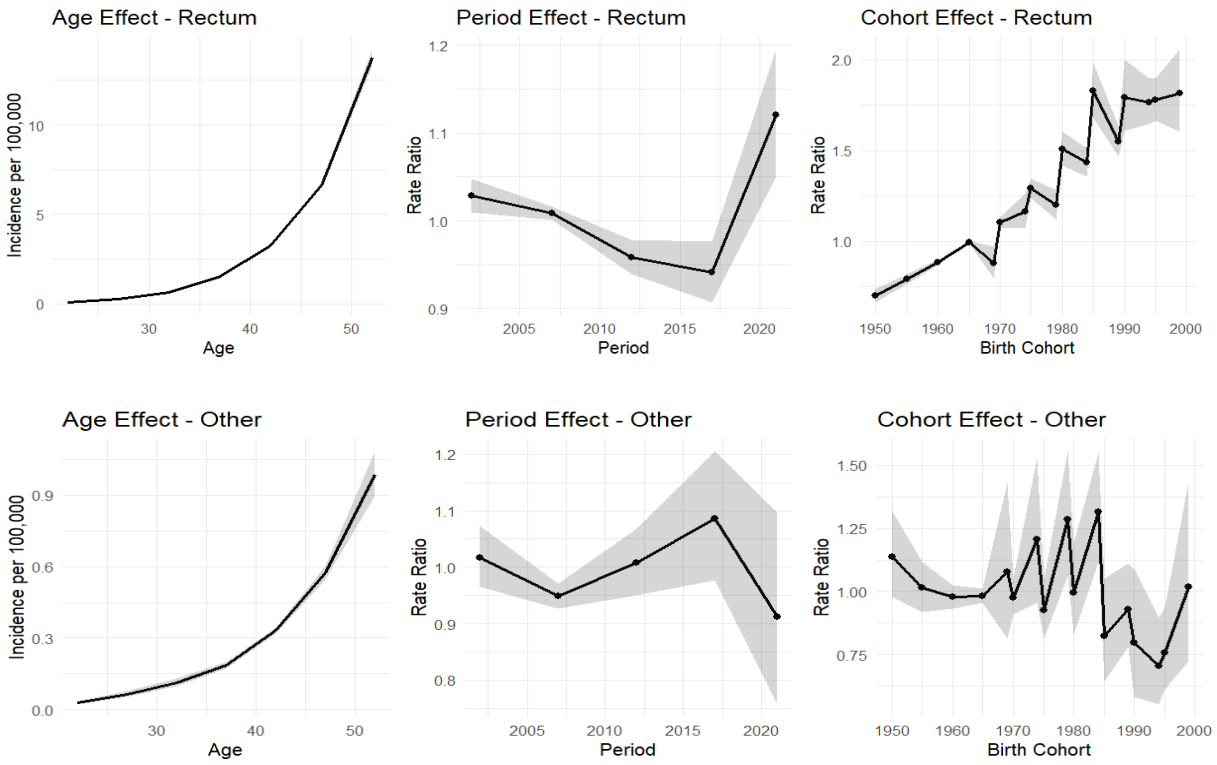

Cohort Effect - AIAN
Rate Ratio
0
2
4
6
8
1950
1960
1970
1980
1990
2000
Birth Cohort

C) Income



D) Site




Age Effect - Rectum
Incidence per 100,000
0
5
10
30
40
50
Age
Period Effect - Rectum
Rate Ratio
0.9
1.0
1.1
1.2
2005
2010
2015
2020
Period
Cohort Effect - Rectum
Rate Ratio
1.0
1.5
2.0
1950
1960
1970
1980
1990
2000
Birth Cohort
Age Effect - Other
Incidence per 100,000
0.0
0.3
0.6
0.9
30
40
50
Age
Period Effect - Other
Rate Ratio
0.8
0.9
1.0
1.1
1.2
2005
2010
2015
2020
Period
Cohort Effect - Other
Rate Ratio
0.75
1.00
1.25
1.50
1950
1960
1970
1980
1990
2000
Birth Cohort

APPENDIX -SUPPLEMENTARY MATERIAL

Supplementary Methods

To give descriptive context for the APC analyses, we examined EO-CRC incidence trends by period of diagnosis, birth cohort, age group, sex, race and ethnicity, income level, and tumor location. Incidence rate ratios (IRRs) quantified relative differences across subgroups, periods, and cohorts; IRRs above 1 indicated higher incidence relative to the reference group, and those below 1 indicated lower incidence.

Because age, period, and cohort are linearly dependent, APC models cannot uniquely separate the overall linear temporal trend into independent period and cohort components. We addressed this non-identifiability using the ACP parameterization in Epi package, which allocates the linear drift to the cohort effect and estimates period effects as deviations from that trend. Period and cohort effects were presented as IRRs relative to the 2010–2014 diagnosis period and the 1965 birth cohort, respectively.

To assess whether incidence patterns differed by sex, race and ethnicity, income level, and tumor location, we fitted Poisson regression models with a population offset. Subgroup differences in temporal patterns were evaluated using likelihood ratio tests comparing nested models with and without interaction terms between subgroup variables and the age, period, and cohort components. All tests were two-sided; statistical significance was defined as $p < 0.05$.

Supplementary Results

Age-specific incidence rates of EO-CRC increased over time across all demographic subgroups defined by sex, race and ethnicity, income and tumor location (Supplementary Figures 1–2). Rates were relatively stable or showed only modest increases from 2000 to 2014, then rose more noticeably from 2015 to 2022, particularly among individuals aged 40–49 years. Among younger adults aged 20–34 years, incidence remained low but trended gradually upward. Likelihood ratio tests confirmed that temporal incidence patterns differed significantly by sex, race and ethnicity, income, and anatomic location ($p < 0.001$), indicating that age, period, cohort components on EO-CRC incidence were not uniform across subgroups.

Period Trends

Supplementary Figure 3 display age-specific EO-CRC incidence rates by diagnostic period across all subgroups. Consistently, the 2015–2019 and 2020–2022 periods show higher incidence rates than earlier periods at every age group, with the separation between periods becoming most apparent from age 40 onward. The 40–49 age group showed higher incidence than younger age groups across all periods and subgroups, reflecting the steep upward trajectory of the curves at that range.

In the 2015–2019 versus 2000–2004 comparison, the 30–34 age group drove the greatest relative increase by sex, with IRRs of 1.34 (95% CI: 1.27, 1.40) among males and 1.32 (95% CI: 1.26, 1.39) among females. The racial and ethnic pattern was less uniform. White individuals saw the steepest increases in the 40–44 (IRR: 1.37; 95% CI: 1.34, 1.41) and 35–39 (IRR: 1.33; 95% CI: 1.28, 1.38) age groups. Among Black individuals, the 35–39 group showed the largest increase (IRR: 1.31; 95% CI: 1.21, 1.41). Hispanic adults had the greatest increases at younger ages — 30–34 (IRR: 1.50; 95% CI: 1.33, 1.70) and 25–29 (IRR: 1.47; 95% CI: 1.23, 1.76). Among Asian/Pacific Islander individuals, the largest point estimate was in the 20–24

age group (IRR: 1.29; 95% CI: 0.69, 2.41), though the wide confidence interval precludes a firm conclusion.

Comparing rates from the 2015-2019 period to 2000-2004, by county income, individuals in low-income counties had the greatest relative increase in the 35–39 age group (IRR: 1.23; 95% CI: 1.19, 1.27); in high-income counties, the 30–34 group showed the largest increase (IRR: 1.31; 95% CI: 1.23, 1.39). By location, rectal cancer showed the largest relative increase of any subsite, with the 30–34 age group most affected (IRR: 1.63; 95% CI: 1.54, 1.72). Proximal colon increases peaked in the 35–39 group (IRR: 1.23; 95% CI: 1.17, 1.28), distal colon in the 25–29 group (IRR: 1.47; 95% CI: 1.32, 1.64), and other (unspecified subsites) in the 40–44 group (IRR: 1.12; 95% CI: 1.02, 1.22).

Births Cohort Trends

Figure 4 shows age-specific EO-CRC incidence rates plotted by birth cohort across all subgroups. Visually, more recently born generations tend to show higher incidence rates than earlier ones, particularly among individuals aged 35–49 years. Figure 5 presents cohort-specific IRRs estimated relative to the 1965 birth cohort. Earlier cohorts (1945–1960) show IRRs at or near 1.0, while cohorts born from the 1970s onward show IRRs progressively above 1.0, reaching approximately 1.2 among those aged 35–49 years. The highest IRRs appear concentrated among individuals born in the late 1970s (1976–1980). Males and females follow broadly parallel trajectories, with males showing slightly higher absolute rates but comparable generational patterns.

Across stratifications by race and ethnicity, income, and anatomic subsite (Figures 4 and 5), cohort patterns are broadly consistent with the overall picture. For rectal and proximal colon cancers in particular, earlier cohorts (1945–1960) show IRRs at or below 1.0, while cohorts born from the 1970s onward show IRRs above 1.0, reaching approximately 1.4 among those aged 30–39 years.

The most recent birth cohorts (1985 and 1990) are a notable exception to this otherwise rising trajectory. In Supplementary Figure 3, incidence rates in the 20–44 age groups appear lower than in the preceding cohorts, and a similar dip is visible in the 30–44 age groups in Supplementary Figure 4, most prominently among males and across several stratified subgroups. This decline, however, should be interpreted cautiously. Individuals born in 1985 and 1990 were only 32–37 and 27–32 years old at the end of the study period, leaving these cohorts incompletely observed; what appears to be a downturn is more plausibly an artifact of right-censoring than evidence of a true generational shift in risk.

Best model for fitting APC

The full APC model provided the best fit to incidence data across most demographic and anatomic subgroups (Supplementary Table 1). Exceptions were observed for the smaller Asian/Pacific Islander and AIAN subgroups, and for income-based subgroups, where the nested Age–Cohort model fit the data better, suggesting that incidence patterns in these groups may be more strongly shaped by age and birth cohort than by period-related changes.

Local and net drift

Net drift estimates indicated a positive average annual percentage change in EO-CRC incidence across all subgroups, with the exception of the "other" tumor location category (−0.52%; 95% CI: −1.25%, 0.21%). Both males and females showed increasing trends, with annual increases of 1.47% (95% CI: 1.24%, 1.70%) and 1.38% (95% CI: 1.14%, 1.62%), respectively (Supplementary Table 2). By race and ethnicity, the steepest increase was observed among White individuals (1.56%; 95% CI: 1.31%, 1.80%), followed by Hispanic (1.38%; 95% CI: 1.14%, 1.62%) and Asian / Pacific Islander populations (1.36%; 95% CI: 0.27%, 2.46%). Black individuals had a more modest but statistically meaningful increase (0.67%; 95% CI: 0.14%, 1.20%). AIAN estimates were too imprecise to interpret meaningfully (0.01%; 95% CI: −3.53%, 3.69%). Higher-income areas showed a somewhat larger annual increase (1.37%; 95% CI: 0.82%, 1.93%) compared to lower-income areas (0.97%; 95% CI: 0.60%, 1.35%), although both were statistically significant. By anatomic subsite, the rectum showed the steepest rise (2.33%; 95% CI: 2.08%, 2.59%), followed by the distal colon (1.57%; 95% CI: 1.24%, 1.90%). Proximal colon showed no meaningful trend (0.07%; 95% CI: −0.25%, 0.39%).

Local drift results revealed that age-specific annual percentage changes were not uniform across age groups, with consistently stronger increases in younger-to-middle adult ages. For both sexes, increases began around ages 25–29, peaking at ages 30–34 in males (1.76%; 95% CI: 1.64%, 1.89%) and 35–39 in females (1.86%; 95% CI: 1.68%, 2.04%) (Figure 3).

Among White individuals, the increase began around ages 25–29 and peaked at 40–44 (2.03%; 95% CI: 1.90%, 2.17%). Hispanic individuals peaked earlier, at ages 30–34 (2.89%; 95% CI: 2.26%, 3.51%). Black individuals showed more modest and less consistent changes, with near-null increases around ages 40–44 (0.12%; 95% CI: −0.15%, 0.40%). Asian/Pacific Islander

populations showed higher increases at younger ages (20–24), declining toward near-null in mid-adulthood with a modest rebound at older ages. AIAN estimates were too variable to draw meaningful conclusions.

By anatomic subsite, the rectum showed the most pronounced increases across nearly all age groups, peaking at ages 30–34 (2.68%; 95% CI: 2.40%, 2.95%) and remaining elevated through ages 45–49. Distal colon cancers showed consistently elevated increases from ages 25–29 onward (2.16%; 95% CI: 1.63%, 2.69%), remaining relatively stable through mid-adulthood before declining at older ages. Proximal colon showed little to no meaningful change across age groups.

Intrinsic Estimator

Results from the Intrinsic Estimator (IE) were consistent in shape across subgroups, suggesting that the underlying age–period–cohort structure of EO-CRC incidence is broadly similar across population strata (Supplementary Figure 6).

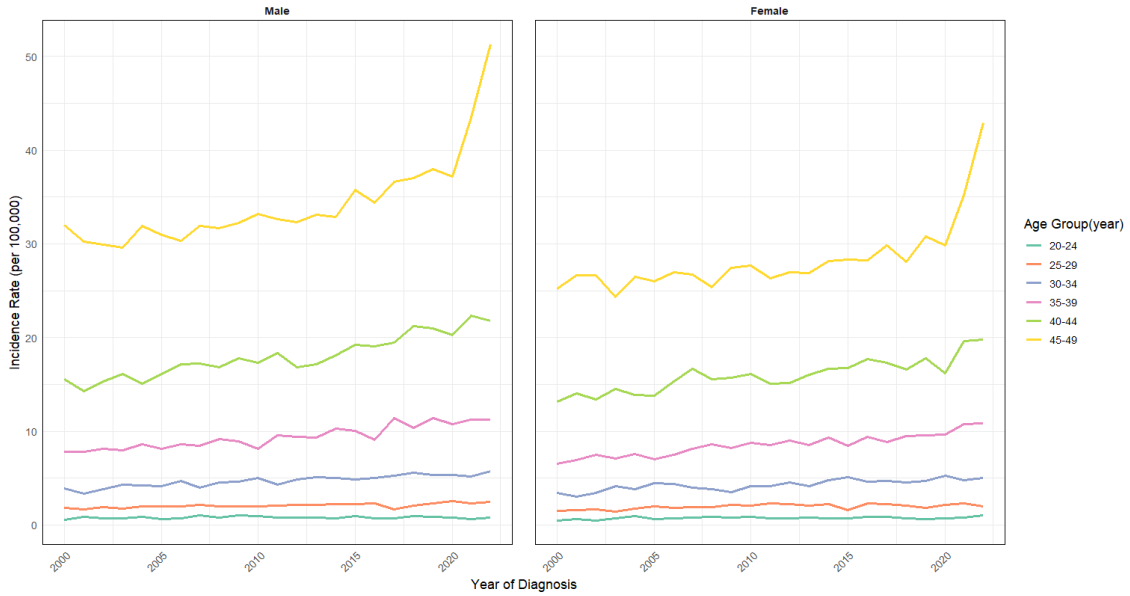
Age effects followed the expected monotonic pattern across all subgroups. Period effects showed a consistent upward trend, somewhat more uniform across strata than the conventional APC estimates. Cohort effects, however, diverged from both the conventional APC and descriptive analyses: rather than the rising gradient seen in more recently born generations, the IE returned a monotonically declining cohort pattern across all subgroups.

