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Prevalence and Predictors of Young-Onset Colorectal Neoplasia: Insights From a Nationally Representative Colonoscopy Registry

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BACKGROUND & AIMS: A disturbing increase in early-onset colorectal cancer (EOCRC) has prompted recent guidelines to recommend lowering the colorectal cancer (CRC) screening starting age from 50 to 45 years old for average-risk individuals. Little is known about the prevalence of colorectal neoplasia in individuals between 45 and 49 years old, or even younger, in the United States. We analyzed a large, nationally representative data set of almost 3 million outpatient colonoscopies to determine the prevalence of, and risk factors for, colorectal neoplasia among patients aged 18 to 54. **METHODS:** Findings from high-quality colonoscopies were analyzed from AMSURG ambulatory endoscopy centers (ASCs) that report their results in the GI Quality Improvement Consortium (GIQuIC) Registry. Logistic regression was used to identify risk factors for EOCRC. **RESULTS:** Increasing age, male sex, White race, family history of CRC, and examinations for bleeding or screening were all associated with higher odds of advanced premalignant lesions (APLs) and CRC. Among patients aged 45 to 49, 32% had any neoplasia, 7.5% had APLs, and 0.58% had CRC. Rates were almost as high in those aged 40 to 44. Family history of CRC portended neoplasia rates 5 years earlier. Rates of APLs were higher in American Indian/Alaskan Natives, but lower among Blacks, Asians, and Hispanics, compared with White counterparts. The prevalence of any neoplasia and APL gradually increased between 2014 and 2019, in all age groups. **CONCLUSIONS:** These data provide support for lowering the screening age to 45 for all average-risk individuals. Early messaging to patients and providers in the years leading up to age 45 is warranted, especially in those with a family history of CRC.

Keywords: Colorectal Neoplasms; Early Detection of Cancer.

Colorectal cancer (CRC) has traditionally been considered a disease of older age. The median age of colon cancer diagnosis is 68 in men and 72 in women, and for rectal cancer is 63 in both men and women.[1] Fortunately, over the last 2 decades, overall CRC incidence rates in individuals aged ≥50 have been steadily declining,[1] which has been attributed to changes in the prevalence of risk factors and improved screening uptake.[2] Curiously, compared with adults aged 55 to 59, individuals aged 50 to 54 have lower rates of colonoscopy use, and their CRC incidence rates have not declined,[2] suggesting a possible procrastination effect for the onset of the first screening colonoscopy.

While CRC incidence has decreased among adults aged ≥55, there has been a troubling increase in the incidence and mortality of CRC in those younger than age 50.[3] As of now, early-onset colorectal cancer (EOCRC) accounts for approximately 12% of all CRC cases,[4] with EOCRC incidence increasing by 2.2% annually from 2012 to 2016, and mortality increasing by 1.3% per year from 2008 to 2017.[4]

The clinical, pathologic, and molecular features of EOCRC appear to be distinct from CRC among patients aged ≥50 (late-onset CRC).[5] Many risk factors that contribute to late-onset CRCs, such as sedentary lifestyle, diabetes mellitus, dietary factors, obesity, and environmental exposures, have all been proposed as EOCRC risk factors; however, they do not explain most cases.[5] Further, only 25% of individuals with EOCRC have a family history of CRC,[5] and 16% carry a pathogenic cancer susceptibility gene.[6]

The disturbing increase in EOCRC rates served as the impetus for the American Cancer Society[7] and now the United States Preventive Services Task Force[8] and American College of Gastroenterology (ACG)[9] to recommend lowering the age to initiate CRC screening from 50 to 45 years old for average-risk patients. This builds on a previous recommendation from the ACG to screen African-Americans at age 45.[10,11] It raises the question about the prevalence of colorectal neoplasia that is found in individuals between 45 and 49 years old, or in the years leading up to the new screening age. The limited data from previous colonoscopy studies

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Abbreviations used in this paper: **ACG, American College of Gastroenterology; ACRN, advanced colorectal neoplasia; ADR, adenoma detection rate; AI/AN, American Indian/Alaska Native; APLs, advanced premalignant lesions; ASCs, ambulatory endoscopy centers; CRC, colorectal cancer; EOCRC, early-onset colorectal cancer; FDR, first-degree relative; FH, family history; GIQuIC, GI Quality Improvement Consortium; SSP, sessile serrated polyp.**

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WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Guidelines recommend lowering the onset of colorectal cancer screening to 45 years old, but little is known about the prevalence of colorectal neoplasia in United States populations between ages 45 and 49 or younger.

NEW FINDINGS

Data from a national colonoscopy registry demonstrated that one-third of individuals aged 45 to 49 had a colorectal neoplasm; 7.5% had an advanced premalignant lesion. A family history of colon cancer conferred a higher risk of colorectal neoplasia.

LIMITATIONS

Data are derived from ambulatory surgery centers and may not reflect procedures performed in other settings.

IMPACT

The findings support screening at age 45 and the importance of family history. Early messaging before age 45 is warranted.

suggest that the prevalence of any adenoma is approximately 10% to 11%[12] and advanced adenomas is 2% to 6%.[13–18]

There are several limitations to the previous studies, such as small sample size from a single institution, non-United States (US) patient populations, predominantly White individuals among US studies, different indications for the colonoscopy, lack of family history information, different age-groupings, and different definitions of colorectal pathology, which typically lack the inclusion of serrated polyps.

The present study was conducted to address these questions. We analyzed a large, nationally representative data set of almost 3 million outpatient colonoscopies to determine the prevalence of, and risk factors for, colorectal neoplasia among patients aged 18 to 49. This allows us to describe in detail the pathologic findings among individuals aged 45 to 49, as well as those younger than age 45, in whom 6% of EOCRC cases arise.[19]

Materials and Methods

Study Design

We conducted a retrospective analysis of colonoscopy data from AMSURG ambulatory endoscopy centers (ASCs) that report their results in the GI Quality Improvement Consortium (GIQuIC) Registry. Deidentified data were provided for statistical analysis through a data-use agreement with the Icahn School of Medicine at Mount Sinai.

