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Original Article

Temporal trends in early-onset colorectal cancer incidence (2000-2020) by age group and five geographic regions in the state of Georgia

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Abstract: The increase of early-onset colorectal cancer (CRC) among younger adults is a major public health concern. However, little is known about variations in CRC incidence across different age groups within small geographic areas in Georgia. We examined temporal trends of CRC incidence in Clayton, East Central, West Central, Northeast, and Southeast regions, by age groups. Annual incidence rates for CRC in individuals aged 15+ years during 2000-2020 in the five regions of Georgia were included. Temporal trends were examined within the five regions and stratified by age group. Joinpoint regression was employed to calculate the annual percent change and corresponding 95% confidence intervals (CIs). Among 20,215 CRC diagnoses, CRC incidence declined over time for East Central (-2.33%; 95% CI, -3.03, -1.64), Northeast (-1.63%; 95% CI, -2.15, -1.04), Southeast (-1.63%; 95% CI, -2.30, -0.96), and West Central (-1.53%; 95% CI, -2.04, -1.03) Georgia. In the 15-44 age group, a notable increase of CRC incidence was found in Clayton, Northeast, and Southeast regions with a range of 2.2%-3.4%. However, adults aged 60+ years experienced a significant decrease in CRC incidence for most Georgia regions (all *p*-value <0.05), except for the Clayton region. In conclusion, CRC incidence declined during 2000-2020 in most Georgia regions. However, early-onset CRC is a major concern in Georgia as young adults (<45 years) living in Clayton, Northeast, and Southeast Georgia experienced significant annual increases in CRC incidence. Targeted CRC screening and awareness campaigns should be prioritized for adults <45 years and in the most impacted areas in Georgia.

Keywords: Colorectal cancer, incidence, time trends, Joinpoint regression analysis, young adults

Introduction

Colorectal cancer (CRC) is the third most common cancer diagnosed and leading cause of cancer death among men and women in Georgia [1]. Systematic screening efforts in Georgia have led to a decline in the incidence and mortality of CRC. Since 2000, the average annual rate of incidence reduction has been 2.3%, while mortality experienced a rapid decrease of 2.3% per year during the period from 2002 to 2013 [1]. However, from 2008 through 2013, a significant greater burden of CRC mortality were found in Clayton, East Central, West Central, Northeast, and Southeast Georgia [1]. The higher CRC incidence rates were also observed in West Central Georgia [1]. Variations in CRC incidence and/or mortality rates across the Georgia regions may be attributed to barriers to screening and treatment, such as the lack of transportation to CRC treatment centers and/or screening facilities [2].

Historical evidence substantiates that the risk of CRC increases with increasing age [3]. During 2015 and 2019, incidence rates increased by 80%-100% with each 5-year age group until age 50 years and then by 20%-30% from ages 55-59 years and older nationally [3]. Several

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studies recently highlighted increasing incidence among individuals younger than 50 years in the United States (US) [4-6]. Early-onset CRC (defined as CRC diagnosed before the age of 50 years) has been reported to be increasing most rapidly in the southeastern US (e.g., Georgia, Alabama, Florida, South Carolina, North Carolina, Tennessee, Mississippi, Louisiana) [7]. From 2001 to 2017, a meaningful 1.5% increase in CRC incidence rates was observed among Georgians aged 50 years and younger [7]. Factors that may contribute to early-onset CRC include differences in diet and the prevalence of obesity, alcohol use, and current smoking, as well as access to health care services and CRC screening [8-11]. Among some racial and ethnic minority groups, genetic differences as well as various social determinants of health may also play an important role in early-onset CRC [10, 12-15].

A few studies have examined temporal trends of early-onset CRC incidence by geographic areas and age group, but they mainly focused on the entire US [4] or non-US populations [16]. Unanswered questions remain about the variation in early-onset CRC incidence in small geographic regions across various states in the US. A detailed analysis of CRC incidence within small areas is essential to inform future research on CRC etiopathogenesis (e.g., interactions between gene, lifestyle, and environment factors), understand the role of social determinants more relevant to a specific area, and to guide the development of culturally tailored CRC screening programs [17]. Because the United States Preventive Services Taskforce (USPSTF) and American Cancer Society (ACS) have lowered their endorsement to initiate CRC screening at age 45 years due to increasing early-onset CRC incidence [18], additional research examining CRC incidence rate change is needed in the high burden regions of Georgia specifically. Therefore, we sought to examine temporal trends in CRC incidence in Clayton, East Central, Northeast, Southeast, and West Central regions of Georgia, stratified by age groups.

Material and methods

Study design and data source

Population-based cancer incidence data in the US are collected by the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER) program. Thus, we obtained data on CRC incidence cases and rates among adults aged 15 years or older and diagnosed between 2000 and 2020 from the Incidence-SEER Research Plus Data, 17 Registries, Nov 2022 Sub (2000-2020) through SEER*Stat software (version 8.4.1.2; https://seer.cancer.gov/seerstat/). We included individuals aged 15-17 years due to age-adjusted estimates by standardizing to the US 2000 Census population. CRC subsets were determined using the International Classification of Diseases for Oncology, Third Edition (ICD-O-3)/World Health Organization 2008 definition for colon and rectal cancers. The following ICD-O-3 codes were included: C18.0 (cecum), C18.2-C18.9 (ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, large intestine [not otherwise specified]), C19.9 (rectosigmoid junction), C20.9 (rectum), and C26.0 (malignant neoplasm of intestinal tract, part unspecified) [19]. We examined time trends in CRC within the five regions of Georgia (Clayton, East Central, Northeast, Southeast, and West Central regions) as well as time trends by age group (15-44, 45-59, 60-74, and 75+ years). The five regions of Georgia were defined by using Georgia public health districts, including one county in the Clayton region, 13 counties in the East Central, 16 counties in the West Central, 22 counties in the Southeast, and 10 counties in the Northeast regions [1]. All data were publicly available and de-identified. Thus, this study was considered exempt from our Institutional Review Board (IRB) and ethical board approval.