Supplementary Figures and Tables

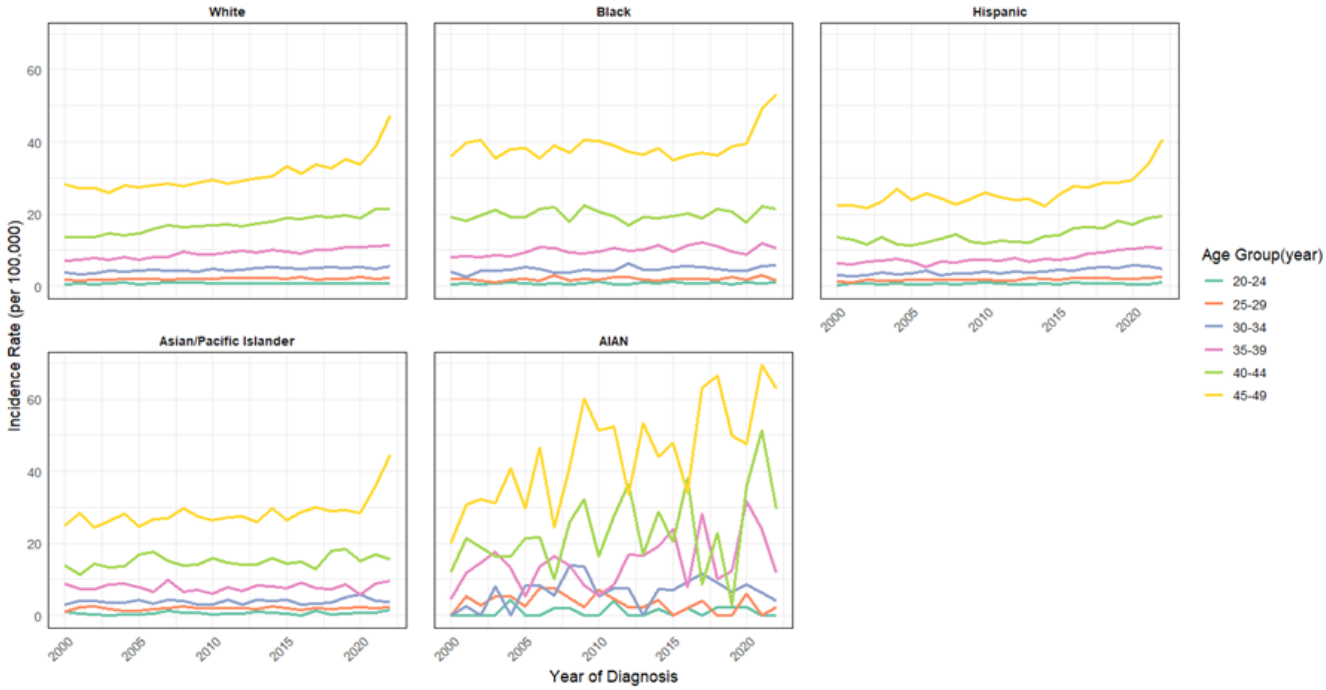
List of Supplementary Figures and Tables

Figure 1. Trends in age-specific colorectal cancer incidence in the United States from 2000 to 2022, stratified by sex, race, income, tumor location.

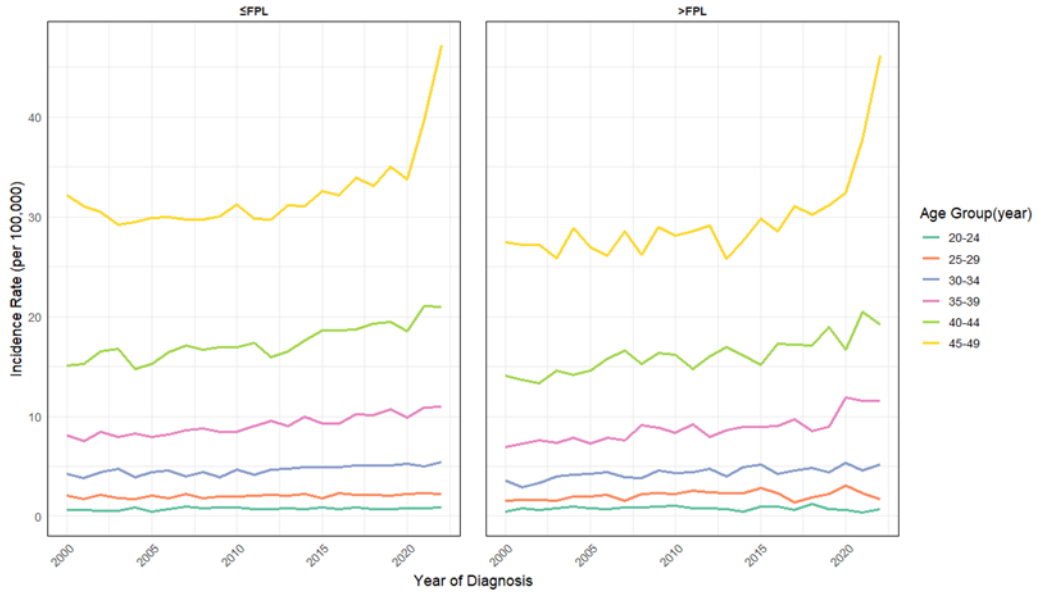
A) Sex



B) Race



C) Income



D) Location

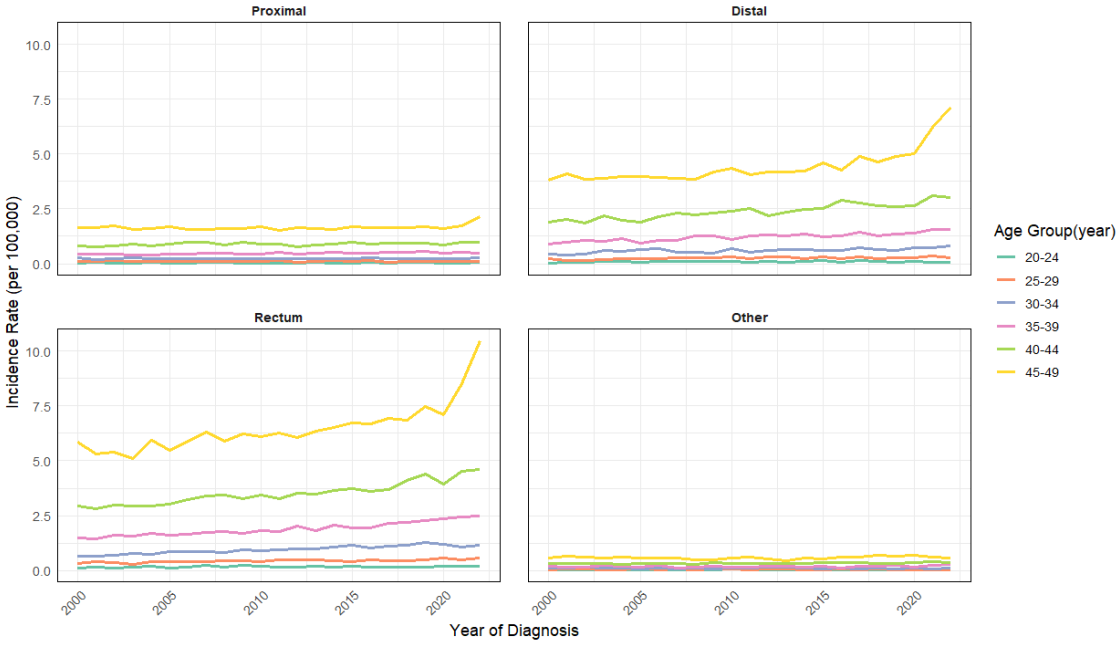
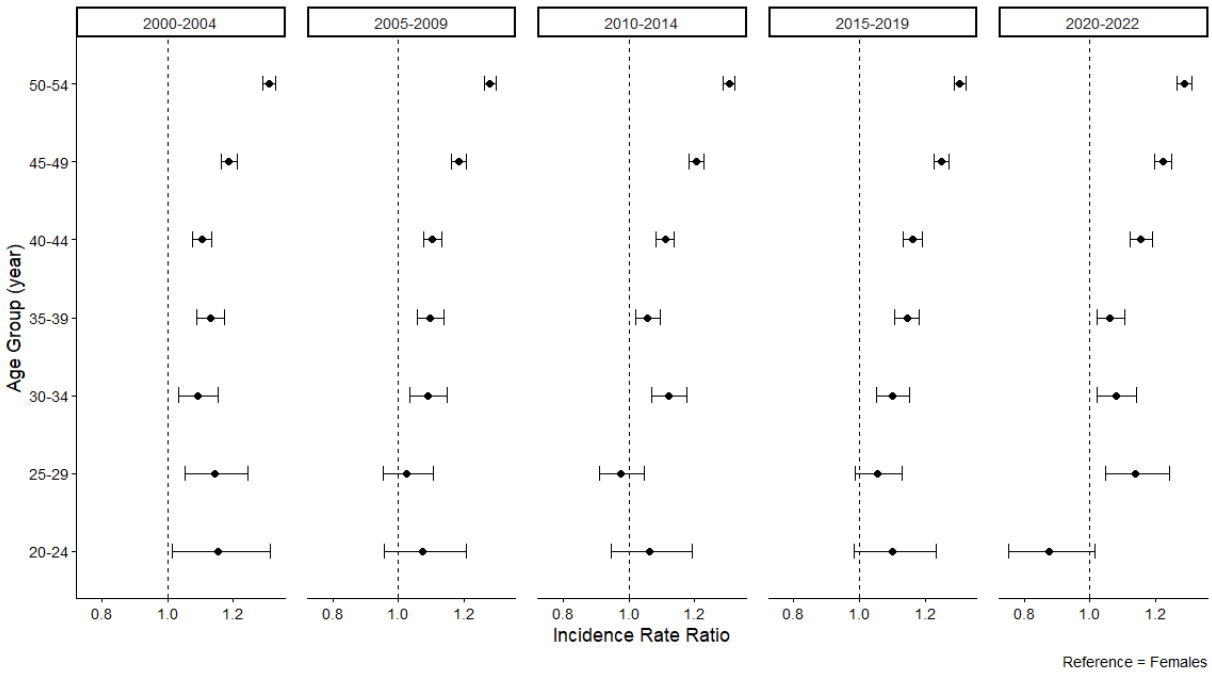
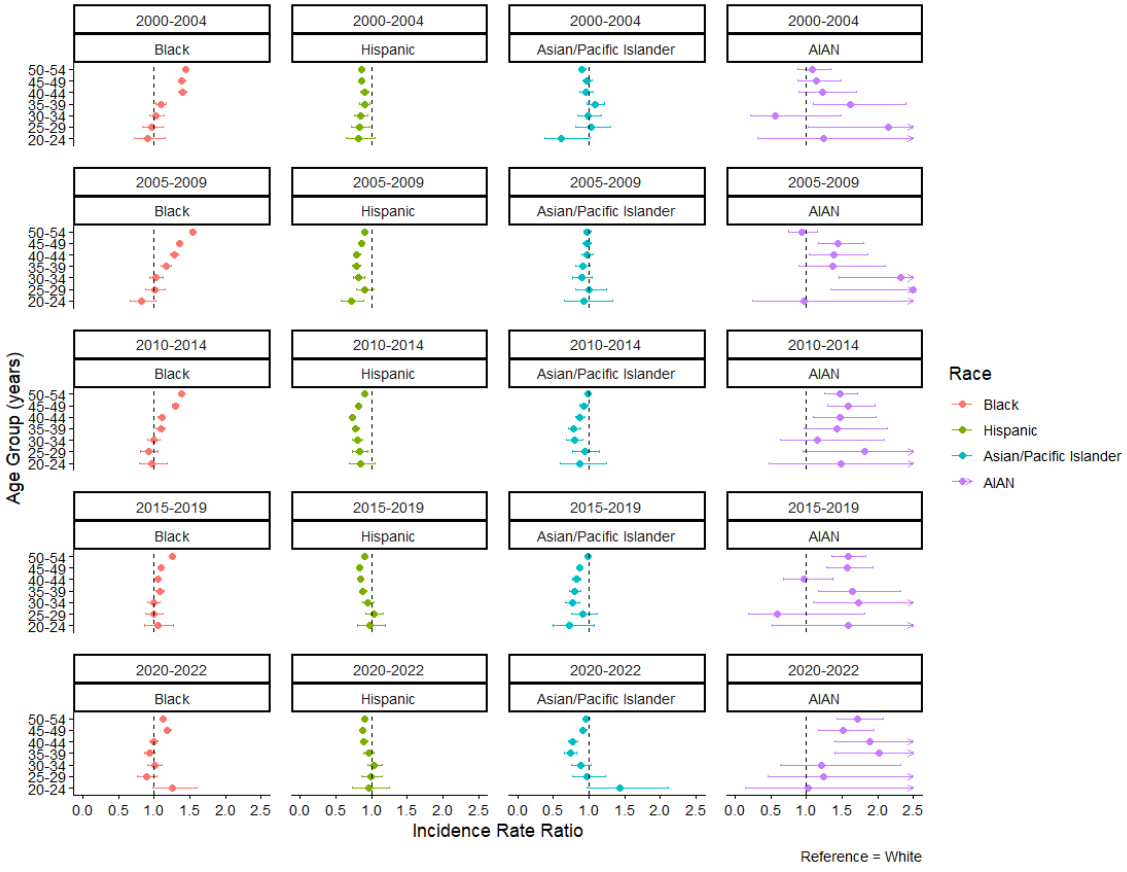


Figure 2. Forest plots of age-specific colorectal cancer incidence in the United States, 2000–2022, comparing demographic and clinical characteristics.