Data Source

The GIQuIC registry was founded as a collaboration between the ACG and the American Society for Gastrointestinal Endoscopy. The registry sources endoscopy data from approximately one-third of practicing gastroenterologists in the United States. GIQuIC audits of >7000 colonoscopy records from >140 providers between 2017 and 2020 demonstrated an accuracy rate of >99% on all risk factors—both personal and family history of CRC or other findings that put the patient at high risk (personal communication; Luke Williams, MD, MPH, GIQuIC Manager of Data Quality and Analytics).

AMSURG is among the largest ASC management companies in the US, and AMSURG colonoscopy cases account for approximately 25% of all cases included in the GIQuIC national registry. The overall average adenoma detection rate (ADR) among endoscopists whose procedures are included in the present study is 36.9%. Each provider's ADR (using the standard definition of ADR in individuals aged ≥50 undergoing screening colonoscopies) was compared with their neoplasia prevalence detection (Supplementary Figure 1).

The data presented here were collected from procedures performed at 123 AMSURG ASCs across 29 states between January 1, 2014, and February 5, 2021.

Study Sample

Screening and diagnostic colonoscopies were included in the analysis if they were performed on patients aged 18 to 54 at AMSURG ASCs and recorded using GIQuIC reporting standards. If a patient had multiple colonoscopies, only the first colonoscopy recorded was included. Only high-quality colonoscopies were included, defined as procedures with adequate bowel preparation quality, photo documentation of cecal landmarks, and a withdrawal time >6 minutes.

To generate a data set that best represents the general population, we used several exclusion criteria (Supplementary Table 1). We excluded colonoscopies performed for surveillance or therapeutic reasons. Similarly, we excluded higher-risk patients with a personal history of colorectal polyps, CRC, inflammatory bowel disease, an inherited CRC syndrome (eg, familial adenomatous polyposis syndrome, hereditary non-polyposis CRC/Lynch syndrome, serrated polyposis syndrome), or a documented family history of inflammatory bowel disease in a first-degree relative (FDR).

Definitions

Young Onset. The young-onset age-group was defined as patients aged 18 to 49. Patients aged 50 to 54 were analyzed as a comparator group.

Family History. Family history (FH) of CRC refers to patients with an FDR with a history of CRC before age 60 or 2 FDRs with history of CRC at any age. FH of polyps refers to patients with a FDR with an advanced adenoma, sessile serrated polyp (SSP), or traditional serrated adenoma before age 60 or with 2 FDRs with a history of advanced adenoma, SSP, or traditional serrated adenoma at any age. A patient who had both a FH of CRC and a FH of polyps was categorized as only having a FH of CRC.

Indication. Procedures were grouped into 3 general indication categories: diagnostic-bleeding, diagnostic-other, and screening. Diagnostic-bleeding colonoscopies comprised those performed to evaluate frank blood in stool, melena, iron-deficiency anemia, and follow-up of stool-based screening tests (all of which detect occult blood). Diagnostic-other included all other diagnostic indications that met inclusion criteria (eg, evaluation of abdominal pain, diarrhea, constipation, and change in bowel habits). Screening colonoscopies were recorded as such by endoscopists in the GIQuIC registry.

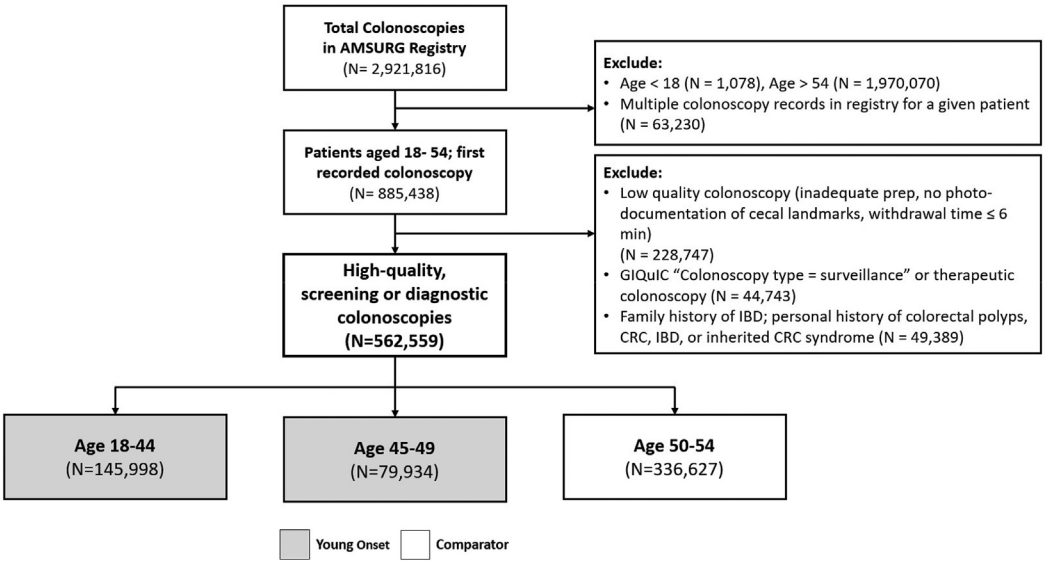

Figure 1. Consolidated Standards of Reporting Trials flow diagram. From a nationally representative database of 2,921,816 colonoscopies, the main analysis was performed on 225,932 procedures among patients aged 18 to 49 years ("young-onset" group). An additional 336,627 colonoscopies performed among patients aged 50 to 54 served as a comparator group. IBD, inflammatory bowel disease.

The GIQuIC Colonoscopy Data Collection form lists 3 "Colonoscopy Types" (screening, surveillance, diagnostic) and several "Colonoscopy Indications" (which add additional specificity) that can determine which of the 3 general indication categories (defined above) to which a case should be assigned. To best categorize a case into our framework of screening, diagnostic-bleeding, and diagnostic-other, all information documented by endoscopists was considered, including free-text entries. If endoscopists select a colonoscopy indication of "Other, specify:" they can submit free-text entries. All unique submissions to the free-text data field were identified and then tokenized to determine the most frequently occurring words among the free text. These results were used to select high-frequency words and terms that could be used to ascertain information regarding FH and colonoscopy indication from the free-text entries (Supplementary Table 1). The following order of priority was used to classify cases into 1 of the 3 general indication categories: (1) "exclude" for those that meet exclusion criteria, (2) "diagnostic-bleeding" for colonoscopy indication or free-text evidence of bleeding, (3) "screening" for colonoscopy indication, colonoscopy type, or free-text evidence of a screening case, (4) "diagnostic-other" for all other cases that met inclusion criteria.