Statistical analysis

Annual CRC incidence rates were obtained by using standard formulae implemented in SEER*Stat software, with the number of cases as the numerator and the corresponding population size (based on the US Census Bureau data) as the denominator. The corresponding 95% confidence intervals (CIs) were calculated via the Tiwari method [20]. We first presented incident CRC and age-adjusted CRC incidence rates (using the 2000 US standard population) with 95% CI stratified by the five regions of Georgia.

Further, we examined for temporal trends in rates by five regions of Georgia and four age

Table 1. Annual frequencies and age-adjusted incidence rats of colorectal cancer among individuals aged 15 years or older in the five regions of Georgia, 2000-2020 (n=20, 215)

Year	Clayton		East Central		Northeast		Southeast		West Central	
	n	ADIR (95% CI)[a]	n	ADIR (95% CI)[a]	n	ADIR (95% CI)[a]	n	ADIR (95% CI)[a]	n	ADIR (95% CI)[a]
2000	61	53.5 (40.0, 69.7)	217	70.2 (61.2, 80.3)	183	75.5 (64.9, 87.3)	232	65.5 (57.3, 74.4)	175	67.6 (57.9, 78.3)
2001	51	45.5 (33.2, 60.6)	194	63.1 (54.5, 72.7)	159	64.2 (54.5, 75.0)	245	67.7 (59.4, 76.7)	183	69.9 (60.1, 80.7)
2002	83	71.5 (56.0, 89.7)	232	74.0 (64.8, 84.2)	166	64.8 (55.2, 75.5)	261	69.9 (61.6, 78.9)	185	70.0 (60.3, 80.9)
2003	65	52.1 (39.3, 67.4)	241	76.2 (66.8, 86.5)	180	68.9 (59.1, 79.8)	290	75.6 (67.1, 84.9)	189	71.5 (61.6, 82.5)
2004	83	62.6 (48.9, 78.6)	225	68.1 (59.4, 77.7)	200	72.1 (62.3, 82.9)	237	60.4 (52.9, 68.7)	203	74.8 (64.8, 85.9)
2005	88	71.0 (55.7, 88.8)	202	60.0 (51.9, 68.9)	195	67.6 (58.3, 77.9)	259	62.6 (55.1, 70.8)	168	59.9 (51.1, 69.7)
2006	86	62.6 (49.2, 78.3)	238	69.1 (60.5, 78.5)	178	57.1 (48.9, 66.3)	250	58.6 (51.5, 66.5)	193	67.7 (58.4, 78)
2007	92	66.0 (52.1, 82.2)	204	59.3 (51.3, 68.1)	197	60.7 (52.3, 69.9)	265	59.5 (52.4, 67.2)	179	61.0 (52.3, 70.7)
2008	103	70.3 (56.6, 86.3)	244	68.3 (59.9, 77.6)	191	58.7 (50.6, 67.8)	235	51.2 (44.7, 58.3)	197	66.3 (57.3, 76.3)
2009	88	56.9 (44.9, 71.1)	208	57.1 (49.4, 65.5)	186	54.1 (46.5, 62.7)	269	58.1 (51.2, 65.6)	199	65.4 (56.5, 75.2)
2010	83	53.7 (41.9, 67.7)	186	48.5 (41.7, 56.2)	184	53.3 (45.8, 61.8)	242	50.9 (44.6, 57.9)	192	63.4 (54.7, 73.2)
2011	98	61.1 (48.6, 75.6)	196	50.2 (43.3, 58.0)	227	64.5 (56.2, 73.6)	267	54.2 (47.7, 61.2)	166	53.3 (45.4, 62.2)
2012	100	65.0 (51.8, 80.3)	200	50.9 (44.0, 58.7)	222	58.8 (51.2, 67.3)	262	51.8 (45.6, 58.7)	186	58.6 (50.3, 67.8)
2013	83	52.0 (40.5, 65.6)	220	54.0 (47.0, 61.9)	186	48.4 (41.6, 56.0)	274	54.2 (47.8, 61.2)	190	57.5 (49.4, 66.5)
2014	103	61.7 (49.5, 75.7)	192	46.4 (39.9, 53.7)	203	52.4 (45.3, 60.3)	270	52.4 (46.2, 59.2)	194	59.3 (51.1, 68.5)
2015	107	64.2 (51.7, 78.8)	217	51.3 (44.5, 58.8)	228	56.1 (48.9, 64.1)	311	58.6 (52.2, 65.7)	206	60.6 (52.4, 69.7)
2016	125	65.1 (53.4, 78.6)	209	48.3 (41.8, 55.5)	232	55.3 (48.3, 63.1)	235	43.0 (37.6, 49.1)	207	63.4 (54.9, 73.0)
2017	114	60.5 (49.1, 73.6)	194	44.7 (38.5, 51.7)	235	53.7 (46.9, 61.3)	281	51.3 (45.4, 57.8)	171	50.7 (43.2, 59.1)
2018	119	60.4 (49.3, 73.3)	197	44 (37.9, 50.8)	232	52.6 (45.9, 60)	321	57.2 (51, 64)	183	52.8 (45.2, 61.3)
2019	112	58.6 (48.1, 70.7)	229	50.9 (44.3, 58.1)	238	51.3 (44.8, 58.4)	316	54.7 (48.7, 61.3)	171	49.3 (42, 57.6)
2020	92	46.6 (37.0, 57.9)	238	52.9 (46.2, 60.4)	242	50.9 (44.6, 57.9)	266	45.3 (39.9, 51.3)	186	55 (47.2, 63.8)
Total	1946	59.5 (56.7, 62.5)	4483	56.2 (54.6, 57.9)	4264	57.5 (55.8, 59.3)	5599	56.1 (54.6, 57.6)	3923	61.1 (59.2, 63.1)

Abbreviations: n, number of new cases; ADIR, Age-adjusted incidence rate; CI, confidence interval. [a]Rates are per 100,000 and age-adjusted to the 2000 US Standard Population.