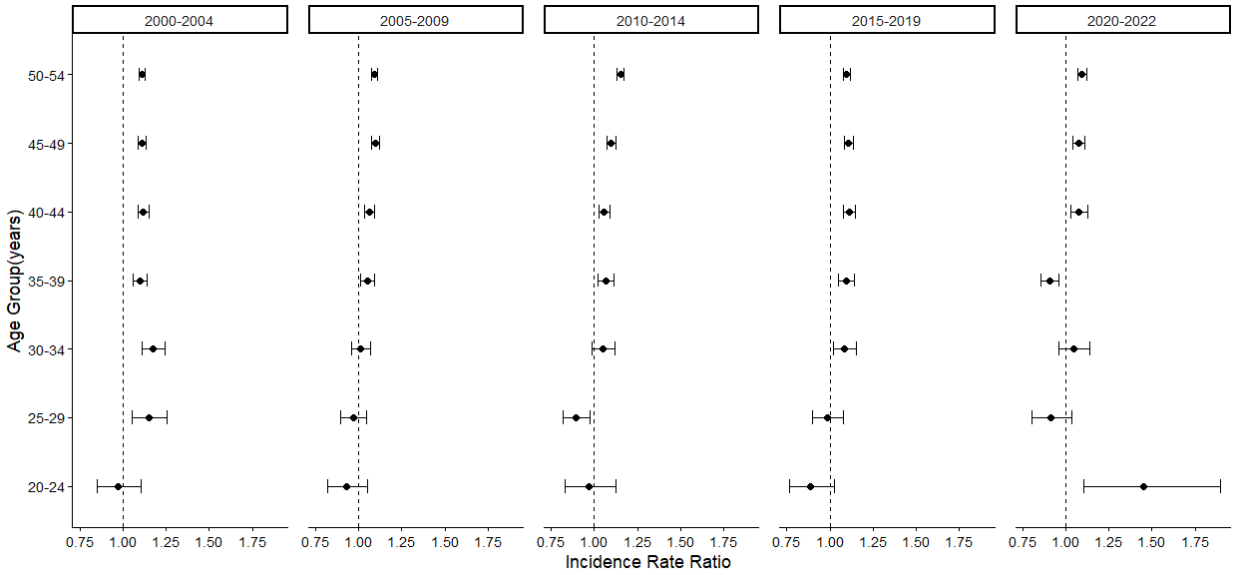
A) Sex



B) Race

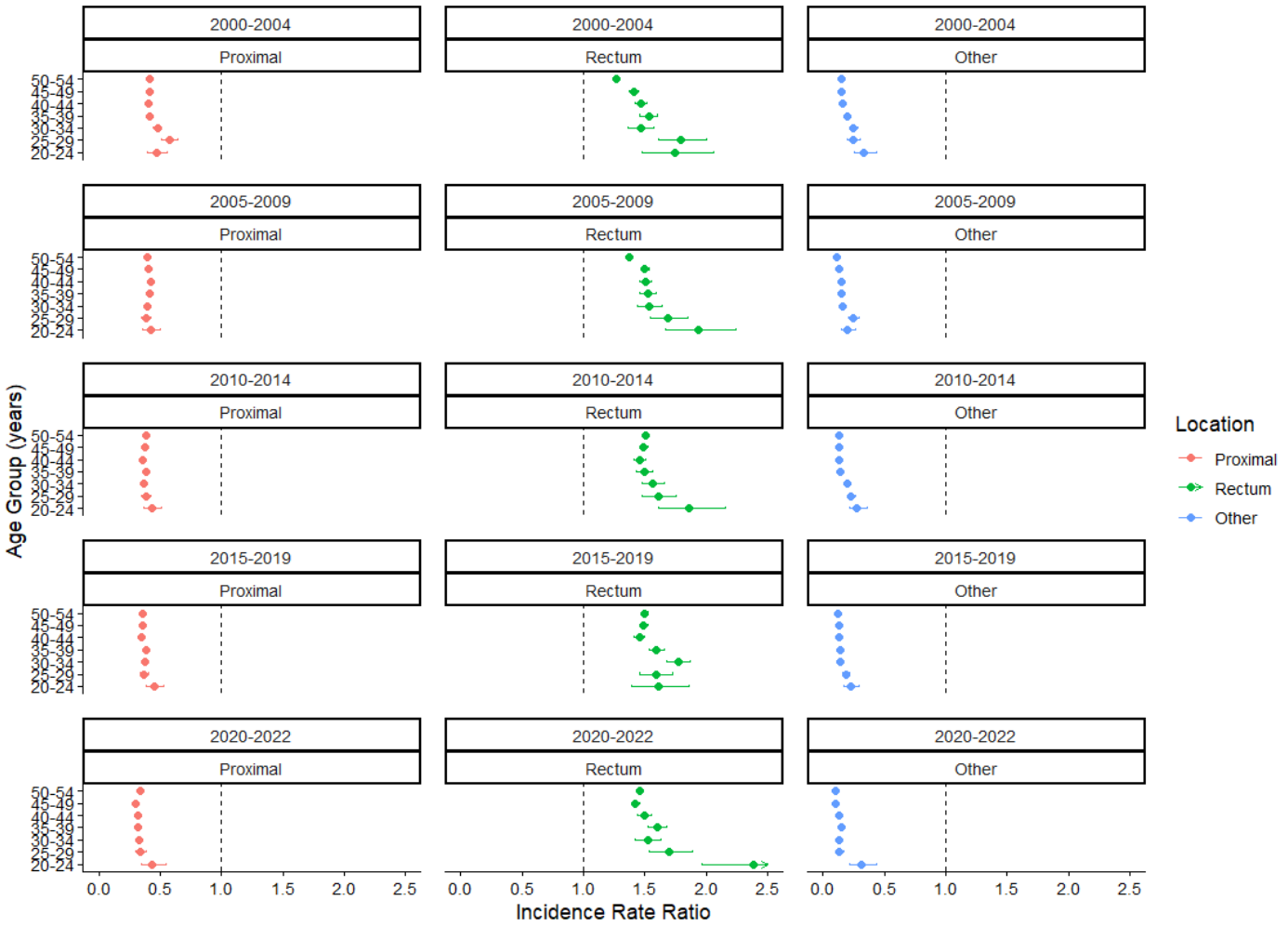


C) Income



Reference: Above Federal Poverty Level

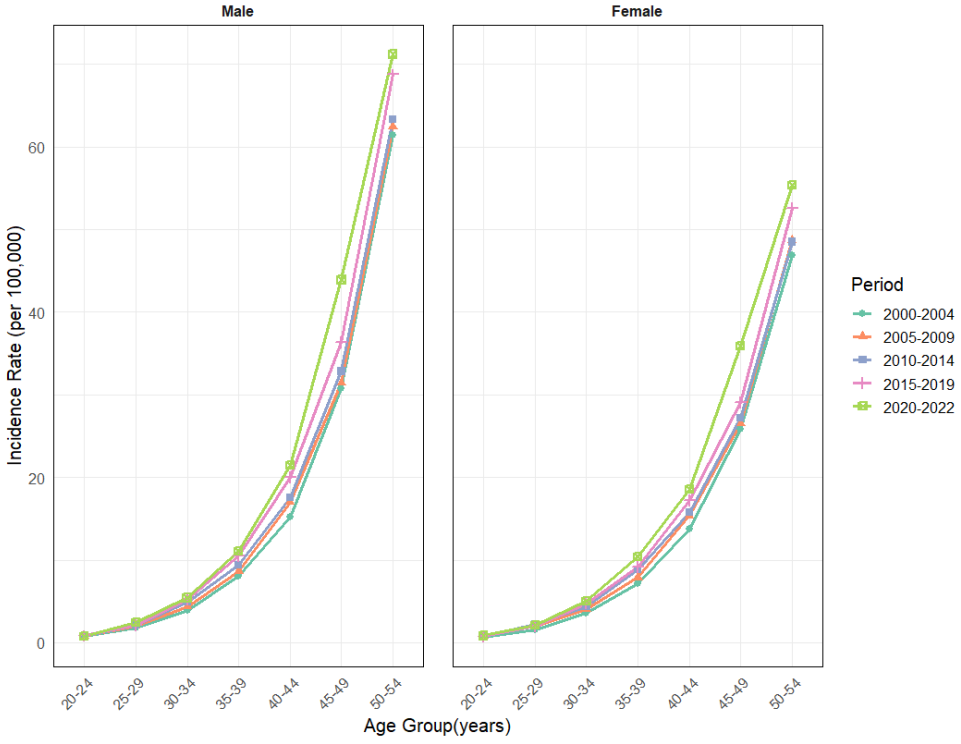
C) Location



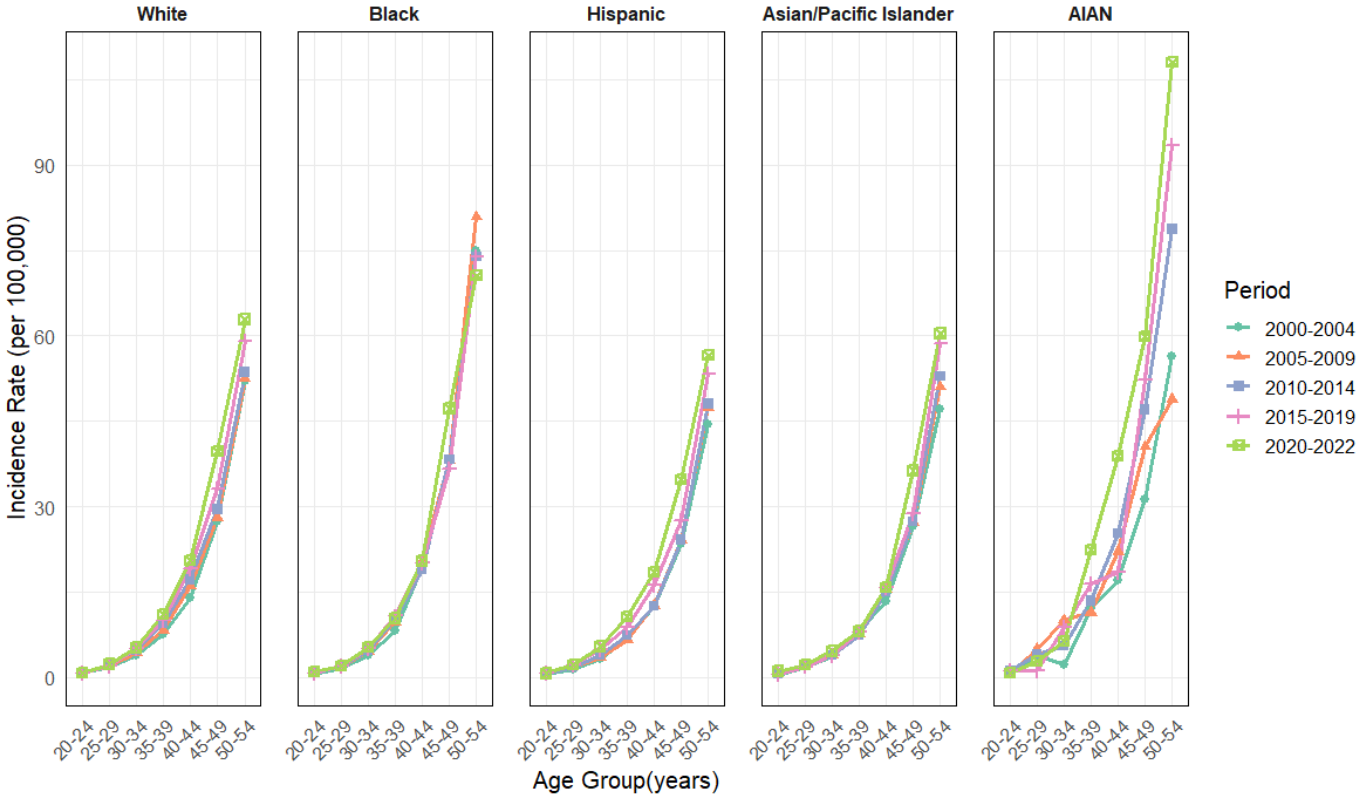
Reference: Distal colon. Arrows indicate confidence intervals extending beyond the displayed x-axis range.

Figure 3. Age-specific colorectal cancer incidence in the United States, 2000–2022, by age group and period of diagnosis, stratified by demographic and tumor location.