Race, Ethnicity. Patient race was recorded according to the GIQuIC registry as White, African-American, Asian, American Indian/Native Alaskan, or other. "Patient declined to provide," "unknown," and "other" were considered "other/unknown." Ethnicity was recorded as Hispanic/Latino and not Hispanic/Latino; patients who declined were classified as "unknown/patient declined."

Neoplastic Findings. The neoplastic findings reported in GIQuIC were categorized in 4 groups: CRC, advanced premalignant lesions (APL), advanced colorectal neoplasia (ACRN), and any neoplasia. APL included advanced adenomas (adenoma ≥10 mm, or with high-grade dysplasia, or villous component), advanced SSPs (≥10 mm, or any size with dysplasia), or traditional serrated adenomas. ACRN consisted of all APL and adenocarcinomas (CRC). Any neoplasia was the most comprehensive and included all adenomas, SSPs, and CRC.

Statistical Methods

Statistical analyses were performed using Python 3.85 software (Python Software Foundation, https://www.python.org/psf/), with the pandas, NLTK, NumPy, and statsmodels packages. Logistic regression was used to determine predictors associated with ACRN. The following covariates were included in a preliminary model and subsequently removed if they were not significant at an $\alpha = 0.05$: age, sex, race, ethnicity, FH of CRC, FH of polyps, and indication.

Prevalence is reported as an unadjusted percentage for 6 age-groups (18–29, 30–34, 35–39, 40–44, 45–49, and 50–54 years) for 3 neoplasia groupings (any neoplasia, APL, and CRC). The z-test was used to compare prevalence between the 40 to 44 and 45 to 49 age-groups and between the 45 to 49 and 50 to 54 age-groups.

For graphical representation and ease of comparison, "Hispanic or Latino" ethnicity was included alongside race. However, in this population, those with Hispanic or Latino ethnicity did not identify with one particular race group, so race and ethnicity were analyzed as 2 separate variables.

To analyze time trends in neoplasia prevalence, the z-test with a Bonferroni correction ($\alpha = 0.05/10 = 0.005$) was used to compare the prevalence of any neoplasia and APL in 2014 and 2019 among the 5 young-onset age-groups. Data for 2020 were not included to avoid any theoretical influence of the severe acute respiratory syndrome coronavirus 2 pandemic on colonoscopic data.

Results

Baseline Patient and Procedure Characteristics

During the study period, AMSURG-associated endoscopists recorded 2,921,816 colonoscopies according to

Table 1. Patient Characteristics

Patient characteristics	Patient age-group, No. (%)				
	18–39 years (n = 94,822)	40–44 years (n = 51,176)	45–49 years (n = 79,934)	50–54 years (n = 336,627)	Total (N = 562,559)
Sex					
Female	56,747 (59.8)	30,306 (59.2)	47,127 (59.0)	181,797 (54.0)	315,977 (56.2)
Male	38,075 (40.2)	20,870 (40.8)	32,807 (41.0)	154,830 (46.0)	246,582 (43.8)
Race					
White	61,264 (64.6)	31,647 (61.8)	47,694 (59.7)	202,835 (60.3)	343,440 (61.0)
African American	7733 (8.2)	5028 (9.8)	10,042 (12.6)	30,804 (9.2)	53,607 (9.5)
Asian	2600 (2.7)	1768 (3.5)	2457 (3.1)	11,093 (3.3)	17,918 (3.2)
AI/AN	271 (0.3)	140 (0.3)	197 (0.2)	721 (0.2)	1329 (0.2)
Other/unknown	22,954 (24.2)	12,593 (24.6)	19,544 (24.5)	91,174 (27.1)	146,265 (26.0)
Ethnicity					
Hispanic/Latino	7000 (7.4)	4356 (8.5)	6141 (7.7)	25,497 (7.6)	42,994 (7.6)
Not Hispanic/Latino	49,072 (51.8)	26,187 (51.2)	42,191 (52.8)	175,407 (52.1)	292,857 (52.1)
Unknown/patient declined	38,750 (40.9)	20,633 (40.3)	31,602 (39.5)	135,723 (40.3)	226,708 (40.3)
Family history of					
Colorectal cancer	5268 (5.6)	5406 (10.6)	7490 (9.4)	10,946 (3.3)	29,110 (5.2)
Polyp(s)	1097 (1.2)	1415 (2.8)	2084 (2.6)	4425 (1.3)	9021 (1.6)
Indication					
Diagnostic–other	8661 (9.1)	13,197 (25.8)	24,541 (30.7)	16,250 (4.8)	358,456 (63.7)
Diagnostic–bleeding	39,650 (41.8)	17,855 (34.9)	22,295 (27.9)	16,877 (5.0)	96,677 (17.2)
Screening	46,511 (49.1)	20,124 (39.3)	33,098 (41.4)	303,500 (90.2)	107,426 (19.1)

GIQuIC documentation standards (Figure 1). Of these, 562,559 procedures met inclusion criteria for being the first recorded, high-quality, screening, or diagnostic colonoscopy. Of these, 145,998 were performed on patients aged 18 to 44, 79,934 on those aged 45 to 49, and 336,627 on those aged 50 to 54.

Demographic characteristics were similar across these age groups (Table 1). More female patients underwent colonoscopy across all age groups. Most patients were White, followed by African American, and then Asian. Latino patients represented 7.6% of the cohort. Compared with patients aged 50 to 54, there was a higher proportion of FH of CRC and polyps among patients aged <50.

Among patients aged 18 to 44, the most frequent indication was diagnostic-other (45.6%), followed by diagnostic-bleeding (39.4%), with only a minority being done for apparent screening. Colonoscopies performed to follow-up a positive fecal occult blood test or fecal immunochemical test were rare (total of 56 cases) and were included in the diagnostic-bleeding category. Among patients aged 45 to 49, the most frequent indication was screening (41.4%), followed by diagnostic-other (30.7%). Among those aged 50 to 54, 90% of procedures were performed for screening.