groups, using Joinpoint regression analysis. The average percent change (APC) and average annual percent change (AAPC) in CRC incidence over each study period (2000-2020) by these five regions and age groups were calculated. The APC for each single linear segment and the AAPC for the entire study period (2000-2020) were calculated for each Joinpoint model. Monte Carlo permutation tests were performed to examine trends for each combination of Joinpoints, and the trend that provided the best fit to the data were selected [21]. We reported both AAPCs, which are more meaningful for comparisons between groups, and APCs, which provide a complete characterization of the trend over time, to provide an integrated information of CRC incidence trends. Finally, a parallelism test was used to examine whether AAPCs between the five regions and stratified by age group were different in direction and magnitude. A statistically significant *p*-value on this test indicated that the two trends in terms of AAPCs compared were significantly different from each other [22]. The Joinpoint Regression Program version 4.9.0.1, which was developed by Surveillance, Epidemiology, and End Results, National Cancer Institute, Bethesda, MD, was used to conduct analysis. Trends were described as increasing or decreasing when the APC or AAPC was statistically significant based on a two-sided *p*-value <0.05.

Results

Incidence by regions across 20 years

There were 20,215 cases of CRC diagnosed at aged 15 years or older in the five regions of Georgia from 2000 through 2020 (**Table 1**). A total of 1,946 CRC cases were diagnosed among individuals who resided in Clayton, 4,483 in East Central, 4,264 in Northeast, 5,599 in Southeast, and 3,923 West Central regions. Among study eligible cases, age-adjusted CRC incidence rates were highest in West Central (61.1 per 100,000; 95% CI, 59.2, 63.1), followed by Clayton (59.5 per 100,000; 95% CI, 56.7, 62.5), Northeast (57.5 per 100,000; 95% CI, 55.8, 59.3), East Central (56.2 per 100,000; 95% CI, 54.6, 57.9),

Table 2. APCs and AAPCs in CRC incidence rates by the five regions of Georgia and age group, 2000-2020

Regions/Age group	Joinpoint Segment Start-End	APC (95% CI)	AAPC (95% CI)	*P*-value[a]
All age group				
Clayton	2000-2020	-0.28 (-1.20, 0.65)	-0.28 (-1.20, 0.65)	0.540
East Central	2000-2020	**-2.33 (-3.03, -1.64)**	**-2.33 (-3.03, -1.64)**	<0.001
Northeast	2000-2020	**-1.63 (-2.15, -1.04)**	**-1.63 (-2.15, -1.04)**	<0.001
Southeast	2000-2020	**-1.63 (-2.30, -0.96)**	**-1.63 (-2.30, -0.96)**	<0.001
West Central	2000-2020	**-1.53 (-2.04, -1.03)**	**-1.53 (-2.04, -1.03)**	<0.001
15-44 years				
Clayton	2000-2020	**3.43 (0.38, 6.58)**	**3.43 (0.38, 6.58)**	0.029
East Central	2000-2020	0.29 (-2.05, 2.69)	0.29 (-2.05, 2.69)	0.800
Northeast	2000-2020	**2.53 (0.63, 4.46)**	**2.53 (0.63, 4.46)**	0.011
Southeast	2000-2020	**2.23 (0.23, 4.27)**	**2.23 (0.23, 4.27)**	0.031
West Central	2000-2020	1.56 (-1.03, 4.22)	1.56 (-1.03, 4.22)	0.224
45-59 years				
Clayton	2000-2020	0.46 (-1.28, 2.23)	0.46 (-1.28, 2.23)	0.586
East Central	2000-2020	-0.42 (-1.52, 0.69)	-0.42 (-1.52, 0.69)	0.439
Northeast	2000-2020	0.25 (-0.72, 1.23)	0.25 (-0.72, 1.23)	0.599
Southeast	2000-2020	-0.32 (-1.18, 0.55)	-0.32 (-1.18, 0.55)	0.453
West Central	2000-2020	0.09 (-1.11, 1.29)	0.09 (-1.11, 1.29)	0.883
60-74 years				
Clayton	2000-2020	-0.88 (-2.44, 0.70)	-0.88 (-2.44, 0.70)	0.255
East Central	2000-2020	**-2.94 (-3.76, -2.11)**	**-2.94 (-3.76, -2.11)**	<0.001
Northeast	2000-2020	**-2.23 (-3.18, -1.27)**	**-2.23 (-3.18, -1.27)**	<0.001
Southeast	2000-2020	**-2.29 (-3.24, -1.32)**	**-2.29 (-3.24, -1.32)**	<0.001
West Central	2000-2020	**-1.89 (-2.64, -1.11)**	**-1.89 (-2.64, -1.11)**	0.001
75+ years				
Clayton	2000-2020	-1.21 (-2.68, 0.29)	-1.21 (-2.68, 0.29)	0.108
East Central	2000-2020	**-3.93 (-5.10, -2.75)**	**-3.93 (-5.10, -2.75)**	<0.001
Northeast	2000-2020	**-3.23 (-4.12, -2.34)**	**-3.23 (-4.12, -2.34)**	<0.001
Southeast	2000-2020	**-2.81 (-3.73, -1.88)**	**-2.81 (-3.73, -1.88)**	<0.001
West Central	2000-2020	**-3.09 (-3.79, -2.38)**	**-3.09 (-3.79, -2.38)**	<0.001

Abbreviations: CRC, colorectal cancer; APC, annual percent change; AAPC, average annual percent change; CI, confidence interval. Bold texts indicate the statistical significance. [a]Monte Carlo permutation tests were used.

Southeast (56.1 per 100,000; 95% CI, 54.6, 57.6) regions.