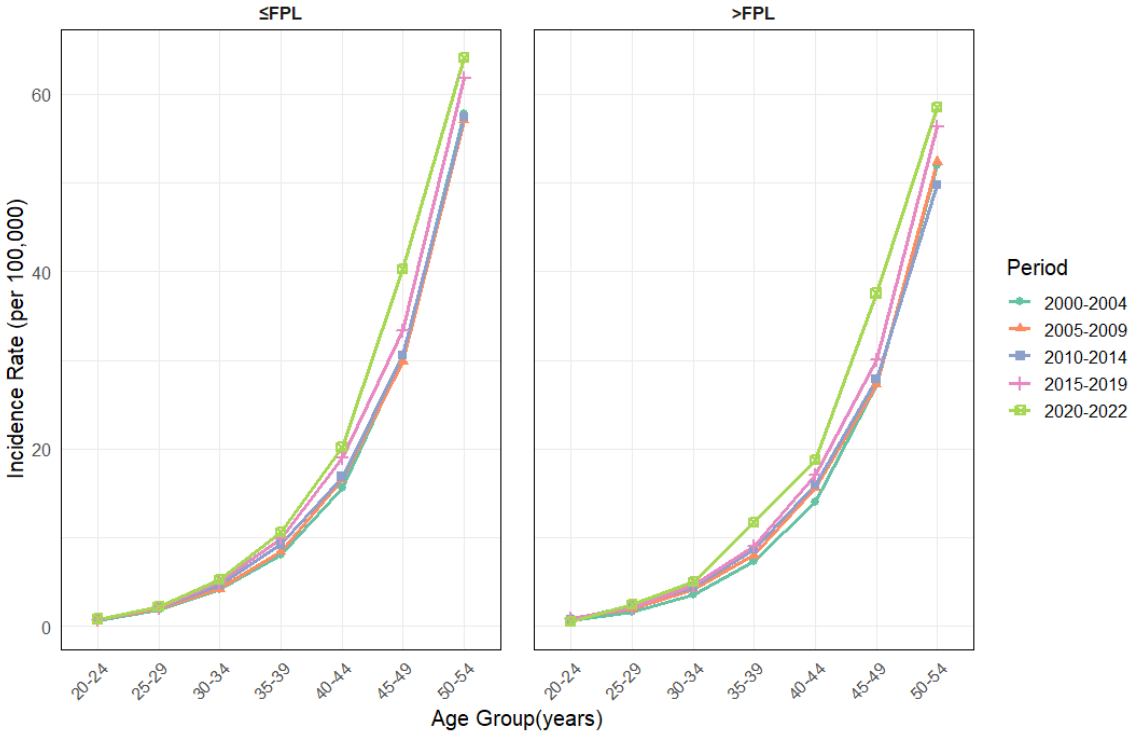
A) Sex



B) Race



B) Income



B) Location

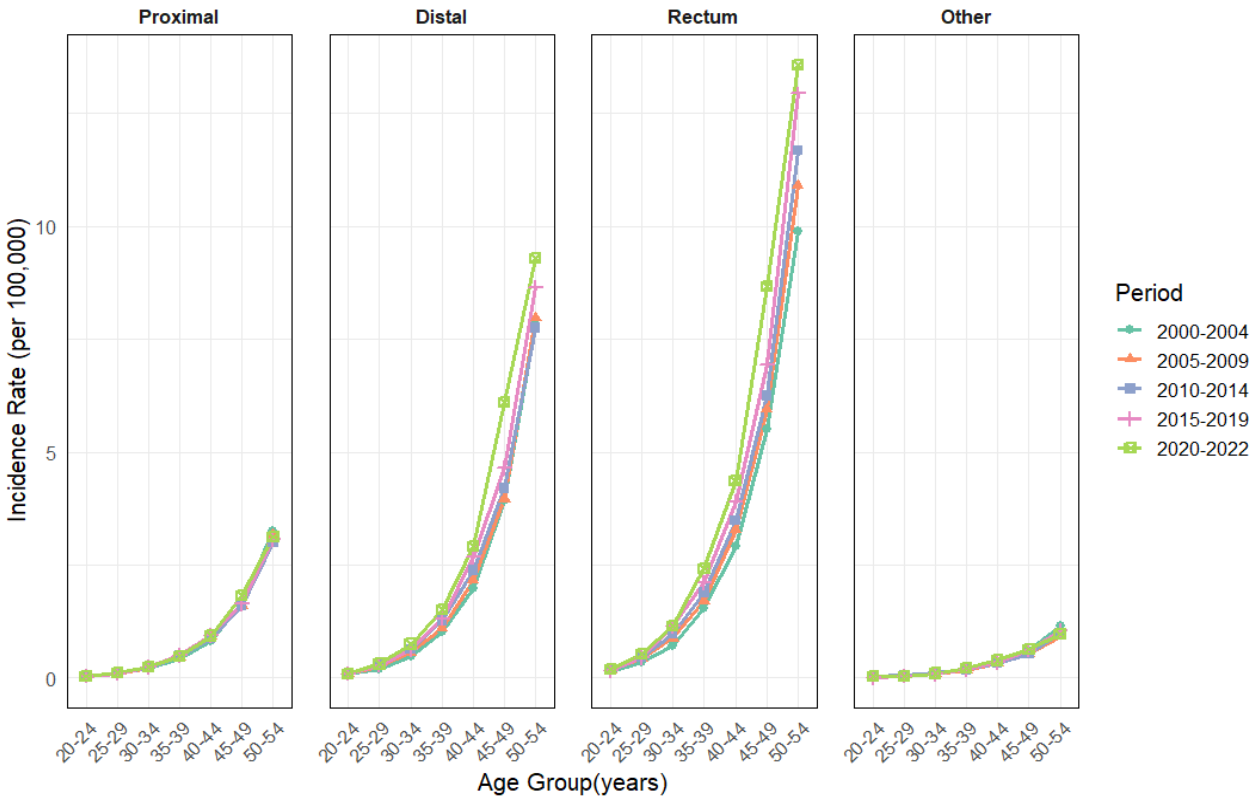
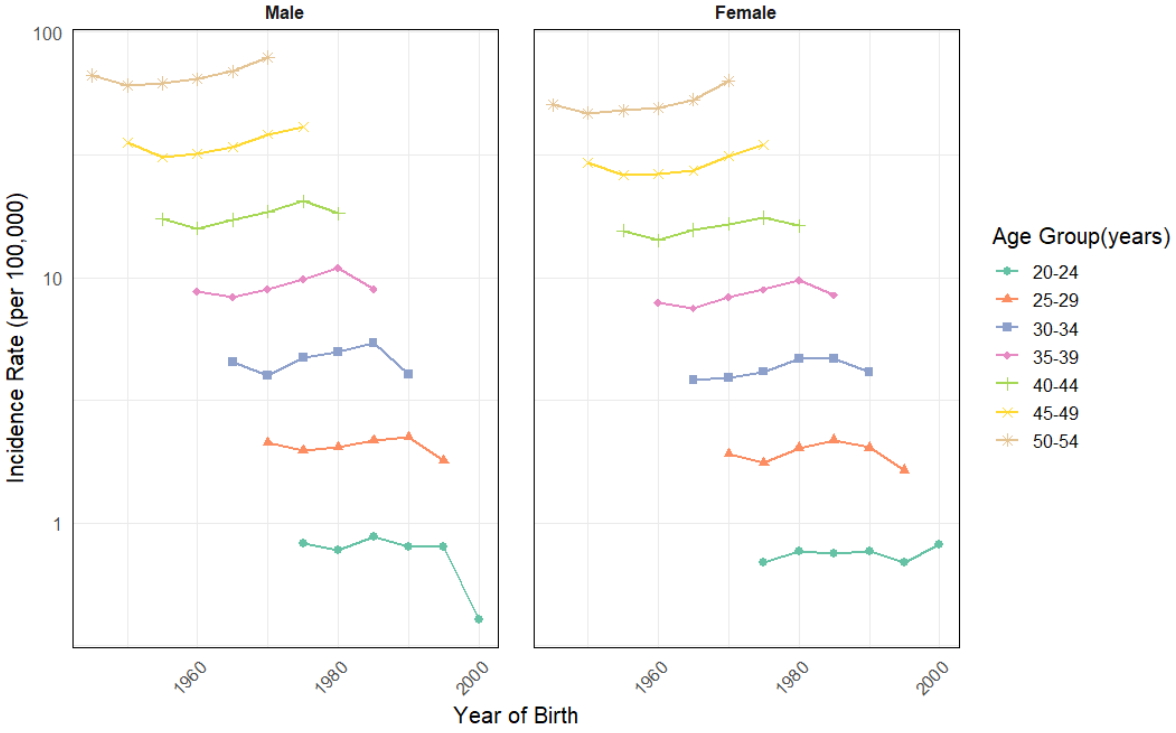
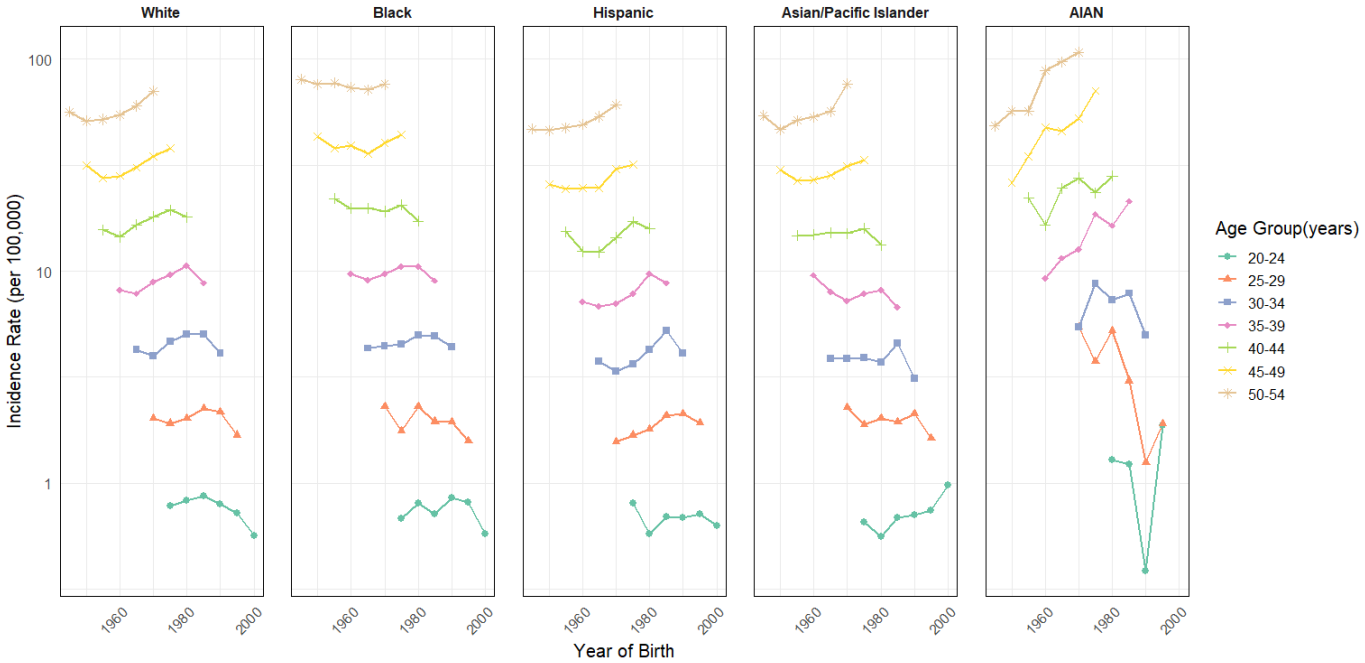


Figure 4. Age-specific colorectal cancer incidence in the United States, 2000–2022, by age group and year of birth, stratified by demographic and tumor location.

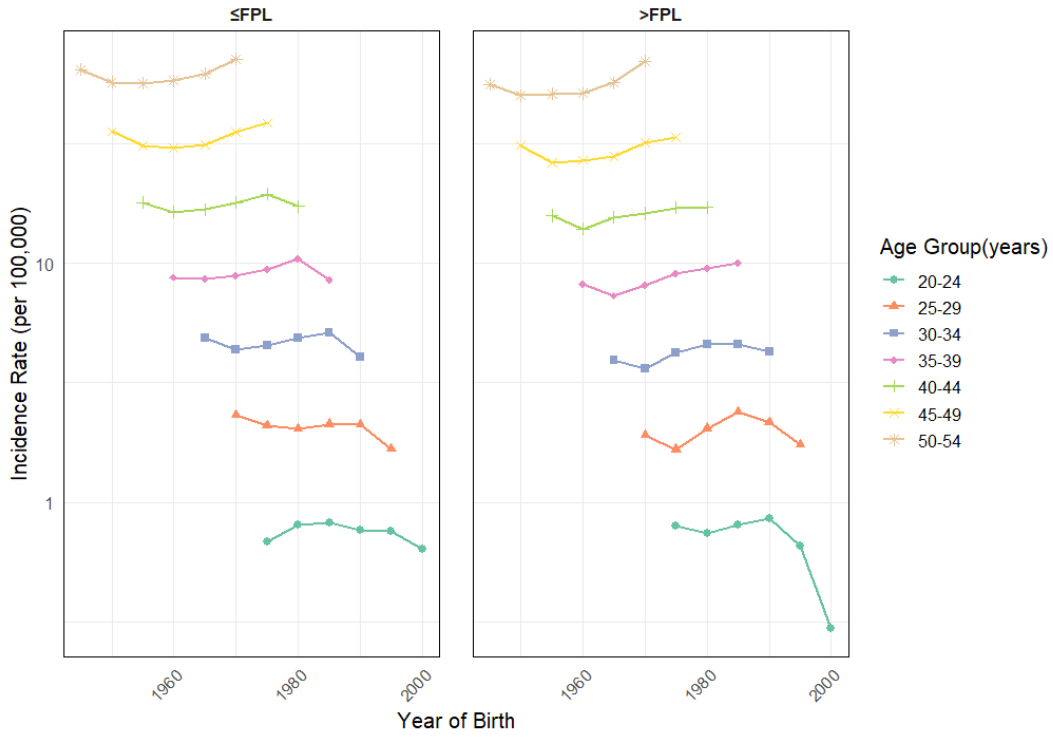
A) Sex



B) Race



C) Income


≤FPL
>FPL
Incidence Rate (per 100,000)
10
1
1960
1980
2000
Year of Birth
Age Group(years)
20-24
25-29
30-34
35-39
40-44
45-49
50-54