Predictors of Advanced Colorectal Neoplasia

Multivariable logistic regression identified 5 characteristics that were predictive of ACRN (APL + CRC) on first-recorded colonoscopy: increased age, male sex, White race, FH of CRC or polyps, and an indication of diagnostic-bleeding or screening (Table 2). After adjustment, each 1-year increase in age was associated with an 8% increase in the odds of finding ACRN. Male sex was associated with 67% higher odds compared with female sex. Compared with White patients, African American patients had 25% lower odds and Asian patients had 11% lower odds of finding ACRN. Those with a FH of CRC or of polyps had 21% and 33% higher odds of ACRN, respectively, compared with patients with no FH. Patients who underwent colonoscopy for diagnostic-bleeding or screening had 15% and 20% higher odds of finding ACRN, respectively, compared with those who underwent diagnostic-other procedures. Ethnicity failed to meet criteria for inclusion in the final model ($P = .725$).

Prevalence of Neoplasia by Age-Group, Sex, Family History of Colorectal Cancer, and Indication Groupings

In the young-onset age-group, prevalence of neoplastic findings increased with increasing age for all 3 categories of any neoplasia, APL, and CRC (Figure 2*a*). Among patients aged 45 to 49, approximately 32% had any neoplasia, 7.5% had APL, and 0.58% had CRC. Among those aged 40 to 44, 26.59% had any neoplasia, 5.76% had APL, and 0.53% had CRC. For comparison, the prevalence of any neoplasia, APL, and CRC were 37.72%, 9.48%, and 0.32%, respectively, for the 50 to 54 group. There was a statistically significant

Table 2. Predictors of Advanced Colorectal Neoplasia Among Patients Aged 18 to 49

Predictor	Odds ratio	95% CI	*P*
Age (per year)	1.08	1.07–1.08	**<.01**
Sex			
Female	Reference	—	—
Male	1.67	1.63–1.70	**<.01**
Race[a]			
White	Reference	—	—
African American	0.76	0.73–0.79	**<.01**
Asian	0.89	0.84–0.94	**<.01**
AI/AN	1.04	0.85–1.28	.67
Family history			
None	Reference	—	—
Colorectal cancer	1.21	1.16–1.26	**<.01**
Polyp(s)	1.33	1.24–1.43	**<.01**
Indication			
Diagnostic–other	Reference	—	—
Diagnostic–bleeding	1.15	1.12–1.18	**<.01**
Screening	1.20	1.16–1.24	**<.01**

NOTE. Bold *P* values are statistically significant.
CI, confidence interval.
[a]Ethnicity was excluded from the final model for failing to meet inclusion criteria for multivariable regression (Hispanic/Latino vs not Hispanic Latino: $P = .725$).

difference in any neoplasia and APL prevalence between the 40 to 44 and 45 to 49 age-groups as well as between the 45 to 49 and 50 to 54 age groups ($P < 10^{-10}$ for all). For CRC, there was a statistically significant difference comparing those 45 to 49 years old with those 50 to 54 years old ($P < 10^{-10}$) but no statistically significant difference between those 40 to 44 and those 45 to 49 years old.

Male patients manifested a higher prevalence of pathology across all age-groups and neoplasia groupings (Figure 2*b*; Supplementary Table 2). Except for CRC, in all other pathologic categories, the prevalence of neoplasia was seen in men approximately 10 years younger than those in women.

Among 45 to 49 year olds, rates of CRC were comparable between White, African American, and Hispanic/Latino patients (0.56%–0.61%), whereas prevalence was higher in Asian patients; there were no cases of CRC among American Indian/Alaska Native (AI/AN) (Figure 2*c*; Supplementary Table 3). Similar trends were seen among 40 to 44 year olds for Whites, African Americans, and Asians, although rates of CRC were highest among Hispanic patients. In the same 2 age-groups, lower rates of APL were observed among African American, Hispanic/Latino, and Asian patients (40–44: 4.08%–5.76%; 45–49: 5.85%–7.67%) compared with Whites, whereas AIs/ANs had the highest rates of APL.

Individuals with a FH of CRC had a higher prevalence of any neoplasia and APL for all age groups (Figure 3*a*). In fact, the rates of any neoplasia and APL in those with a FH of CRC were similar to those of individuals 5 years older without a FH of CRC. Patients with a positive FH had a lower prevalence of CRC compared with those with no FH across most young-onset age-groupings.

Compared with patients undergoing diagnostic-other procedures, those who underwent diagnostic-bleeding procedures had a higher prevalence of all 3 neoplasia groupings