Incidence by regions and age group

Table 2 describes APCs and AAPCs in overall CRC incidence rates by the five regions of Georgia and age group during 2000 and 2020. Because zero Joinpoints were found in each region, APCs and AAPCs were the same. We found that age-adjusted CRC incidence rates declined by 2.33% in East Central (95% CI, -3.03, -1.64), 1.63% in Northeast (95% CI, -2.15, -1.04), 1.63% in Southeast (95% CI, -2.30, -0.96), and 1.53% in West Central (95% CI, -2.04, -1.03) regions from 2000 to 2020. The Clayton region demonstrated a stable trend with a 0.28% non-significant decline of CRC incidence (95% CI, -1.20, 0.65).

When exploring age difference, among individuals aged 15-44 years, increased CRC incidence rates were observed over the study period by 3.43% in Clayton (95% CI, 0.38, 6.58), 2.53% in Northeast (95% CI, 0.63, 4.46), and 2.23% in Southeast (95% CI, 0.23, 4.27)

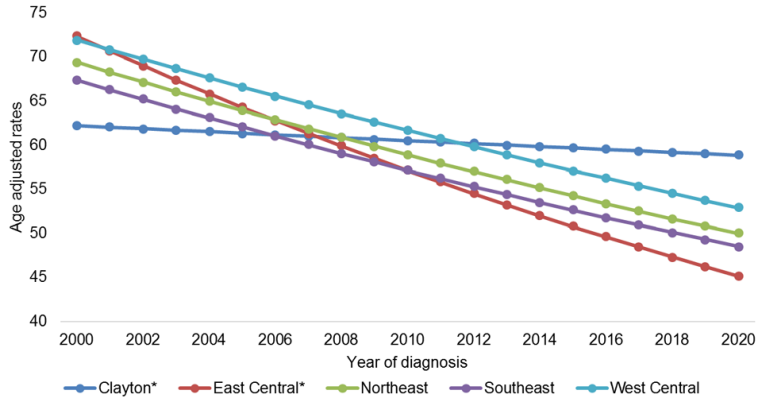

Figure 1. Age-adjusted colorectal cancer incidence rates by the five regions of Georgia, 2000-2020. Notes: 1) Rates are per 100,000 and age-adjusted to the 2000 US Standard Population. 2) Zero Joinpoints were found in each region. 3) **P*-value <0.05 on the parallelism test indicated that the trends of average annual percent change (AAPC) between the reference group (West Central) were significantly different.

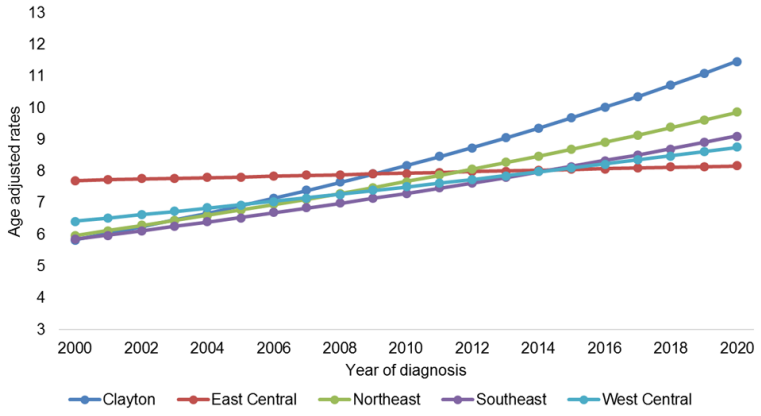

Figure 2. Age-adjusted colorectal cancer incidence rates at 15-44 age group by the five regions of Georgia, 2000-2020. Notes: 1) Rates are per 100,000 and age-adjusted to the 2000 US Standard Population. 2) Zero Joinpoints were found in each region. 3) **P*-value <0.05 on the parallelism test indicated that the trends of average annual percent change (AAPC) between the reference group (West Central) were significantly different.

regions (**Table 2**). Among adults aged 45-59 years, all regions demonstrated stable trends for CRC incidence during 2000 and 2020 (all *p*-value >0.05). Conversely, there was a reduction of CRC incidence from 2000 to 2020 for individuals aged 60-74 years and 75 years or older. Among adults aged 60-74 years, CRC incidence reduced by 2.94% in East Central (95% CI, -3.76, -2.11), 2.23% in Northeast (95% CI, -3.18, -1.27), 2.29% in Southeast (95% CI, -3.24, -1.32), and 1.89% in West Central (95% CI, -2.64, -1.11) regions. Further, among those aged 75+ years, CRC incidence were dramatically reduced by 3.93% in East Central (95% CI, -5.10, -2.75), 3.23% in Northeast (95% CI, -4.12, -2.34), 2.81% in Southeast (95% CI, -3.73, -1.88), and 3.09% in West Central (95% CI, -3.79, -2.38) regions.

Comparison of AAPCs by regions

Figure 1 illustrates the time trends in Joinpoint-predicted CRC incidence rate per 100,000 for Clayton, East Central, West Central, Northeast, and Southeast regions. The rate of increase was statistically significant in Clayton when compared with the West Central (AAPC, 1.25%; *p*-value =0.013) region. Conversely, East Central demonstrated a slightly significant reduction for CRC incidence when compared to the West Central region (AAPC, -0.81%; *p*-value =0.05).

Comparison of AAPCs by regions and age group

When examining age differences, East Central demonstrated a significant decline in CRC incidence with 1.06% (*p*-value =0.049) reduction in 60-74 age group (**Figure 4**) in comparison to West Central region. Further, Clayton reported a significant increase in CRC incidence with 2.73% (*p*-value =0.003) increasing in 75+ age group (**Figure 5**). Finally, no statistical significance was found when comparing the 15-44- and 45-59-year age groups in these regions (all *p*-value >0.05; **Figures 2**, **3**).