D) Location

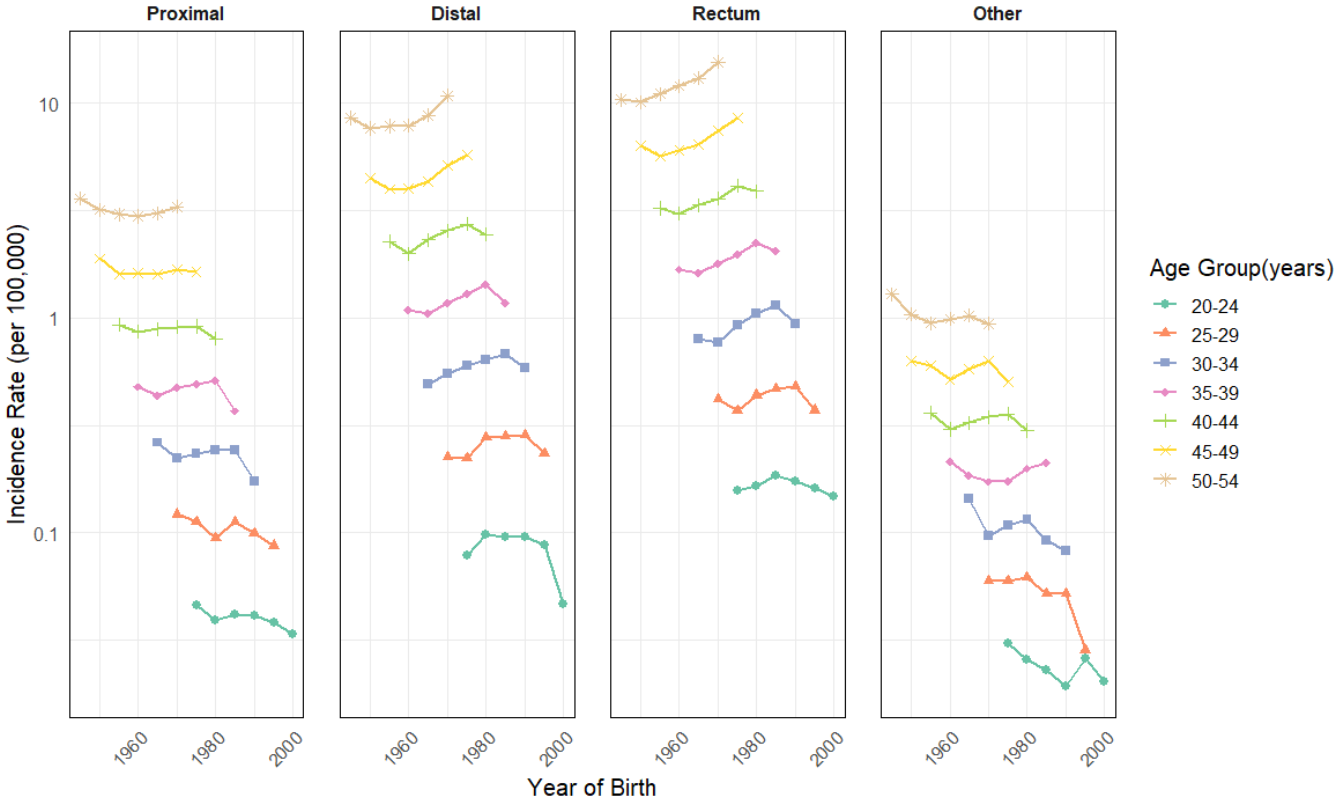
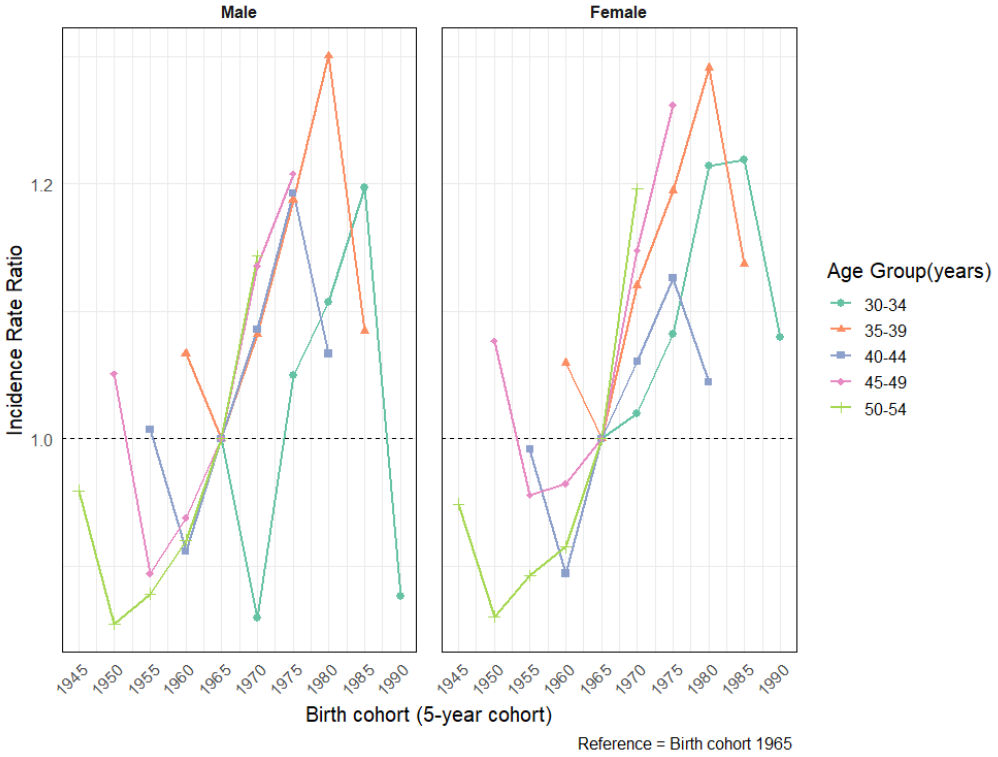
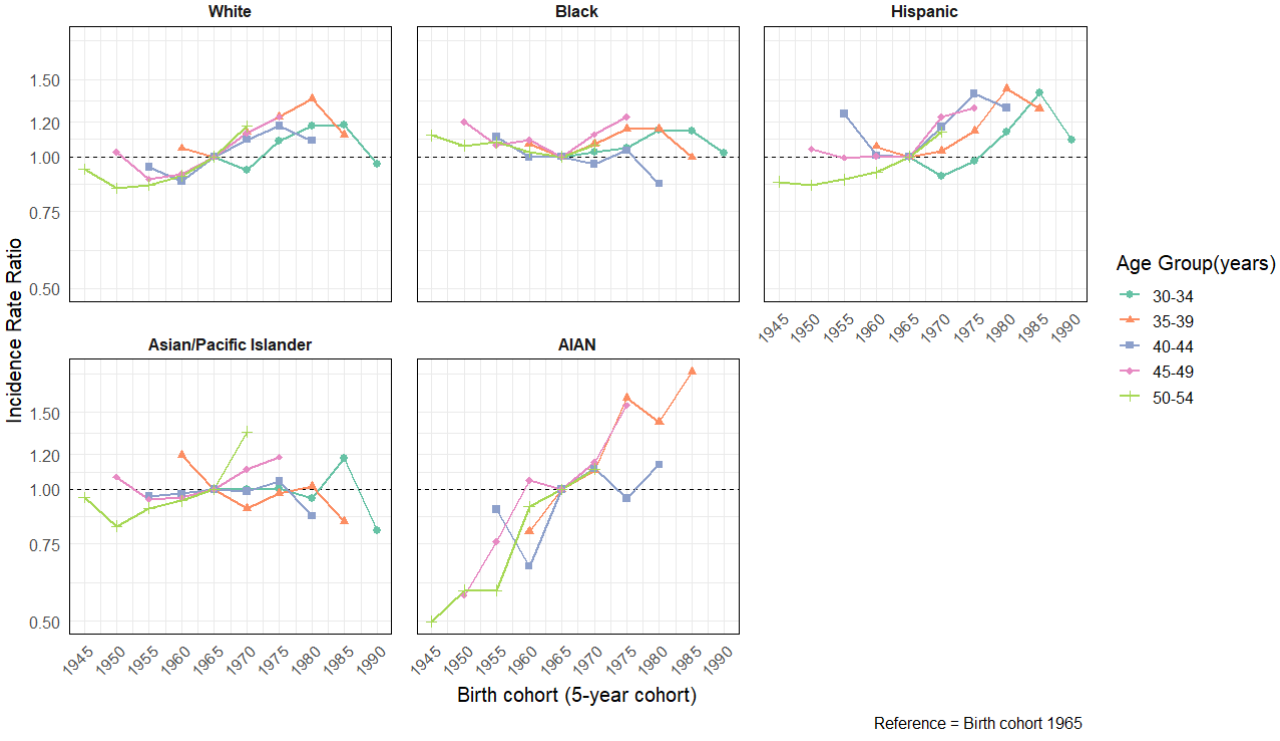

Proximal
Distal
Rectum
Other
Incidence Rate (per 100,000)
10
1
0.1
1960
1980
2000
Year of Birth
Age Group(years)
20-24
25-29
30-34
35-39
40-44
45-49
50-54

Figure 5. Age-specific incidence rate ratios for colorectal cancer by age group and birth cohort in the United States, 2000–2022, stratified by demographics and tumor location.

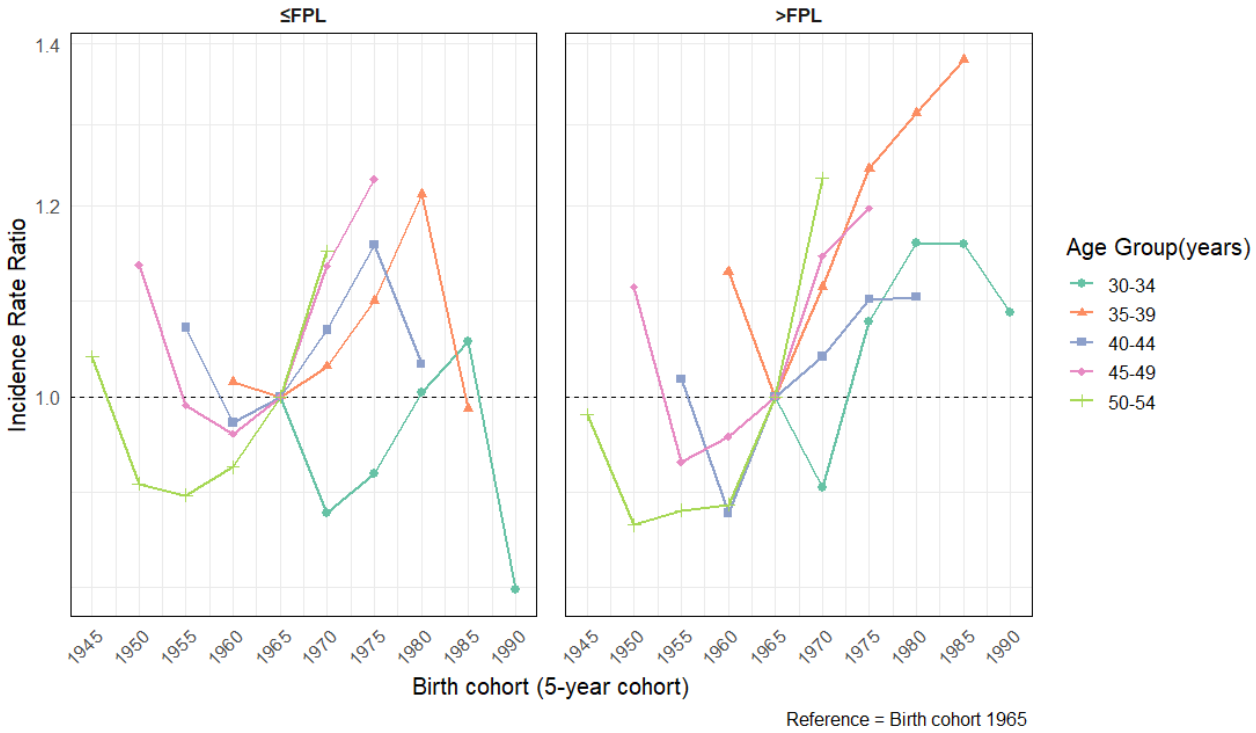
A) Sex



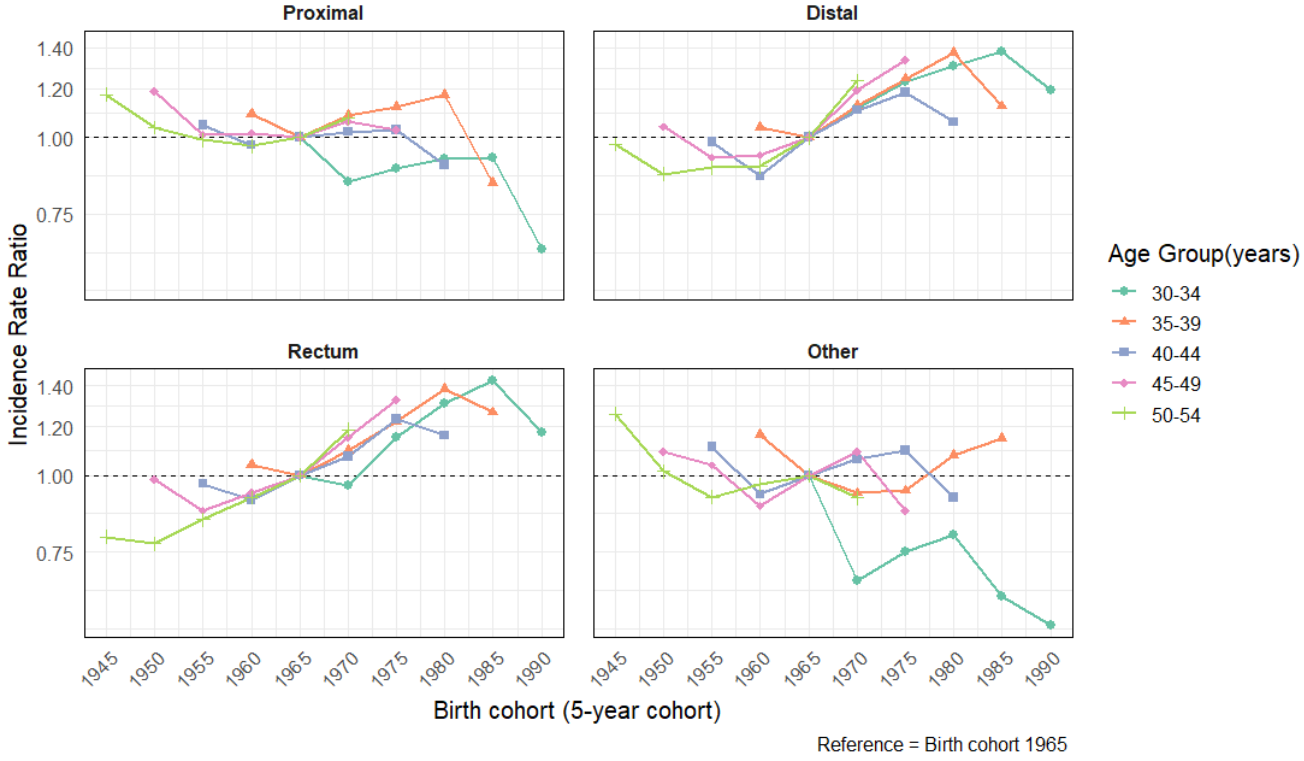
B) Race



C) Income



D) Location

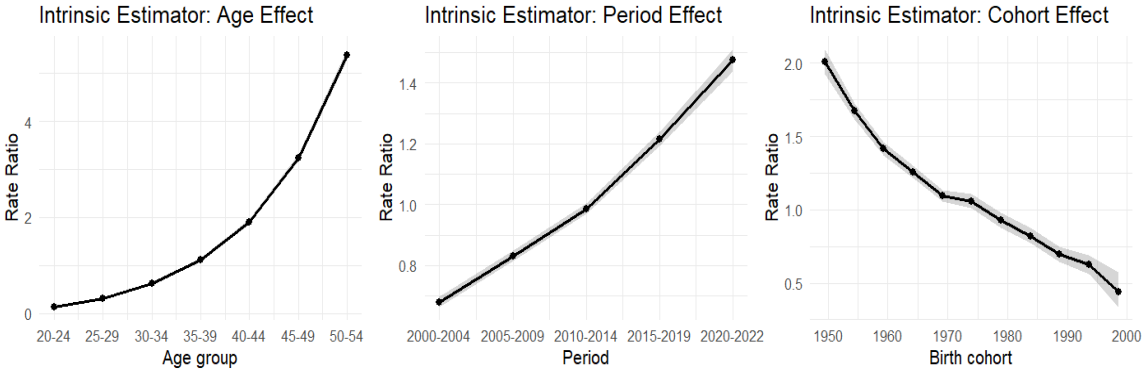


Note: IRRs for EO-CRC by 5-year birth cohort are shown separately for demographic characteristic and tumor location across age groups. All estimates are relative to the 1965 birth cohort (reference = 1.0, dashed line)

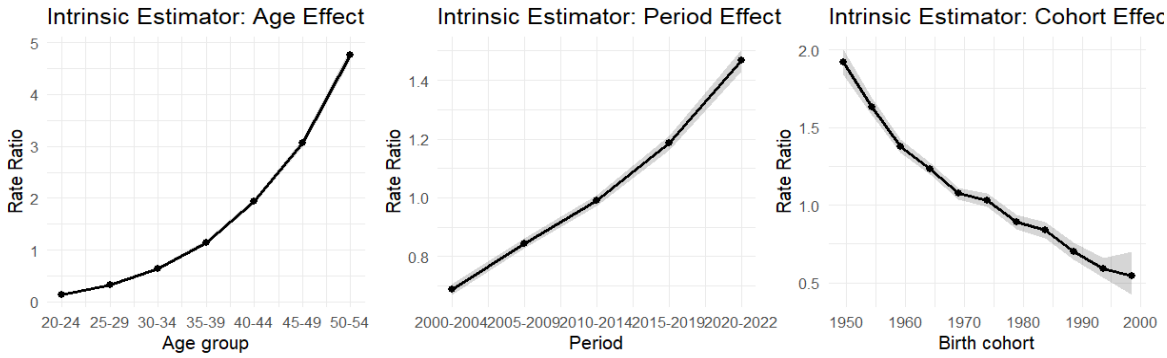
Figure 6. Age–period–cohort effects on colorectal cancer incidence estimated using the intrinsic estimator in the United States, 2000–2022, stratified by demographic factors (1A by sex, 1B by race / ethnicity, 1C by county-level income) and tumor location (1D). Period and cohort effect estimates are incidence rate ratio relative to 2010-2014 for period effect, and 1965 birth cohort for cohort effect. Shaded areas represent 95% confidence intervals.