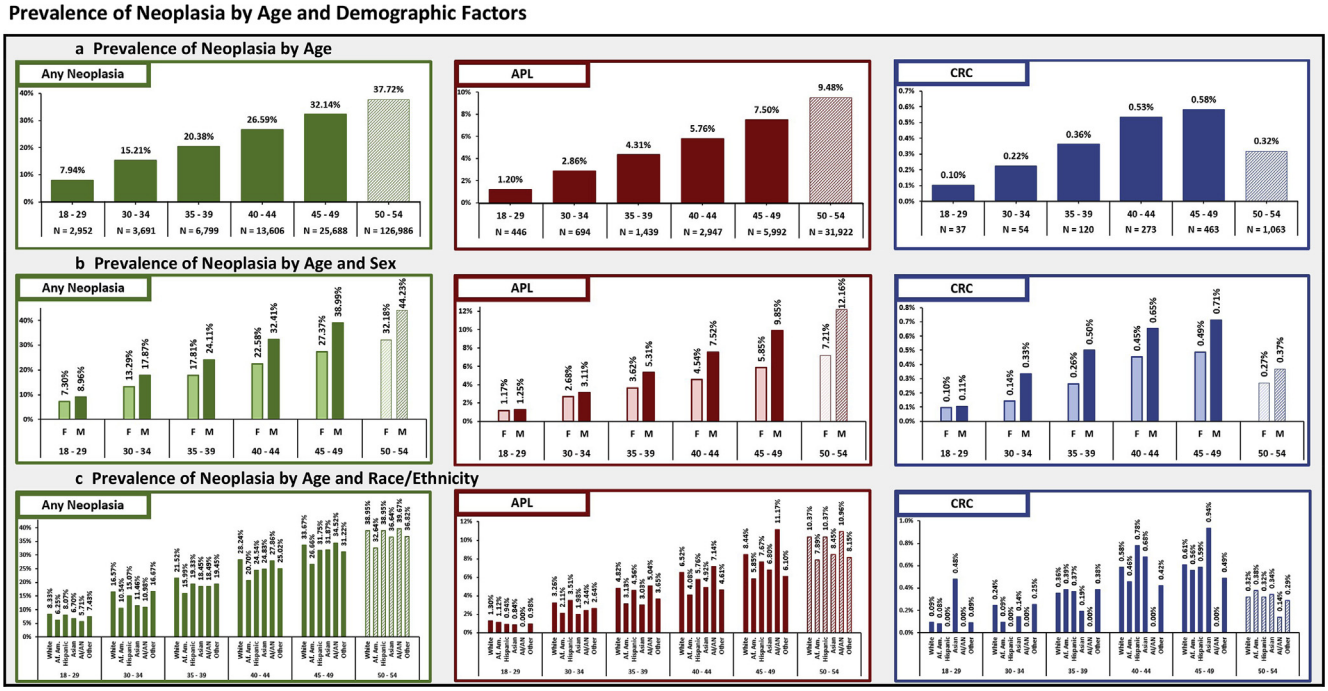

Figure 2. Prevalence any neoplasia, APL, and CRC by (*a*) age alone, (*b*) age and sex, and (*c*) age and race/ethnicity. Hispanic or Latino ethnicity did not identify with 1 particular race group, so race and ethnicity were analyzed as 2 separate variables. Hispanic or Latino ethnicity was included alongside race. Af. Am., Black/African American; F, female; M, male.

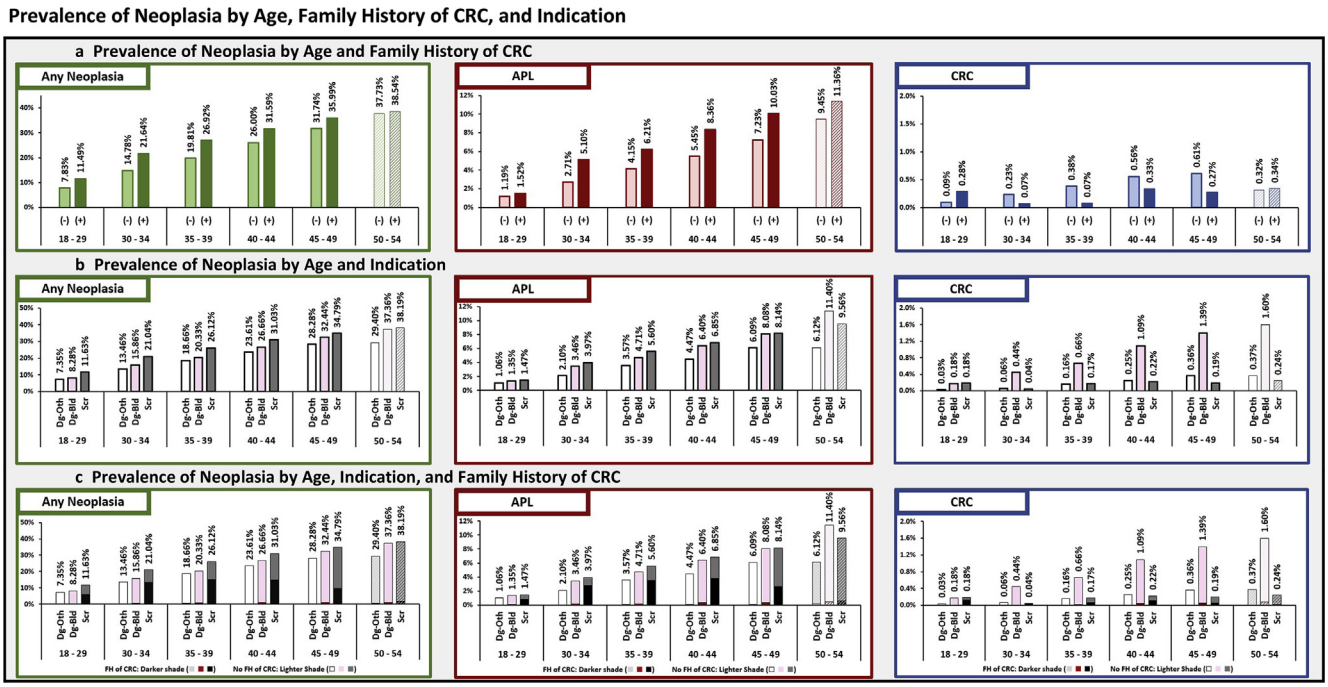

Figure 3. Prevalence of the 3 neoplasia groupings by: (*a*) age and FH of CRC, (*b*) age and colonoscopy indication, and (*c*) both FH of CRC and colonoscopy indication. Panel *c* is identical to *b* with positive FH of CRC indicated by *dark shaded bars*. Dg-Bld, diagnostic-bleeding; Dg-Oth, diagnostic-other; Scr, screening.

(Figure 3*b*; Supplementary Table 4). This effect was most pronounced in the CRC group. For those undergoing screening colonoscopies, there was also a higher prevalence of any neoplasia and APLs compared with the diagnostic-other group, with prevalence rates at least as high as for diagnostic-bleeding procedures. This was not observed for the prevalence of CRC, where the prevalence of CRC was similar between screening and diagnostic-other procedures. This was even true among those aged 50 to 54, suggesting that CRC was being detected more because of a diagnostic-bleeding rather than a screening examination.

Simultaneous examination of FH and indication reveals 87% of patients aged 18 to 49 with a positive FH for CRC, which was not the case in the 50 to 54 group (Supplementary Figure 2). Compared with diagnostic-bleeding and diagnostic-other procedures, a higher proportion of screening procedures with findings of neoplasia were performed on patients with a positive FH (Figure 3*c*).