Discussion

This is the first study to examine temporal trends of CRC incidence (early-onset CRC included) in these five regions of Georgia. CRC incidence rates significantly decreased in East

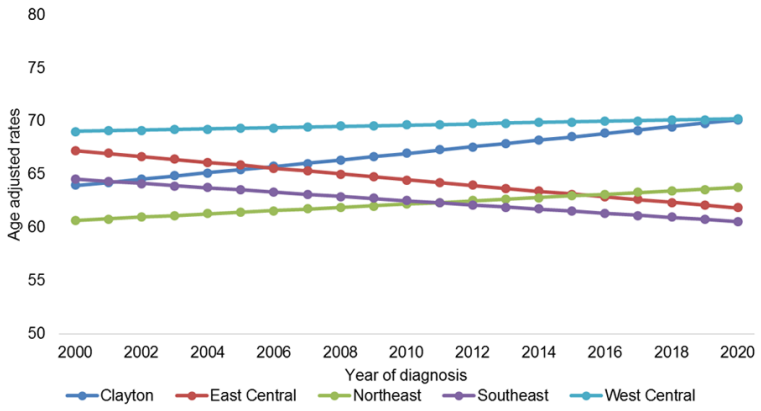

Figure 3. Age-adjusted colorectal cancer incidence rates at 45-59 age group by the five regions of Georgia, 2000-2020. Notes: 1) Rates are per 100,000 and age-adjusted to the 2000 US Standard Population. 2) Zero Joinpoints were found in each region. 3) **P*-value <0.05 on the parallelism test indicated that the trends of average annual percent change (AAPC) between the reference group (West Central) were significantly different.

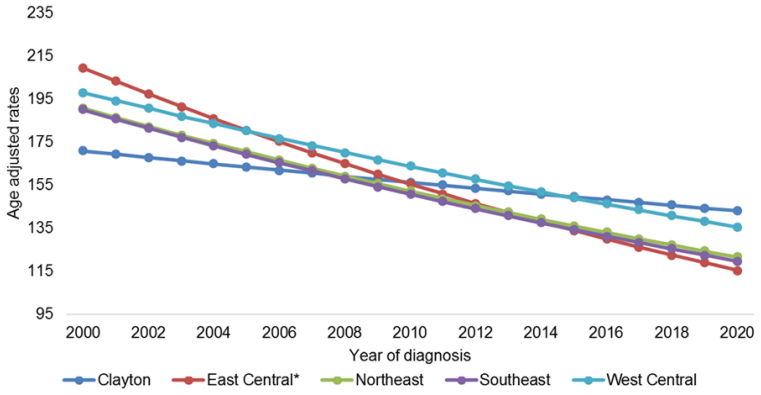

Figure 4. Age-adjusted colorectal cancer incidence rates at 60-74 age group by the five regions of Georgia, 2000-2020. Notes: 1) Rates are per 100,000 and age-adjusted to the 2000 US Standard Population. 2) Zero Joinpoints were found in each region. 3) **P*-value <0.05 on the parallelism test indicated that the trends of average annual percent change (AAPC) between the reference group (West Central) were significantly different.

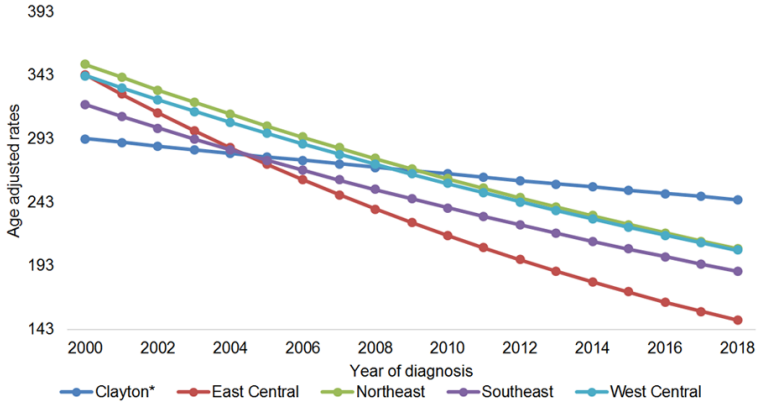

Figure 5. Age-adjusted colorectal cancer incidence rates at 75 or older age group by the five regions of Georgia, 2000-2020. Notes: 1) Rates are per 100,000 and age-adjusted to the 2000 US Standard Population. 2) Zero Joinpoints were found in each region. 3) **P*-value <0.05 on the parallelism test indicated that the trends of average annual percent change (AAPC) between the reference group (West Central) were significantly different.

Central, Northeast, Southeast, and West Central regions as well as among our older age group (60+ years) from 2000 to 2020. During the study period, a noteworthy increase in CRC incidence was observed among individuals aged 15-44 years in the Clayton, Northeast, Southeast regions. Despite not being statistical significance, West Central individuals aged 15-44 years also demonstrated a slightly increasing trend. This rising incidence of early-onset CRC underscore the importance of implementing targeted and age-specific screening and awareness programs for early-onset CRC in the identified regions, aiming to detect and address this concerning trend among younger populations. Early detection and intervention strategies could potentially mitigate the impact of CRC in these age groups and improve overall public health outcomes.

Place-based difference

CRC incidence was highest in West Central Georgia and lowest in Southeast Georgia during 2000-2020 period. Place-based differences in CRC incidence may be attributed to socioeconomic status at area-level (e.g., poverty, unemployment status, and lower education), availability of CRC screening, and access to primary care facilities [23, 24]. We observed that CRC incidence rates significantly de-

clined from 2000 to 2020 in East Central, Northeast, Southeast, and West Central regions. Possible explanation is that community-level CRC screening programs have been implemented in Georgia, particularly in the southwest regions [25]. For instance, since 2006, the Cancer Coalition of South Georgia has operated the Community Cancer Screening Program to increase CRC screening among uninsured and underinsured patients of federally qualified community health centers (FQHCs) and other clinics [25]. Moreover, the Georgia Colorectal Cancer Roundtable (GCCRT), which is a statewide multiorganizational collaborative comprised of leading organizations (e.g., East Georgia Center Coalition, West Central Georgia Cancer Coalition, Northwest Georgia Regional Cancer Coalition), has continuously worked towards the improving CRC outcomes in Georgia since 2015. Particularly, they encourage the use of patient navigation through cancer screening program to ensure cancer screening options are provided to underserved population in Georgia [25]. All considered, these local initiatives have the potential to enhance screening uptake, thereby contributing to a reduction in CRC incidence in the specific regions of Georgia where they are implemented.