A) Sex

Male

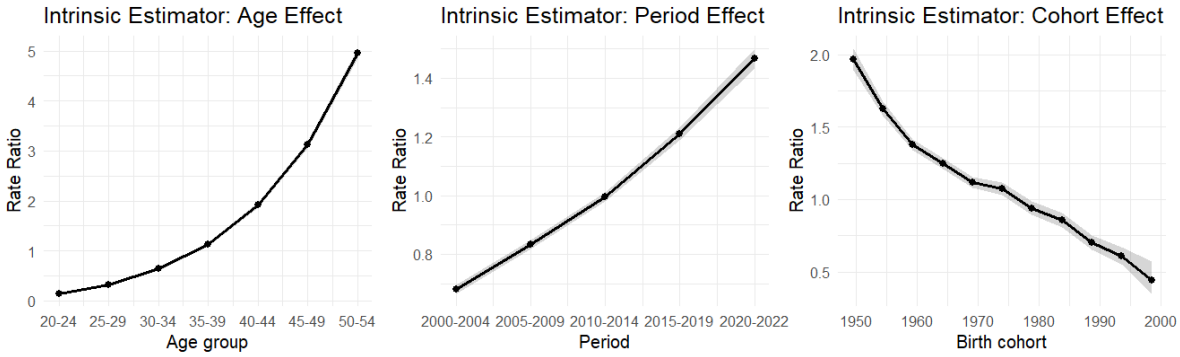


Female

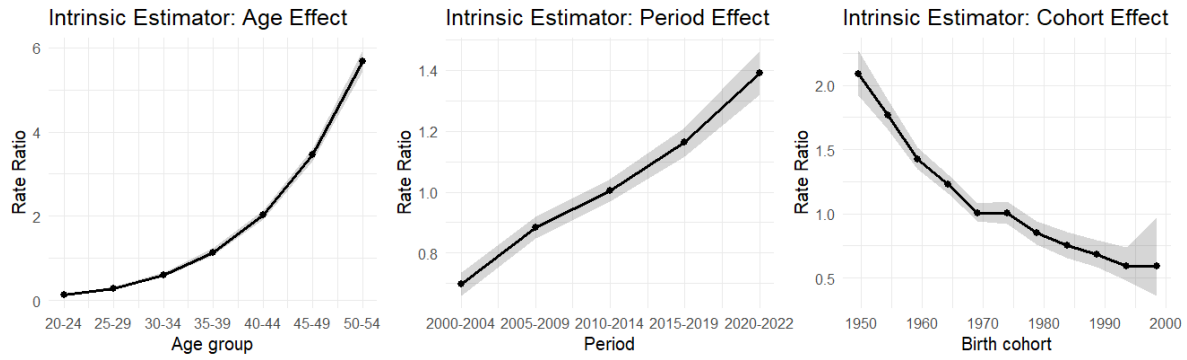


B) Race

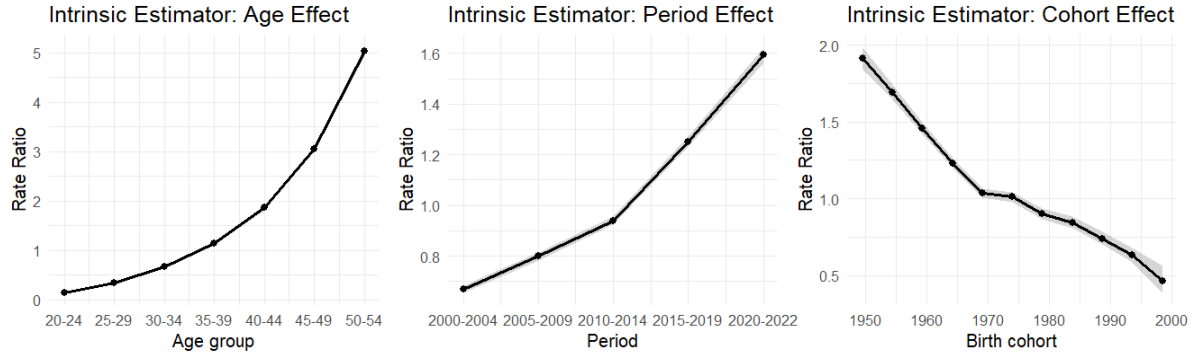
White



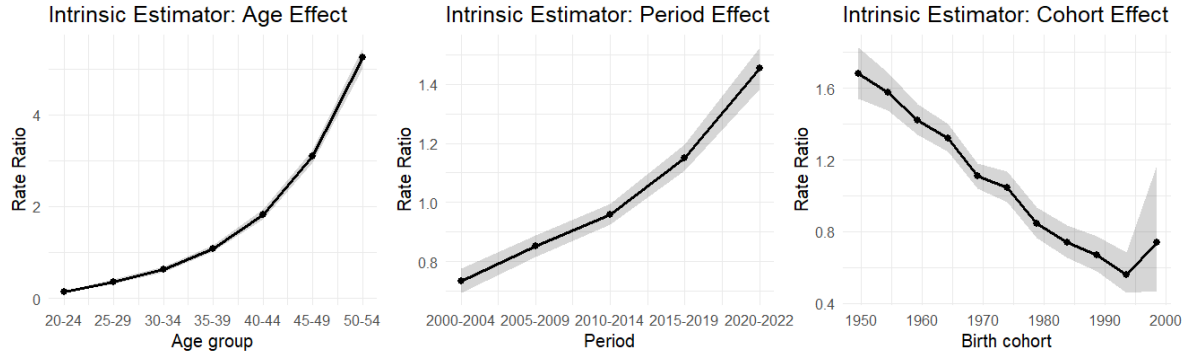
Black



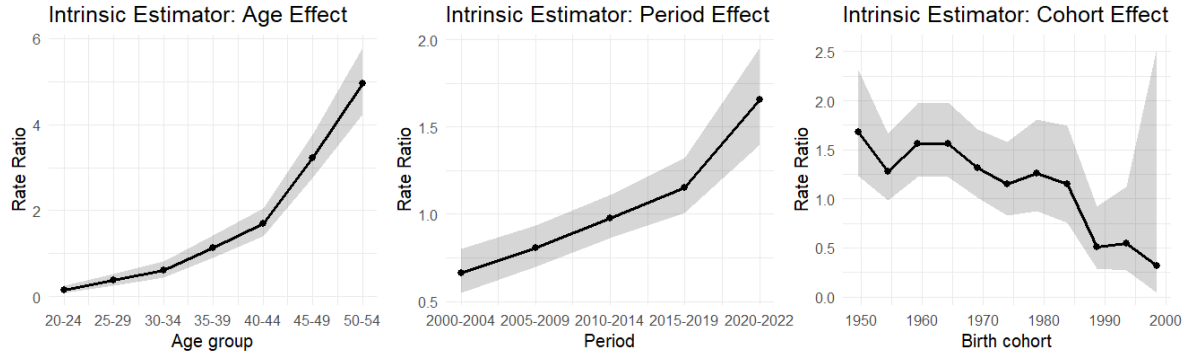
Hispanic



Asian/ Pacific Islander

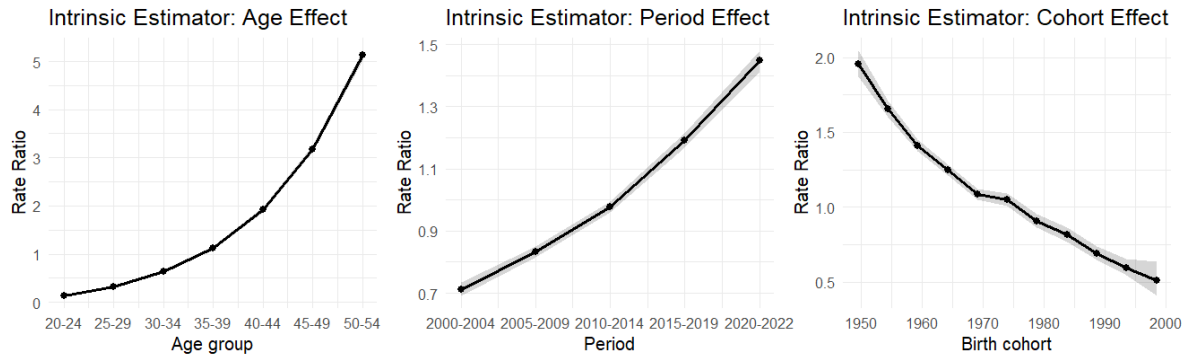


AIAN

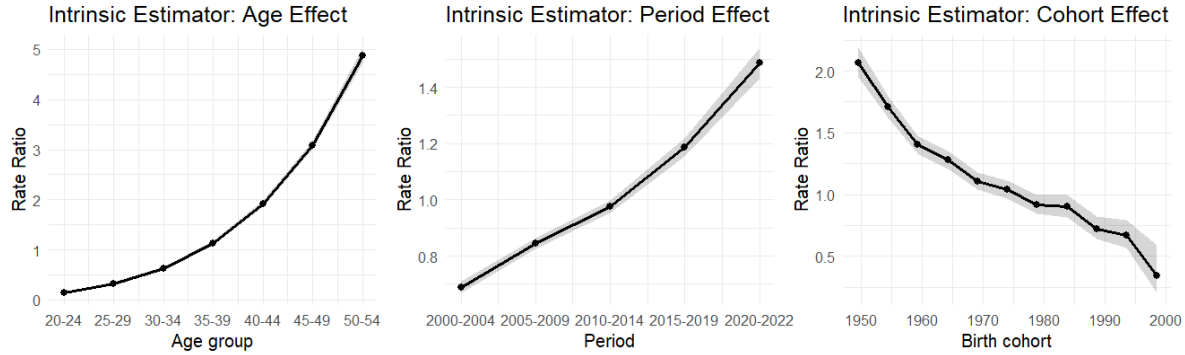


C) Income

≤FPL

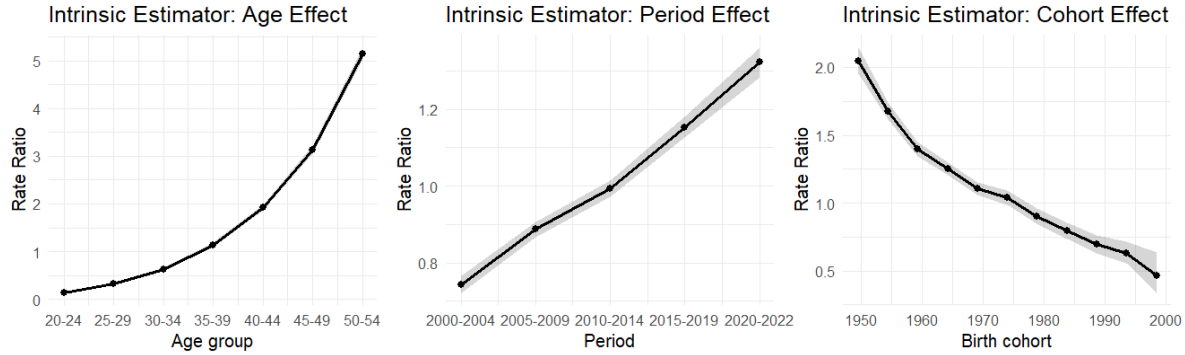


>FPL

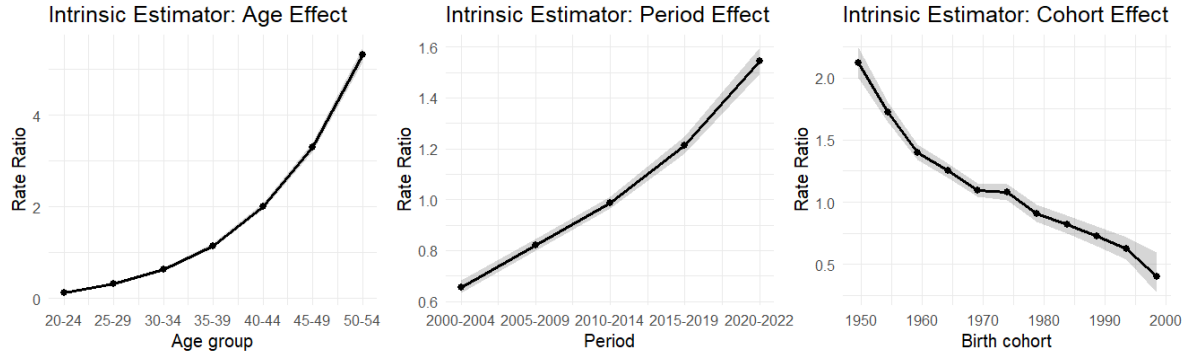


D) Location

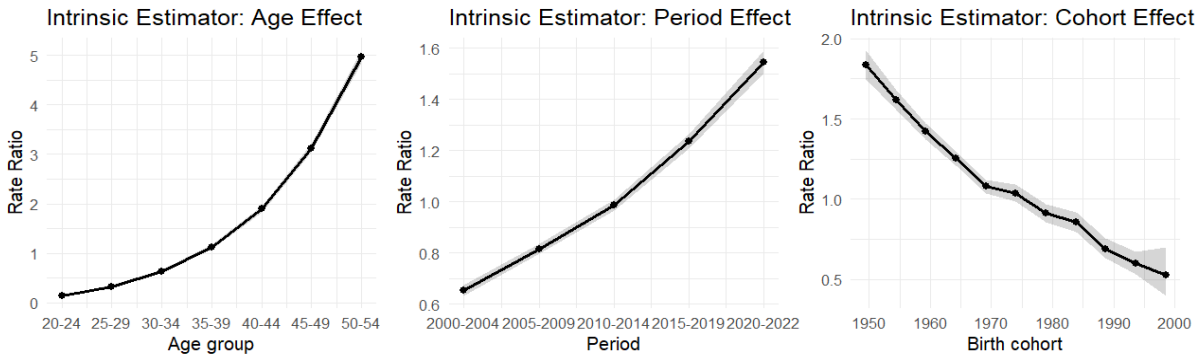
Proximal



Distal



Rectum



Other

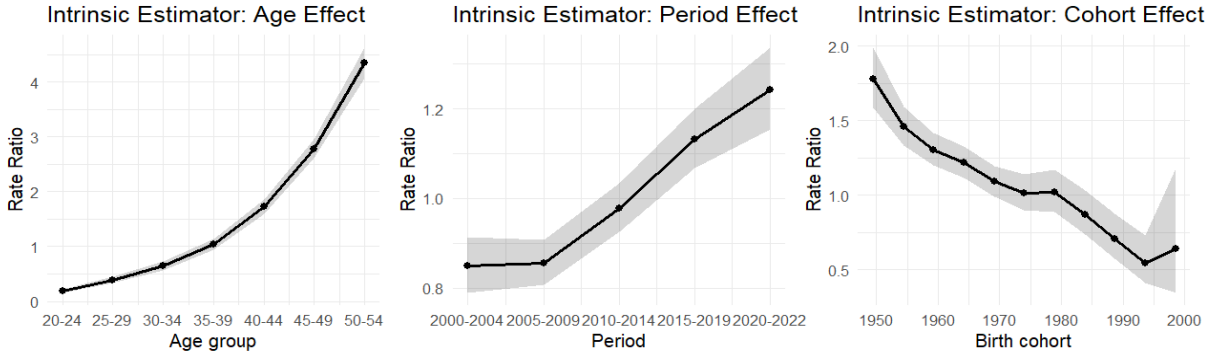
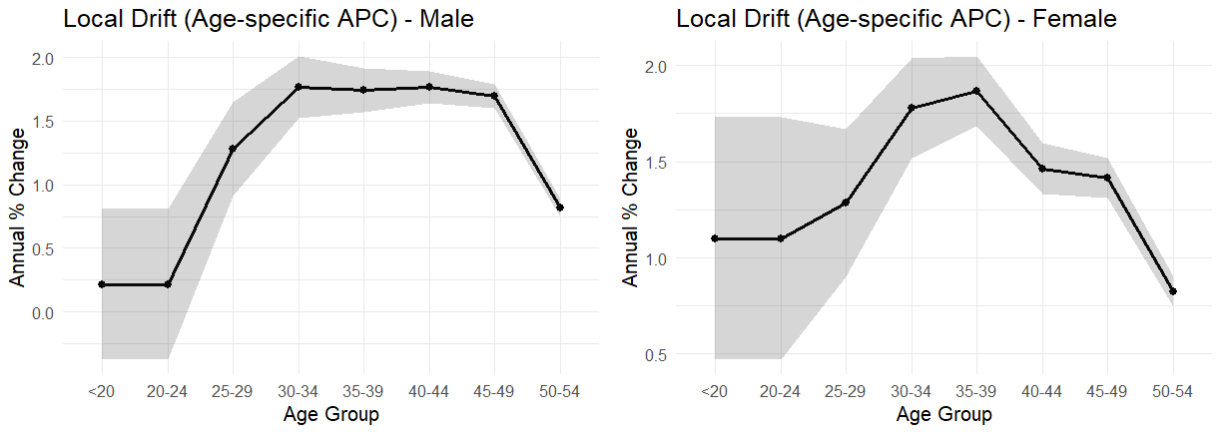
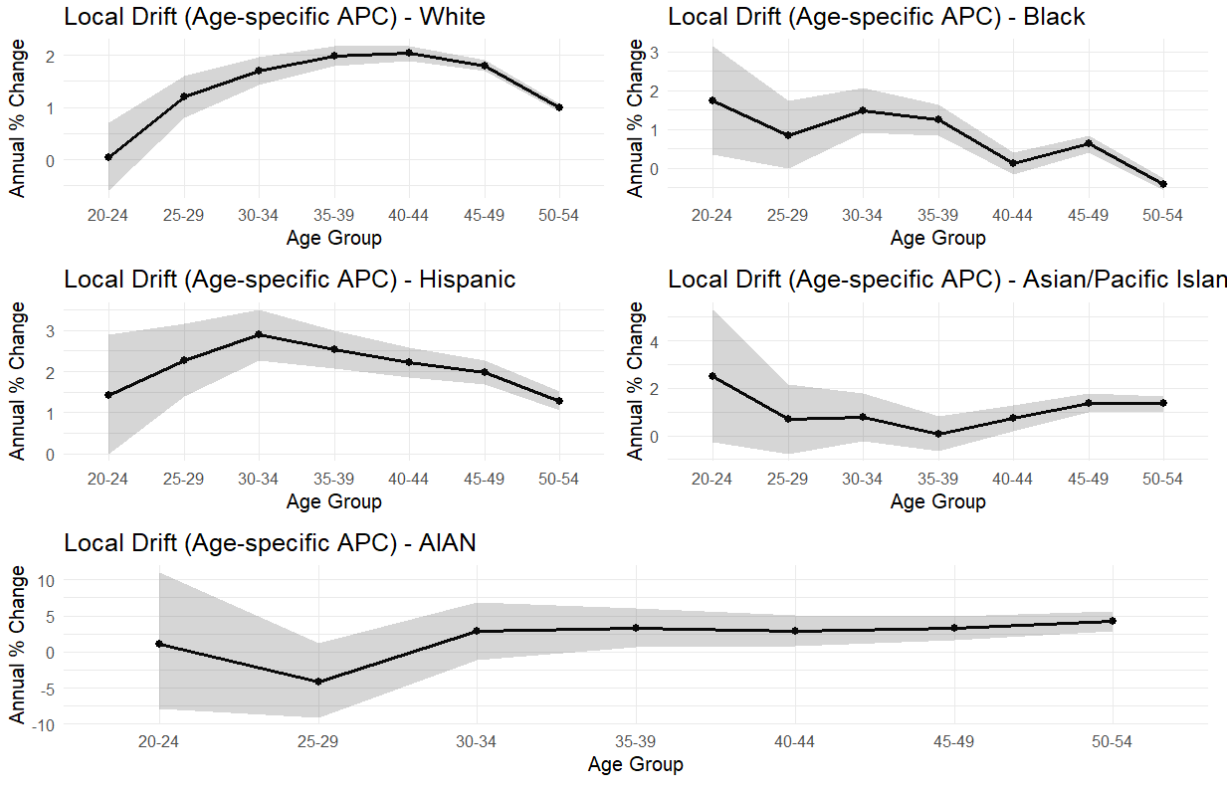


Figure 7. Local drift in early-onset colorectal cancer incidence in the United States, 2000–2022, stratified by demographic factors and tumor location

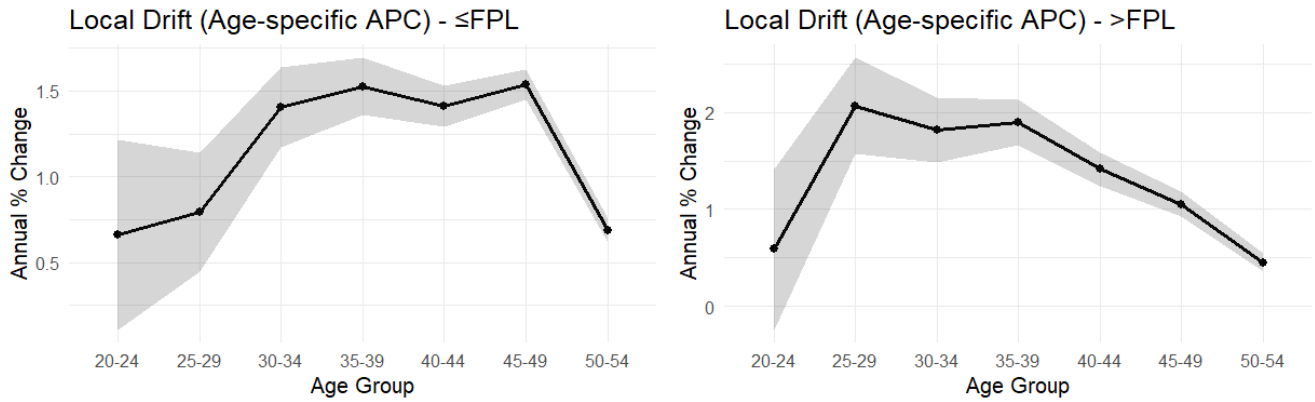
A) Sex



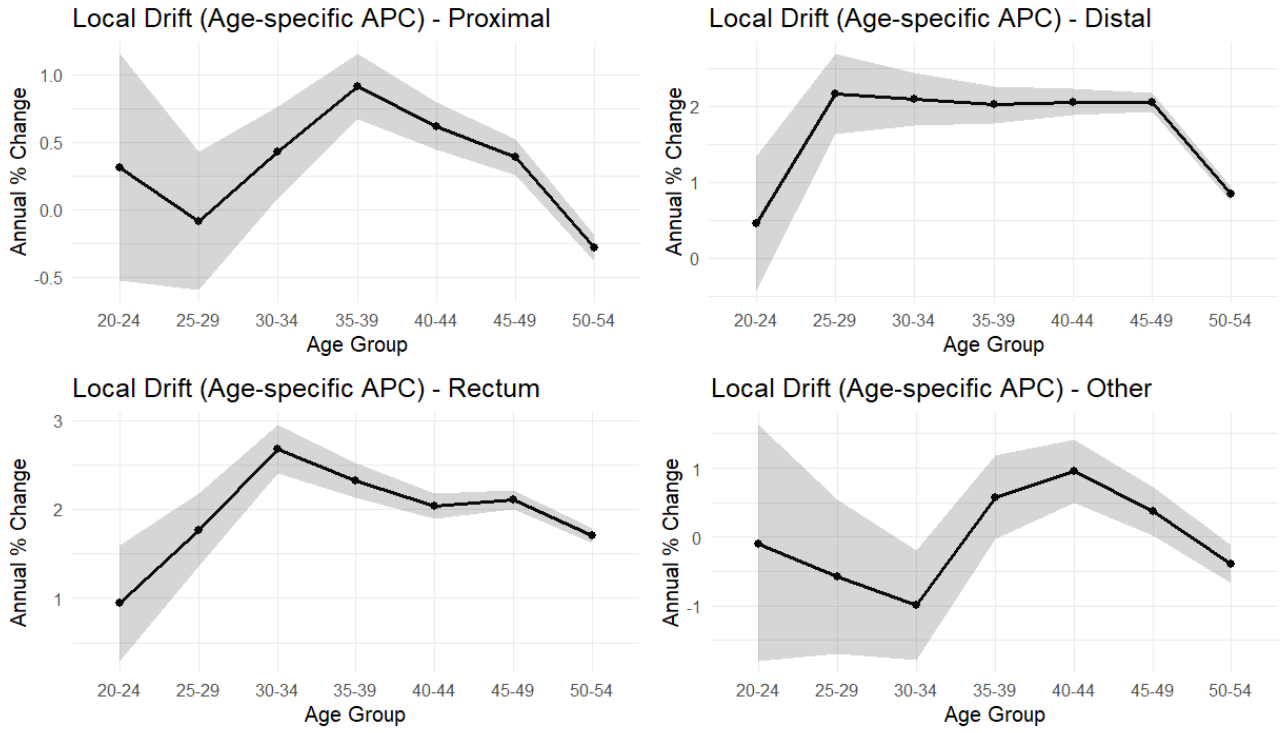
B) Race



C) Income



D) Location



Note: Local drift represents the age-specific annual percent change (APC) in incidence rates. Values above 0 indicate increasing trends over time, while values below 0 indicate decreasing trends. Shaded areas represent 95% confidence intervals.

Table 1. Goodness-of-fit statistics for the best-fitting age–period–cohort models of ealy-onset colorectal cancer incidence by demographic factor and tumor location.

Characteristic	Subgroup	Model	AIC	Deviance	df	p_value	H0
Sex	Male	Age-Period-Cohort	752.52	208.63	8	<0.001	PE|Cohort
		Age-Cohort	909.35	369.47	10	<0.001	CE|drift
		Age-Period	38266.23	37762.34	28	<0.001	CE|Period
		Age-drift	39205.19	38707.31	31	<0.001	zero drift
		Age-drift	39205.19	38707.31	31	<0.001	PE|drift.
		Age	92371.49	91875.61	32	<NA>	
	Female	Age-Period-Cohort	453.65	42.89	10	<0.001	PE|Cohort
		Age-Cohort	469.84	63.08	12	<0.001	CE|drift
		Age-Period	809.10	426.34	24	<0.001	CE|Period
		Age-drift	984.86	608.10	27	<0.001	zero drift
		Age-drift	984.86	608.10	27	<0.001	PE|drift.
		Age	3102.69	2727.93	28	<NA>	
Race	White	Age-Period-Cohort	442.28	33.29	10	0.0658	PE|Cohort
		Age-Cohort	443.72	38.73	12	<0.001	CE|drift
		Age-Period	893.36	512.37	24	<0.001	CE|Period
		Age-drift	1047.18	672.19	27	<0.001	zero drift
		Age-drift	1047.18	672.19	27	<0.001	PE|drift.
		Age	4117.95	3744.96	28	<NA>	
	Black	Age-Period-Cohort	375.15	18.37	10	< 0.001	PE|Cohort
		Age-Cohort	404.24	51.46	12	< 0.001	CE|drift
		Age-Period	586.75	257.96	24	< 0.001	CE|Period
		Age-drift	630.20	307.42	27	0.00506	zero drift
		Age-drift	630.20	307.42	27	< 0.001	PE|drift.
		Age	636.06	315.27	28	<NA>	
	Hispanic	Age-Period-Cohort	352.78	5.93	10	<0.001	PE|Cohort
		Age-Cohort	384.25	41.41	12	<0.001	CE|drift
		Age-Period	425.74	106.90	24	<0.001	CE|Period