Prevalence of Neoplasia by Year of Procedure

The prevalence of any neoplasia and APL gradually increased between 2014 and 2019 for patients aged 35 to 39, 40 to 44, 45 to 49, and 50 to 54 (Figure 4). Given the low number of CRC cases among patients aged <50, a consistent time trend was not observed. Between 2014 and 2019, among patients aged 45 to 49, there was an 12.2% increase in any neoplasia and a 52.6% increase in APL, which were both statistically significant ($P < .001$). During the same time period, among patients aged 40 to 44, there was an 8.3% increase in any neoplasia and a 33.6% increase in APL, although those increases did not reach statistical significance.

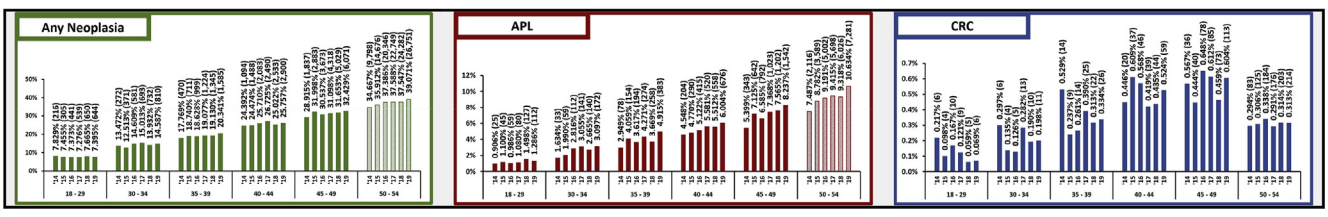

Figure 4. The prevalence of the 3 neoplasia groupings is provided by age-group clusters, with each cluster having a breakdown by year of procedure. Data labels indicate the prevalence and the number of cases with a positive finding for a given neoplasia grouping for each year. The z-test for proportions with the Bonferroni correction ($\alpha = 0.05/10 = 0.005$) was used to compare neoplasia prevalence between 2014 and 2019 for young-onset age-groups. A statistically significant difference was detected for any neoplasia age 35 to 39 ($P = .004$) and age 45 to 49 ($P < .001$) and for APL age 35 to 39 ($P < .001$) and age 45 to 49 ($P < .001$).

Table 3. Prevalence of Colorectal Neoplasia Among Individuals Age 40 to 49: Studies from the United States With Young Age-Groupings

Study (Time period)	Age-group, *y*	No.	Adenomas, n (%)	Advanced adenoma, n (%)	CRC, n (%)	Colonoscopy indication	Comments
Present study (2014–2021)	40–44 45–49 [40–49]	51,176 79,934 131,110	8351 (16.3) 15,830 (19.8) 24,181 (18.4)	2420 (4.7) 5131 (6.4) 7551 (5.8)	273 (0.5) 463 (0.6) 736 (0.6)	Screening, diagnostic. Included FH CRC & polyps	Female: 55% White: 60%; Black: 10%; Hispanic: 8%; Asian: 3%; AI/AN: 0.2%; other/unknown: 27%
Yen (2012–2019)	40–44 45–49 [40–49]	93 141 234	40 (43.0)[a] 81 (57.4)[a] 121 (51.7)[a]	2 (2.2)[b] 10 (7.1)[b] 12 (5.1)[b]	0 (0.0) 0 (0.0) 0 (0.0)	Screening, diagnostic, and surveillance.	Referred population of veterans Female: 18.9% White: 70.0%
Butterly (2004–2018)	40–44 45–49 [40–49]	1288 1869 3157	154 (12.0) 257 (13.8) 411 (13.0)	36 (2.8) 61 (3.3) 97 (3.1)	2 (0.2) 9 (0.5) 11 (0.3)	Screening. Excluded bleeding; anemia; FH CRC	SSPs included large hyperplastic polyps, proximal HPs >5 mm. Pts referred into registry. Female: 62% White: 91%
Yip (2014)	40–44 45–49 [40–49]	940 1500 2440	—	51 (5.4) 103 (6.9) 154 (6.3)	—	—	Only included polyps >9 mm. Female: 52%
Imperiale (2018–2019)	45–49	816	253 (31)	42 (5.1)	0 (0)	Screening, asymptomatic.	Female: 47% White: 84%; Black: 11%; Hispanic: 5.8%; Asian: 3.8%; AI-AN: 0.1%
Krigel (2007–2017)	[40–49]	2261	215 (9.5)	37 (1.6)		Diagnostic. Included FH CRC	Female: 60% White: 46%; Black: 8%; Hispanic: 16%
Gupta (1999–2009)	40–44 45–49 [40–49]	314 326 640	29 (9.2) 70 (21.5) 99 (15.5)	8 (2.5) 13 (4.0) 21(3.3)	—	FDR with CRC	Advanced adenomas defined as size ≥10 mm Female: 58% White: 78%; Black: 6%; Hispanic: 4%; Asian: 8%
Overholt (2007)	[40–49]	1688	281 (16.7)	—	8 (0.5)	Screening, diagnostic & surveillance	AMSURG ASCs; 1-month data. Female: 57%
Thoma (2004–2008)	[40–49]	247	25 (10.1)	5 (2.0)	0 (0)	Screening, diagnostic Excluded weight loss, anemia, bleeding	Female: 57% White: 48%; Black: 14%; Hispanic: 24%
Imperiale (1995–2000)	[40–49]	906	79 (8.7)	32 (3.5)	0 (0)	Screening; asymptomatic	Employer-based program Female: 39%
Guillem (1980–1990)	[40–49]	48	4 (8.3)	…	…	FDR with CRC; asymptomatic	Female: 63%

[a]Includes sessile serrated lesions
[b]Includes advanced serrated lesions, traditional serrated adenomas.

Prevalence of Any Neoplasia by Provider-Specific Adenoma Detection Rate

With increasing provider-specific ADRs, there was a concomitant statistically significant increase in prevalence of any neoplasia, which includes all premalignant and malignant lesions (Supplementary Figure 2). However, the colonoscopy count per provider did not correlate significantly with any neoplasia prevalence.

Discussion

Despite rising EOCRC rates and the consequent recommendations to lower the screening age to 45, there are limited data on the prevalence of premalignant colorectal lesions among individuals younger than age 50. This is mostly because colonoscopies in those younger than age 50 have mainly been done for diagnostic reasons, with so-called screening examinations being reserved for individuals who have a positive FH of CRC. A recommendation to begin screening at age 45 for African Americans was put forward by the ACG (2009)[10,11] and more recently for all individuals regardless of race/ethnicity by the American Cancer Society (2018),[20] the US Preventive Services Task Force (2021),[8] and the ACG (2021).[9] The present study provides real-world data on the prevalence of colonoscopically detected neoplastic findings among individuals of all races and ethnicities younger than age 50 using data from 2014 to 2021.