Conversely, we observed a slightly increasing incidence rate in the Clayton region compared to the West Central region. Clayton residents possibly experience barriers to the access of appropriate medical resources because 18% of Clayton residents reported having no health insurance, compared with 14% of Georgians, overall [26, 27]. The Clayton region also has a greater proportion of Black inhabitants than Georgia as a whole (73.6% vs. 33.1%). Importantly, this region has lower socio-economic resources than Georgia, with 19% of Clayton residents reporting living below the poverty level compared to 14% of Georgians [26]. Therefore, our findings suggest that local policies for ongoing investment in early detection screening modalities for CRC should be prioritized for individuals living in the Clayton region. Worth further consideration, other factors that may also contribute to the observed differences of incidence across these regions include lifestyle-related factors (e.g., diet and obesity) [28], environmental exposures (e.g., agricultural runoff and industrial pollution) [29], and/or occupational exposures (e.g., mineral dust and trace elements) [30].

Age difference

We observed increased CRC incidence trends in the 15-44 age group in Clayton, Northeast, and Southeast regions. According to the USPSTF and ACS screening recommendations, CRC screening should start at age 45 years among all groups, primarily based on increasing incidence among those aged younger than 50 years. Several prior research has confirmed this increased trend in young adults. This is particularly concerning because Bailey et al. have estimated a 90% increase in the incidence rates of colon cancers among adults aged 20-34 by the year 2030 [6]. More importantly, survival after early-onset CRC diagnosis was significantly worse in the Southern US, particularly for men [11]. In line with several studies, Shah et al. reported that CRC incidence rates increased from 2001 to 2017 among the US adults aged 20-49 years [31]. Similarly, a prior study using the SEER data showed a steady rise in the incidence of CRC in those under the age of 50 years, with the most dramatic rise being observed in the 20-29 age group [6]. Another study using the SEER database from 1980 to 2016 also concluded an increase in the incidence of rectal cancer, particular in those aged 30-39 years [32]. Contributors to these concerning trends among young individuals remain unknowns but suggest an underlying common environmental risk factor for early-onset CRC, and several potential risk factors have been identified, including diet, exposure to antibiotics, obesity, tobacco use, and current smoking [4, 33]. Therefore, more research examining the etiology of early-onset CRC focusing on lifestyle, environmental factors, and the microbiome is needed [34].

Unlike the results in our study across the age group of 15-44 years, reduction in CRC incidence rates among individuals aged 60-74 and 75+ years in East Central, Northeast, Southeast, and West Central regions was discovered. In line with a US study, individuals aged 50 or older demonstrated reduced CRC incidence from 1998 to 2019, with about 3%-5% reduction annually in the late 2000s [3]. Similar to the findings in our 45-59 age group, Decker and colleagues found that CRC inci-

dence rates were stable for those aged 45-54 years [16]. The reduced CRC incidence trends in Georgia are likely related to the increased CRC screening utilization over the past 20 years [35]. According to a study conducted in Georgia, there was an increase in the utilization of colonoscopy or sigmoidoscopy for CRC screening between 1997 and 2018, with rates increasing from 48.1% to 71.2% [35]. Further, a study from Northeastern Georgia reported that adults aged 51 or older (51-60 years: 77.9%; 61-70 years: 85.7%; 71+ years: 85.7%) had greater CRC screening utilization compared to adults aged 41-50 years (32.8%) [36], which may also explain our declined trends in age group of 45+ years. Several factors associated with CRC screening uptake have been reported, including education, insurance coverage, and geographic location [10].

A major strength of this study was to examine time trends of CRC incidence within the small regions of Georgia. Findings from our study will guide all relevant stakeholders (e.g., Georgia Department of Public Health, community organizations, local communities) for prioritizing CRC prevention efforts in the most impacted regions and age groups in Georgia. Although race differences may have potential impact on CRC incidence, the declined trends of CRC incidence were observed during 2000-2020 in each race group (non-Hispanic White, non-Hispanic Black, and non-Hispanic Other) with 1.4%-2.0% of reduction in our study (Supplementary Table 1). Similarly, the reduced trends of CRC incidence were also found in several regions of Georgia except for Clayton region for non-Hispanic White and Black (Supplementary Table 1). However, the reduced trends were only observed in East Central and West Central regions for non-Hispanic Other (Supplementary Table 1). Despite these declining trends, our study suggests more research integrating area-level characteristics may further elucidate the differences of CRC incidence across these five regions.

Finally, there are a few limitations that should be noted. First, our study was based on cancer registry data and information on individual risk factors was not available. Therefore, we are unable to provide any direct evidence about the effect of specific exposures in the reported trends. Yet, by including the data from the SEER program, we were able to report more representative findings of the Georgia population in our targeted regions. Next, because the cancer registries collected data prospectively and independently of our study hypotheses, our results may not be influenced by a recall or information bias. However, we included multiple year data to examine the rate of change within our five regions of Georgia. This is particularly important because the rate of changes have dramatically increased in younger groups (15-44 years) and the rates/trends have varied geographically in these five regions. Lastly, due to unavailable information, we were unable to evaluate whether CRC screening programs at the community-level impact the rate of changes in Georgia. Evidence exists confirming that the initiation of organized CRC screening programs has demonstrated significantly increased screening utilization and decreased CRC incidence [37]. More research that considers and addresses multifaceted factors (e.g., socioeconomic demographics at individual and area-level, lifestyle, and environmental factors) is necessary to further elucidate exposures to these trends, particularly for Clayton region and the age group of 15-44 years in Georgia.