		Age-drift	506.67	193.82	27	<0.001	zero drift
		Age-drift	506.67	193.82	27	<0.001	PE|drift.
		Age	1158.19	847.35	28	<NA>	
	Asian/Pacific Islander	Age-Cohort	322.67	13.37	12	<0.001	CE|drift
		Age-Period-Cohort	323.80	10.50	10	0.2379	PE|Cohort
		Age-Period	333.82	48.51	24	<0.001	CE|Period
		Age-drift	338.94	59.64	27	<0.001	zero drift
		Age-drift	338.94	59.64	27	0.0111	PE|drift
		Age	449.12	171.81	28	<NA>	
	AIAN	Age-drift	226.54	41.08	27	<0.001	zero drift
		Age-drift	226.54	41.08	27	0.629	PE|drift
		Age-Period	230.80	39.34	24	0.0969	CE|Period
		Age-Cohort	233.66	18.21	12	0.0868	CE|drift

		Age-Period-Cohort	237.62	18.16	10	0.976	PE|Cohort
		Age	289.03	105.57	28	<NA>	
		Age-Cohort	443.53	0.00	0	<0.001	CE|drift
		Age-Period-Cohort	443.53	0.00	0	<NA>	PE|Cohort
	≤FPL	Age-Period	964.99	569.46	24	<0.001	CE|Period
		Age-drift	1347.73	958.20	27	<0.001	zero drift
		Age-drift	1347.73	958.20	27	<0.001	PE|drift
Income		Age	3642.72	3255.19	28	<NA>	
		Age-Cohort	408.88	0.00	0	<0.001	CE|drift
		Age-Period-Cohort	408.88	0.00	0	<NA>	PE|Cohort
	>FPL	Age-Period	794.36	433.48	24	<0.001	CE|Period
		Age-drift	959.09	604.21	27	<0.001	zero drift
		Age-drift	959.09	604.21	27	<0.001	PE|drift
		Age	1754.17	1401.29	28	<NA>	
		Age-Period-Cohort	446.30	55.76	10	<0.001	PE|Cohort
		Age-Cohort	467.40	80.86	12	<0.001	CE|drift
	Proximal	Age-Period	645.30	282.76	24	<0.001	CE|Period
		Age-drift	702.29	345.75	27	<0.001	zero drift
		Age-drift	702.29	345.75	27	<0.001	PE|drift.
		Age	718.99	364.45	28	<NA>	
		Age-Period-Cohort	423.23	31.79	10	0.0274	PE|Cohort
		Age-Cohort	426.42	38.99	12	<0.001	CE|drift
	Distal	Age-Period	920.14	556.70	24	<0.001	CE|Period
		Age-drift	1167.53	810.10	27	<0.001	zero drift
		Age-drift	1167.53	810.10	27	<0.001	PE|drift
Location		Age	3158.04	2802.61	28	<NA>	
		Age-Period-Cohort	445.27	38.04	10	0.00254	PE|Cohort
		Age-Cohort	453.22	49.99	12	< 0.001	CE|drift
	Rectum	Age-Period	719.54	340.31	24	< 0.001	CE|Period
		Age-drift	785.68	412.44	27	< 0.001	zero drift
		Age-drift	785.68	412.44	27	< 0.001	PE|drift
		Age	5695.71	5324.48	28	<NA>	
		Age-Period-Cohort	375.31	47.21	10	<0.001	PE|Cohort
		Age-Cohort	399.16	75.06	12	<0.001	CE|drift
	Other	Age-Period	422.69	122.59	24	<0.001	CE|Period
		Age	483.28	191.18	28	<NA>	
		Age-drift	484.82	190.72	27	0.498	zero drift
		Age-drift	484.82	190.72	27	<0.001	PE|drift

df: degree of freedom; AIAN: American Indian and Alaska Native: PE: Period effect; CE: Cohort effect
H0: Indicates the null hypothesis tested in likelihood ratio comparisons between nested APC models. Zero drift tests for no overall temporal trend, while the remaining terms evaluate whether period or cohort effects significantly improve model fit beyond drift or after adjustment for each other.