In this large, nationally representative study of patients younger than age 50, we found that the prevalence of any neoplasia and APL among those aged 45 to 49 was almost as high as those of 50 to 54 year olds, and the rates of CRC were even higher. Moreover, among 40 to 44 year olds, rates of APL were almost as high as those aged 45 to 49, and again, CRC rates were comparably high. Together, these findings support the recent recommendations to lower the screening age to 45 and suggest that early messaging of young individuals should begin in the years leading up to the younger screening age.[21] It is also worth noting that even among 30 to 39 year olds, 15% to 20% already had any neoplasia, 2% to 4% had APL, and 0.2% to 0.4% had CRC.

Previous colonoscopy studies reporting the prevalence of precancerous polyps in individuals younger than age 50 vary in their age-groupings, sample size, definition of advanced neoplasia, and colonoscopy indications.[12] Among US populations, most studies grouped together 40 to 49 year olds, demonstrating prevalence rates of 8.3% to 20.5% for adenomas, 2.0% to 6.3% for advanced adenomas, and up to 0.6% for adenocarcinomas (Table 3).[13–18,22–25] Our data fit within the higher range of these prevalence rates, possibly because we included colonoscopies performed for screening, FH of CRC/polyps, diagnostic evaluation of warning signs and symptoms, and abnormal results on imaging/stool tests. When considering only 45 to 49 year olds, we found an advanced adenoma rate of 6.4%, which is similar to the 6.9% from the Clinical Outcomes Research Initiative data set that included diagnostic colonoscopies and individuals with a FH of CRC[18] but not as high as 7.1% among a referral population of predominantly White, male veterans scoped for screening, diagnostic, and surveillance indications.[25] These advanced adenoma rates are higher than the rate of 3.3% reported from the New Hampshire Colonoscopy Registry, which included a less diverse study population and excluded individuals with bleeding, anemia, or FH of CRC,[13] and the rate of 4.0% from a single institution that included only individuals with a FH of CRC.[14] In a meta-analysis of early-onset colorectal neoplasia among asymptomatic, average-risk individuals, Kolb et al[26] determined the pooled rate of advanced neoplasia was 4.1%. That meta-analysis included 4 studies from the US, with 10,700 of the 12,463 cases coming from the Clinical Outcomes Research Initiative data set.

Only 1 other study has reported prevalence rates of SSPs in young individuals by specific age-groups. Butterly et al[13] defined clinically significant serrated polyps as SSPs, traditional serrated adenomas, and hyperplastic polyps >1 cm anywhere in the colon or >5 mm in the proximal colon, finding prevalence rates of 5.1% among 40 to 44 year olds and 5.9% among 45 to 49 year olds. We found slightly lower rates in our cohort.

Despite a well-documented increase in EOCRC incidence over the last 2 decades, there are limited data available on time trends of precancerous lesion prevalence. In an analysis of advanced precancerous lesions (defined as those >9 mm) among adults younger than 50 years old, Yip et al[18] found that between 2005 and 2014, the prevalence of advanced lesions among 45 to 49 year olds increased from 4.8% to 6.9%, an increase of 0.23 percentage points per year.[17] Our data move forward from 2014 to 2019, revealing increases in APL prevalence from 5.40% to 8.24% in that same age-group, an increase of 0.57 percentage points per year. [17]

Male sex has long been known as a CRC risk factor. We found that the odds of ACRN were 67% higher for male patients compared with female patients. For all age and neoplasia groupings, men had a higher disease prevalence than women. Similar to Yip et al,[18] we also observed that men in their 40s have a higher prevalence of ACRN compared with women 10 years older.

In our analysis, White race was found to be an independent predictor of ACRN in adults younger than age 50. In the 45- to 49-year age-group, rates of APL and CRC among African American and Hispanic/Latino patients were lower but almost equal to those of Whites. Surprisingly, rates of CRC among Asians were considerably higher than other groups, despite similar rates of APL. Strikingly, AIs/ANs had the highest rates of APL, but no CRC was detected in our sample. Our findings support the importance of screening all individuals aged 45 with early messaging of individuals 40 to 44, regardless of race and ethnicity. Our findings differ from reported higher incidence rates of CRC for Blacks compared with Whites,[4] which we believe is due to our inclusion of precancerous lesions in addition to CRC, a lack of race/ethnicity data for a sizeable proportion of our patients, and possible selection bias based on colonoscopies being performed at ASCs.

Mixed findings on the association of race with colorectal neoplasia and CRC for individuals of all ages have been reported in the literature.[27,28] There are scant data in the

literature regarding colorectal neoplasia prevalence among racial and ethnic minorities other than Black Americans. A 2018 meta-analysis of 9 studies found no difference in advanced adenoma prevalence between in Black and White patients.[29] A study conducted among Veterans Health Administration patients, who do not face the same access barriers as the general population, also found no association between race/ethnicity and EOCRC.[30] Finally, a microsimulation study that analyzed the effect of increasing CRC risk among younger populations found a similar benefit from lowering the screening age to 45 for both White and Black patients.[31] Collectively, these studies, along with several others, suggest that differences in CRC incidence between Black and White Americans are driven primarily by differences in screening uptake or access as opposed to underlying differences in biology.