In conclusions, place-based differences in CRC incidence were found in these five regions of Georgia, with the decreased trends were observed during 2000 and 2020 in East Central, Northeast, Southeast, and West Central regions. However, Clayton, Northeast, and Southeast regions demonstrated significant increased trends in incidence for early-onset CRC. Findings from our study provide critical evidence to all relevant stakeholders for further developing culturally tailored CRC screening programs and awareness campaigns aimed at CRC early detection and prevention, particularly for adults <45 years and the most impacted regions in Georgia. Future studies including multifaceted factors to the reported trends are also warranted.

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Disclosure of conflict of interest

None.

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References

[1] McNamara C, Bayakly AR and KC W. Georgia Cancer Data Report, 2016. Georgia Department of Public Health, Georgia Comprehensive Cancer Registry; 2016.

[2] Kruse-Diehr AJ, Oliveri JM, Vanderpool RC, Katz ML, Reiter PL, Gray DM 2nd, Pennell ML, Young GS, Huang B, Fickle D, Cromo M, Rogers M, Gross D, Gibson A, Jellison J, Sarap MD, Bivens TA, McGuire TD, McAlearney AS, Huerta TR, Rahurkar S, Paskett ED and Dignan M. Development of a multilevel intervention to increase colorectal cancer screening in Appalachia. Implement Sci Commun 2021; 2: 51.

[3] Siegel RL, Wagle NS, Cercek A, Smith RA and Jemal A. Colorectal cancer statistics, 2023. CA Cancer J Clin 2023; 73: 233-254.

[4] Siegel RL, Fedewa SA, Anderson WF, Miller KD, Ma J, Rosenberg PS and Jemal A. Colorectal cancer incidence patterns in the United States, 1974-2013. J Natl Cancer Inst 2017; 109: djw322.

[5] O'Connell JB, Maggard MA, Liu JH, Etzioni DA, Livingston EH and Ko CY. Rates of colon and rectal cancers are increasing in young adults. Am Surg 2003; 69: 866-872.

[6] Bailey CE, Hu CY, You YN, Bednarski BK, Rodriguez-Bigas MA, Skibber JM, Cantor SB and Chang GJ. Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975-2010. JAMA Surg 2015; 150: 17-22.

[7] Shah RR, Millien VO, da Costa WL Jr, Oluyomi AO, Gould Suarez M and Thrift AP. Trends in the incidence of early-onset colorectal cancer in all 50 United States from 2001 through 2017. Cancer 2022; 128: 299-310.

[8] Coughlin SS. Social determinants of colorectal cancer risk, stage, and survival: a systematic review. Int J Colorectal Dis 2020; 35: 985-995.

[9] Frederiksen BL, Osler M, Harling H, Ladelund S and Jørgensen T. Do patient characteristics, disease, or treatment explain social inequality in survival from colorectal cancer? Soc Sci Med 2009; 69: 1107-1115.

[10] American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020.

[11] Rogers CR, Moore JX, Qeadan F, Gu LY, Huntington MS and Holowatyj AN. Examining factors underlying geographic disparities in early-onset colorectal cancer survival among men in the United States. Am J Cancer Res 2020; 10: 1592-1607.

[12] Carethers JM. Racial and ethnic disparities in colorectal cancer incidence and mortality. Adv Cancer Res 2021; 151: 197-229.

[13] Seagle HM, Keller SR, Tavtigian SV, Horton C and Holowatyj AN. Clinical multigene panel testing identifies racial and ethnic differences in germline pathogenic variants among patients with early-onset colorectal cancer. J Clin Oncol 2023; 41: 4279-4289.

[14] Muller C, Ihionkhan E, Stoffel EM and Kupfer SS. Disparities in early-onset colorectal cancer. Cells 2021; 10: 1018.

[15] Amweg L and Hayman L. Social determinants associated with the rising incidence of early-onset colorectal cancer in the U.S.: a PRISMA systematic review. Curr Dev Nutr 2020; 4: 302.

[16] Decker KM, Lambert P, Bravo J, Demers A and Singh H. Time trends in colorectal cancer incidence from 1992 to 2016 and colorectal cancer mortality from 1980 to 2018 by age group and geography in Canada. Am J Gastroenterol 2023; 118: 338-344.

[17] Rogers CR, Korous KM, Brooks E, De Vera MA, Tuuhetaufa F, Lucas T, Curtin K, Pesman C, Johnson W, Gallagher P and Moore JX. Early-onset colorectal cancer survival differences and potential geographic determinants among men and women in Utah. Am Soc Clin Oncol Educ Book 2022; 42: 1-16.

[18] US Preventive Services Task Force, Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, Donahue KE, Doubeni CA, Krist AH, Kubik M, Li L, Ogedegbe G, Owens DK, Pbert L, Silverstein M, Stevermer J, Tseng CW and Wong JB. Screening for colorectal cancer: US preventive services task force recommendation statement. JAMA 2021; 325: 1965-1977.

[19] Site Recode ICD-0-3/WHO 2008 Definition. Available from https://seer.cancer.gov/sitere-