Table 2. Estimated net drift in early-onset colorectal cancer incidence across demographic and tumor location, United States, 2000-2022

Characteristic	Subgroup	Estimate	95% CI
Sex	Male	1.47%	1.24%, 1.70%
	Female	1.38%	1.14%, 1.62%
Race	White	1.56%	1.31%, 1.80%
	Black	0.67%	0.14%, 1.20%
	Hispanic	1.38%	1.14%, 1.62%
	Asian	1.36%	0.27%, 2.46%
	AIAN	0.01%	-3.53%, 3.69%
Income	≤FPL	0.97%	0.60%, 1.35%
	>FPL	1.37%	0.82%, 1.93%
Location	Proximal	0.07%	-0.25%, 0.39%
	Distal	1.57%	1.24%, 1.90%
	Rectum	2.33%	2.08%, 2.59%
	Other	-0.52%	-1.25%, 0.21%

Note: Net drift represents the overall annual percent change in incidence rates over time, integrating both period and cohort effects across all age groups combined (20 – 49 years).

Table 3. Period effects on early-onset colorectal cancer incidence in the United States, 2000–2022, stratified by demographic factors and tumor location.

Characteristic	Subgroup	Period	IRR	95% CI
Sex	Male	2000-2004	1.01	0.99, 1.03
		2005-2009	1.01	1.00, 1.01
		2010-2014	0.98	0.96, 1.00
		2015-2019	0.99	0.96, 1.02
		2020-2022	1.03	0.97, 1.09
	Female	2000-2004	0.99	0.98, 1.01
		2005-2009	1.02	1.01, 1.02
		2010-2014	0.99	0.97, 1.01
		2015-2019	0.99	0.96, 1.02
		2020-2022	1.01	0.95, 1.08
Race	White	2000-2004	1.01	0.99, 1.02
		2005-2009	1.01	1.00, 1.01
		2010-2014	0.99	0.97, 1.01
		2015-2019	0.98	0.95, 1.02
		2020-2022	1.04	0.97, 1.11
	Black	2000-2004	0.95	0.92, 0.99
		2005-2009	1.04	1.02, 1.05
		2010-2014	1.03	0.99, 1.07
		2015-2019	1.02	0.95, 1.10
		2020-2022	0.94	0.82, 1.06
	Hispanic	2000-2004	1.02	0.98, 1.07
		2005-2009	0.99	0.98, 1.01
		2010-2014	0.95	0.91, 0.99
		2015-2019	1.04	0.96, 1.12
		2020-2022	0.99	0.87, 1.13
	Asian/Pacific Islander	2000-2004	1.07	0.98, 1.17
		2005-2009	1.01	0.98, 1.04
		2010-2014	0.93	0.85, 1.01
		2015-2019	0.91	0.77, 1.06
		2020-2022	1.19	0.93, 1.54
	AIAN	2000-2004	0.93	0.72, 1.20
		2005-2009	1.01	0.90, 1.13
		2010-2014	1.09	0.83, 1.43
		2015-2019	1.15	0.70, 1.90
		2020-2022	0.77	0.32, 1.86

		2000-2004	1.03	1.01, 1.06
		2005-2009	1.00	0.99, 1.01
	≤FPL	2010-2014	0.98	0.96, 0.99
		2015-2019	0.99	0.96, 1.02
		2020-2022	1.03	0.99, 1.07
Income				
		2000-2004	0.99	0.98, 1.00
		2005-2009	1.02	1.01, 1.03
	>FPL	2010-2014	0.99	0.97, 1.02
		2015-2019	1.02	0.97, 1.06
		2020-2022	0.96	0.85, 1.08
		2000-2004	0.96	0.94, 0.98
		2005-2009	1.02	1.01, 1.03
	Proximal	2010-2014	1.02	0.99, 1.05
		2015-2019	1.06	1.01, 1.11
		2020-2022	0.91	0.84, 0.98
		2000-2004	0.99	0.97, 1.02
		2005-2009	1.01	1.00, 1.02
	Distal	2010-2014	1.00	0.97, 1.02
		2015-2019	1.00	0.95, 1.05
		2020-2022	1.00	0.92, 1.08
Location				
		2000-2004	1.03	1.01, 1.05
		2005-2009	1.01	1.00, 1.02
	Rectum	2010-2014	0.96	0.94, 0.98
		2015-2019	0.94	0.91, 0.98
		2020-2022	1.12	1.05, 1.20
		2000-2004	1.02	0.96, 1.07
		2005-2009	0.95	0.93, 0.97
	Other	2010-2014	1.01	0.95, 1.07
		2015-2019	1.09	0.98, 1.21
		2020-2022	0.91	0.76, 1.10

IRR: Incidence Rate Ratio
95% CI: 95% Confidence Interval

Table 4. Cohort effects on early-onset colorectal cancer incidence in the United States, 2000–2022, stratified by demographic factors and tumor location.

Characteristic	Subgroup	Cohort	IRR	95% CI
		1950	0.85	0.81, 0.89
		1955	0.87	0.84, 0.90
		1960	0.90	0.89, 0.91
		1965	0.97	0.97, 0.98
		1969	0.96	0.88, 1.05
		1970	1.05	1.03, 1.08
		1974	1.22	1.14, 1.31
		1975	1.18	1.14, 1.23
	Male	1979	1.22	1.15, 1.29
		1980	1.31	1.24, 1.39
		1984	1.32	1.26, 1.38
		1985	1.42	1.32, 1.53
		1989	1.41	1.34, 1.48
		1990	1.42	1.29, 1.57
		1994	1.55	1.45, 1.66
		1995	1.49	1.40, 1.59
		1999	1.27	1.12, 1.44
Sex				
		1950	0.88	0.83, 0.92
		1955	0.90	0.87, 0.93
		1960	0.91	0.90, 0.92
		1965	0.98	0.97, 0.99
		1969	1.01	0.92, 1.11
		1970	1.03	1.01, 1.06
		1974	1.24	1.15, 1.34
		1975	1.15	1.10, 1.20
	Female	1979	1.19	1.12, 1.27
		1980	1.25	1.17, 1.32
		1984	1.37	1.30, 1.44
		1985	1.41	1.30, 1.52
		1989	1.43	1.36, 1.51
		1990	1.37	1.24, 1.52
		1994	1.40	1.31, 1.51
		1995	1.44	1.35, 1.53
		1999	1.57	1.39, 1.78

		1950	0.84	0.80, 0.88
		1955	0.85	0.82, 0.88
		1960	0.88	0.87, 0.89
		1965	0.97	0.96, 0.98
		1969	0.98	0.89, 1.08
		1970	1.08	1.05, 1.10
		1974	1.22	1.12, 1.32
		1975	1.22	1.17, 1.27
	White	1979	1.24	1.16, 1.32
		1980	1.33	1.25, 1.42
		1984	1.39	1.31, 1.47
		1985	1.48	1.36, 1.61
		1989	1.42	1.34, 1.50
		1990	1.43	1.28, 1.59
		1994	1.50	1.40, 1.62
		1995	1.46	1.36, 1.56
		1999	1.28	1.12, 1.47
		1950	1.07	0.96, 1.19
		1955	1.06	0.98, 1.13
		1960	0.98	0.95, 1.02
		1965	0.98	0.96, 1.00
		1969	1.02	0.84, 1.25
		1970	0.94	0.90, 0.99
Race		1974	1.34	1.14, 1.57
		1975	1.00	0.91, 1.09
	Black	1979	1.09	0.96, 1.24
		1980	1.09	0.96, 1.24
		1984	1.15	1.03, 1.29
		1985	1.13	0.95, 1.35
		1989	1.30	1.16, 1.45
		1990	1.15	0.91, 1.45
		1994	1.24	1.06, 1.46
		1995	1.31	1.13, 1.51
		1999	1.58	1.22, 2.05
		1950	0.82	0.72, 0.93
		1955	0.89	0.82, 0.97
		1960	0.94	0.90, 0.98
		1965	0.97	0.95, 0.99
		1969	1.07	0.87, 1.31
		1970	1.02	0.97, 1.07
	Hispanic	1974	1.35	1.14, 1.59
		1975	1.18	1.08, 1.29
		1979	1.42	1.24, 1.62
		1980	1.31	1.15, 1.50
		1984	1.63	1.46, 1.82
		1985	1.51	1.26, 1.81

	1989	1.77	1.58, 1.98
	1990	1.60	1.26, 2.04
	1994	1.79	1.52, 2.10
	1995	1.76	1.51, 2.06
	1999	1.67	1.26, 2.23
Asian/Pacific Islander	1950	0.72	0.57, 0.91
	1955	0.84	0.72, 0.98
	1960	0.93	0.86, 1.00
	1965	1.06	1.02, 1.09
	1969	0.83	0.56, 1.23
	1970	1.11	0.99, 1.23
	1974	1.06	0.77, 1.46
	1975	1.19	0.99, 1.45
	1979	0.93	0.73, 1.19
	1980	1.28	0.97, 1.69
	1984	0.99	0.81, 1.20
	1985	1.42	0.98, 2.05
	1989	1.23	1.02, 1.48
	1990	1.43	0.89, 2.30
	1994	1.25	0.94, 1.65
	1995	1.35	1.04, 1.76
	1999	1.89	1.19, 2.99
AIAN	1950	0.81	0.39, 1.68
	1955	0.69	0.43, 1.11
	1960	0.95	0.75, 1.20
	1965	1.06	0.93, 1.20
	1969	1.87	0.49, 7.17
	1970	1.01	0.72, 1.42
	1974	1.79	0.58, 5.45
	1975	1.01	0.56, 1.84
	1979	2.56	1.04, 6.29
	1980	1.11	0.47, 2.59
	1984	2.38	1.14, 4.94
	1985	1.15	0.37, 3.58
	1989	1.39	0.61, 3.16
	1990	0.45	0.09, 2.16
	1994	1.03	0.35, 2.97
	1995	1.00	0.37, 2.70
	1999	0.89	0.10, 7.88

		1950	0.88	0.84, 0.92
		1955	0.90	0.87, 0.93
		1960	0.92	0.91, 0.94
		1965	0.98	0.97, 0.98
		1969	0.98	0.91, 1.05
		1970	1.04	1.02, 1.06
		1974	1.21	1.15, 1.28
		1975	1.15	1.10, 1.19
	≤FPL	1979	1.18	1.13, 1.22
		1980	1.24	1.17, 1.31
		1984	1.27	1.23, 1.31
		1985	1.35	1.25, 1.45
		1989	1.34	1.30, 1.40
		1990	1.33	1.21, 1.46
		1994	1.37	1.28, 1.47
		1995	1.38	1.29, 1.46
		1999	1.39	1.25, 1.53
Income				
		1950	0.99	0.95, 1.03
		1955	0.98	0.96, 1.00
		1960	0.95	0.94, 0.96
		1965	1.03	1.01, 1.05
		1969	1.16	0.99, 1.34
		1970	1.07	1.03, 1.11
		1974	1.41	1.23, 1.61
		1975	1.16	1.09, 1.22
	>FPL	1979	1.32	1.17, 1.49
		1980	1.27	1.17, 1.37
		1984	1.68	1.50, 1.87
		1985	1.42	1.29, 1.57
		1989	1.54	1.37, 1.73
		1990	1.38	1.21, 1.57
		1994	1.69	1.52, 1.88
		1995	1.53	1.39, 1.69
		1999	1.04	0.80, 1.35
		1950	1.12	1.05, 1.20
		1955	1.03	0.99, 1.08
		1960	0.96	0.94, 0.98
		1965	0.97	0.96, 0.98
		1969	1.14	1.01, 1.29
		1970	0.96	0.93, 0.99
Location	**Proximal**	1974	1.23	1.11, 1.36
		1975	1.00	0.94, 1.05
		1979	1.14	1.05, 1.24
		1980	1.00	0.92, 1.08
		1984	1.13	1.05, 1.21
		1985	1.00	0.90, 1.11

	1989	1.17	1.09, 1.26
	1990	0.94	0.82, 1.08
	1994	1.11	1.00, 1.22
	1995	1.08	0.99, 1.19
	1999	0.99	0.82, 1.18
	1950	0.88	0.82, 0.94
	1955	0.89	0.85, 0.92
	1960	0.88	0.86, 0.90
	1965	0.96	0.95, 0.97
	1969	1.04	0.92, 1.19
	1970	1.05	1.02, 1.08
	1974	1.38	1.24, 1.53
	1975	1.19	1.12, 1.25
Distal	1979	1.29	1.19, 1.41
	1980	1.28	1.18, 1.39
	1984	1.45	1.35, 1.55
	1985	1.41	1.27, 1.57
	1989	1.61	1.50, 1.72
	1990	1.47	1.28, 1.70
	1994	1.65	1.50, 1.81
	1995	1.57	1.44, 1.72
	1999	1.30	1.07, 1.56
	1950	0.70	0.66, 0.74
	1955	0.79	0.77, 0.82
	1960	0.88	0.87, 0.90
	1965	0.99	0.98, 1.00
	1969	0.88	0.80, 0.97
	1970	1.10	1.08, 1.13
	1974	1.16	1.07, 1.26
	1975	1.29	1.23, 1.35
Rectum	1979	1.20	1.12, 1.28
	1980	1.51	1.42, 1.61
	1984	1.43	1.36, 1.51
	1985	1.83	1.68, 1.99
	1989	1.55	1.47, 1.64
	1990	1.79	1.61, 2.00
	1994	1.77	1.64, 1.90
	1995	1.78	1.66, 1.90
	1999	1.82	1.60, 2.06

	1950	1.14	0.98, 1.32
	1955	1.01	0.92, 1.12
	1960	0.98	0.93, 1.03
	1965	0.98	0.96, 1.01
	1969	1.08	0.81, 1.43
	1970	0.98	0.91, 1.05
	1974	1.21	0.95, 1.53
	1975	0.92	0.81, 1.05
Other	1979	1.28	1.06, 1.56
	1980	1.00	0.83, 1.19
	1984	1.32	1.12, 1.55
	1985	0.82	0.65, 1.05
	1989	0.93	0.78, 1.11
	1990	0.80	0.58, 1.09
	1994	0.70	0.55, 0.90
	1995	0.76	0.61, 0.94
	1999	1.02	0.72, 1.44