code/icdo3_dwhoheme/index.html. Accessed on Jul 1, 2023.
[20] Tiwari RC, Clegg LX and Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res 2006; 15: 547-569.
[21] Kim HJ, Fay MP, Feuer EJ and Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000; 19: 335-351.
[22] Kim HJ, Fay MP, Yu B, Barrett MJ and Feuer EJ. Comparability of segmented line regression models. Biometrics 2004; 60: 1005-1014.
[23] Hines R, Markossian T, Johnson A, Dong F and Bayakly R. Geographic residency status and census tract socioeconomic status as determinants of colorectal cancer outcomes. Am J Public Health 2014; 104: e63-71.
[24] Wray AJD and Minaker LM. Is cancer prevention influenced by the built environment? Cancer 2019; 125: 3299-3311.
[25] Honeycutt S, Green R, Ballard D, Hermstad A, Brueder A, Haardorfer R, Yam J and Arriola KJ. Evaluation of a patient navigation program to promote colorectal cancer screening in rural Georgia, USA. Cancer 2013; 119: 3059-3066.
[26] QuickFacts Clayton County, Georgia. Available from: https://www.census.gov/quickfacts/claytoncountygeorgia. Accessed on Jul 1, 2023.
[27] Kind AJH and Buckingham WR. Making neighborhood-disadvantage metrics accessible - the neighborhood atlas. N Engl J Med 2018; 378: 2456-2458.
[28] Zhang Z, Zhang L, Penman A and May W. Using small-area estimation method to calculate county-level prevalence of obesity in Mississippi, 2007-2009. Prev Chronic Dis 2011; 8: A85.
[29] James W, Jia C and Kedia S. Uneven magnitude of disparities in cancer risks from air toxics. Int J Environ Res Public Health 2012; 9: 4365-4385.
[30] Johnson N, Shelton BJ, Hopenhayn C, Tucker TT, Unrine JM, Huang B, Christian W, Zhang Z, Shi X and Li L. Concentrations of arsenic, chromium, and nickel in toenail samples from Appalachian Kentucky residents. J Environ Pathol Toxicol Oncol 2011; 30: 213-223.
[31] Shah RR, Millien VO, da Costa WL Jr, Oluyomi AO, Gould Suarez M and Thrift AP. Trends in the incidence of early-onset colorectal cancer in all 50 United States from 2001 through 2017. Cancer 2022; 128: 299-310.
[32] Loomans-Kropp HA and Umar A. Increasing incidence of colorectal cancer in young adults. J Cancer Epidemiol 2019; 2019: 9841295.
[33] Rahib L, Wehner MR, Matrisian LM and Nead KT. Estimated projection of US cancer incidence and death to 2040. JAMA Netw Open 2021; 4: e214708.
[34] O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, Heitman SJ, Hilsden RJ and Brenner DR. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2022; 20: 1229-1240, e5.
[35] Ansa BE, Hoffman Z, Lewis N, Datta B, Islam KM and Johnson JA. Evaluation of colonoscopy and sigmoidoscopy utilization for colorectal cancer screening in Georgia, USA. Curr Oncol 2022; 29: 8955-8966.
[36] Springston J and Hou SI. Colon cancer knowledge, screening barriers, and information-seeking in Northeastern Georgia. J Ga Public Health Assoc 2016; 6: 158-162.
[37] Levin TR, Corley DA, Jensen CD, Schottinger JE, Quinn VP, Zauber AG, Lee JK, Zhao WK, Udaltsova N, Ghai NR, Lee AT, Quesenberry CP, Fireman BH and Doubeni CA. Effects of organized colorectal cancer screening on cancer incidence and mortality in a large community-based population. Gastroenterology 2018; 155: 1383-1391, e1385.

Supplementary Table 1. APCs and AAPCs in CRC incidence rates by race group and the five regions of Georgia, 2000-2020

Regions/Age group	Joinpoint Segment Start-End	APC (95% CI)	*P*-value[a]	AAPC (95% CI)	*P*-value[a]
Five Georgia Region					
NHW	2000-2010	**-2.41 (-3.46, -1.34)**	<0.001	**-1.42 (-2.12, -0.72)**	<0.001
NHW	2010-2020	-0.43 (-1.50, 0.66)	0.418		
NHB	2000-2020	**-2.03 (-2.46, -1.61)**	<0.001	**-2.03 (-2.46, -1.61)**	<0.001
NHO	2000-2020	**-1.89 (-3.71, -0.03)**	0.047	**-1.89 (-3.71, -0.03)**	0.047
NHW					
Clayton	2000-2020	1.09 (-0.32, 2.52)	0.123	1.09 (-0.32, 2.52)	0.123
East Central	2000-2020	**-2.10 (-2.93, -1.26)**	<0.001	**-2.10 (-2.93, -1.26)**	<0.001
Northeast	2000-2020	**-1.38 (-1.98, -0.78)**	<0.001	**-1.38 (-1.98, -0.78)**	<0.001
Southeast	2000-2020	**-1.38 (-2.12, -0.64)**	0.001	**-1.38 (-2.12, -0.64)**	0.001
West Central	2000-2020	**-1.34 (-2.02, -0.65)**	0.001	**-1.34 (-2.02, -0.65)**	0.001
NHB					
Clayton	2000-2017	-0.19 (-1.31, 0.95)	0.731	-1.80 (-3.65, 0.08)	0.060
Clayton	2017-2020	-10.47 (-20.65, 1.02)	0.070		
East Central	2000-2020	**-2.66 (-3.65, -1.65)**	<0.001	**-2.66 (-3.65, -1.65)**	<0.001
Northeast	2000-2020	**-2.36 (-3.32, -1.39)**	<0.001	**-2.36 (-3.32, -1.39)**	<0.001
Southeast	2000-2020	**-1.94 (-2.87, -1.01)**	<0.001	**-1.94 (-2.87, -1.01)**	<0.001
West Central	2000-2020	**-1.70 (-2.63, -0.75)**	0.001	**-1.70 (-2.63, -0.75)**	0.001
NHO					
Clayton	2000-2020	3.89 (-0.01, 7.94)	<0.001	3.89 (-0.01, 7.94)	<0.001
East Central	2000-2020	**-4.59 (-8.30, -0.73)**	<0.001	**-4.59 (-8.30, -0.73)**	<0.001
Northeast	2000-2020	-1.78 (-5.58, 2.17)	<0.001	-1.78 (-5.58, 2.17)	<0.001
Southeast	2000-2020	-3.05 (-6.65, 0.70)	0.001	-3.05 (-6.65, 0.70)	0.001
West Central	2000-2020	**-3.96 (-7.74, -0.03)**	<0.001	**-3.96 (-7.74, -0.03)**	<0.001

Abbreviations: CRC, colorectal cancer; APC, annual percent change; AAPC, average annual percent change; CI, confidence interval; NHW, non-Hispanic White; NHB, non-Hispanic Black; NHO, non-Hispanic Other (Native Hawaiian, Other Pacific Islander, Others, Hispanic, Unknown). Bold texts indicate the statistical significance. [a]Monte Carlo permutation tests were used.