FH is a well-established risk factor for colorectal neoplasia, with guidelines recommending earlier screening for patients with an FDR who had CRC before age 60.[9] Although up to 25% of patients with EOCRC may have an FH of CRC,[5] only 4.6% of patients younger than 50 in the present study had a positive FH of CRC. The reasons for this lower proportion are likely due to the use of a specific definition of FH in GIQuIC—1 FDR before age 60 or 2 FDRs—whereas some guidelines, such as National Comprehensive Cancer Network, recommend earlier screening with an FDR at any age, beginning at age 40 or 10 years before CRC detection in the relative (whichever is earlier).[32] However, this finding may also reflect underreporting of FH by providers. Our results show that for all age groups, patients with a positive FH of CRC had a higher prevalence of any neoplasia and ACRN than those without a FH of CRC. And for each 5-year age-group between age 30 and 49, the rates of any neoplasia and APL in those with a FH of CRC were at least as high as those of individuals 5 years older without a FH of CRC. Moreover, patients aged 40 to 49 with a positive FH had a comparable ACRN prevalence to those aged 50 to 54 without a FH of CRC, reaffirming the need to screen patients with an FH earlier than the average-risk population. The New Hampshire colonoscopy study also found a higher rate of advanced neoplasia in patients with an FH of CRC, but included them only in their sensitivity analysis.[13] In smaller studies of asymptomatic individuals between age 40 and 49 who underwent colonoscopy because of a positive FH of CRC, adenoma prevalence was low, ranging from 8% to 12%.[14,22] While we found that both FH of CRC and a FH of polyps were associated with higher odds of ACRN, we calculated prevalence estimates by FH of CRC only, as family history of polyps is less likely to be reliably reported.

Theoretically, people younger than age 50 should have only undergone colonoscopy because of symptoms (diagnostic) or an FH of CRC and polyps (screening). However, studies indicate that younger people have increasingly undergone colonoscopy. The National Health Interview Survey reported that rates of colonoscopy among 40 to 49 year olds increased from 6.4% in 2000 to 13.6% in 2013.[2] Prior studies have used widely differing inclusion criteria for studying colorectal neoplasia among adults younger than 50, which include (1) only screening procedures,[15] (2) only diagnostic procedures,[16] (3) excluding patients with bleeding, anemia, and FH of CRC,[13] or (4) including all diagnostic and screening procedures.[18] Given the dearth of information on this topic, we included all diagnostic and screening procedures for analysis, but excluded surveillance and therapeutic colonoscopies because those would not be an initial examination. In the 45- to 49-year-old age-group, our study found higher rates of APL for both diagnostic and screening examinations compared with previous reports.[18] Arguably, any neoplasia found in a patient younger than 50, regardless of the colonoscopy indication, adds valuable information for understanding prevalence of neoplasia.

Strengths/Limitations

The strengths of our study include the largest sample size to date, a geographically and racially diverse population, with detailed categorization of neoplastic pathology findings based on high-quality colonoscopies. This allowed us to group individuals into smaller age ranges for more granular detail on neoplasia prevalence. By including all colonoscopic indications (other than surveillance or therapeutic interventions), we were able to discern differences in neoplasia prevalence based on colonoscopy indication. We affirm and further elucidate the importance of an FH of CRC as presaging important colorectal pathology.

We acknowledge several limitations of the present investigation. First, although our population is geographically and racially diverse, the data come from ASCs, which might introduce bias related to insurance coverage or patient preference to attend certain endoscopic facilities.

Second, data on race and ethnicity were missing from many records.

Third, although GIQuIC has structured fields for colonoscopy indication, many providers use free-text entries to further clarify the indications. We took care to extensively catalog all free-text entries and to categorize them in the proper colonoscopy indication, yet there are likely inaccuracies in this process.

Fourth, by including all indications for colonoscopy besides those performed for screening, our findings can be viewed as "worst-case" scenarios. However, we would argue that no matter what the reason is for a younger person to have colonoscopy, any finding of colorectal neoplasia provides important insights into the prevalence of precancerous lesions.

Finally, we are unable to report data related to location within the colon for the pathologic findings since this is not available in GIQuIC.

Conclusions

The present analysis of neoplastic colorectal pathology among individuals younger than age 50 suggests that lowering the screening age to 45 for men and women of all races and ethnicities will likely detect important pathology rather frequently. Further, our data also suggest that for individuals with an FDR with CRC, the currently

recommended start age of 40 (or 10 years before the earliest age at diagnosis) is appropriate. Finally, these findings underscore the importance of early messaging to patients and providers in the years leading up to age 45. Awareness of pathology prevalence in individuals younger than age 45 can help guide clinicians in the clinical management of CRC risk. The data herein can be used to inform prediction and cost-effectiveness models for future public health interventions.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://dx.doi.org/10.1053/j.gastro.2021.12.285.

References

1. American Cancer Society. Colorectal Cancer Facts & Figures 2017-2019. Atlanta: American Cancer Society, 2017.
2. Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal cancer incidence patterns in the United States, 1974-2013. J Natl Cancer Inst 2017;109:djw322.
3. Siegel RL, Jakubowski CD, Fedewa SA, et al. Colorectal cancer in the young: epidemiology, prevention, management. Am Soc Clin Oncol Educ Book 2020;40:1–14.
4. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. CA Cancer J Clin 2020; 70:145–164.
5. Patel SG, Ahnen DJ. Colorectal cancer in the young. Curr Gastroenterol Rep 2018;20:15.
6. Pearlman R, Frankel WL, Swanson B, et al. Prevalence and spectrum of germline cancer susceptibility gene mutations among patients with early-onset colorectal cancer. JAMA Oncol 2017;3:464–471.
7. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA Cancer J Clin 2018;68:250–281.
8. US Preventive Services Task Force, Davidson KW, Barry MJ, et al. Screening for colorectal cancer: US Preventive Services Task Force Recommendation Statement. JAMA 2021;325:1965–1977.
9. Shaukat A, Kahi CJ, Burke CA, et al. ACG clinical guidelines: colorectal cancer screening 2021. Am J Gastroenterol 2021;116:458–479.
10. Agrawal S, Bhupinderjit A, Bhutani MS, et al. Colorectal cancer in African Americans. Am J Gastroenterol 2005; 100:515–523; discussion: 514.
11. Rex DK, Johnson DA, Anderson JC, et al. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected] [published correction appears in Am J Gastroenterol 2009;104):1613]. Am J Gastroenterol 2009;104:739–750.
12. Enwerem N, Cho MY, Demb J, et al. Systematic review of prevalence, risk factors, and risk for metachronous advanced neoplasia in patients with young-onset colorectal adenoma. Clin Gastroenterol Hepatol 2021; 19:680–689 e12.
13. Butterly LF, Siegel RL, Fedewa S, et al. Colonoscopy outcomes in average-risk screening equivalent young adults: data from the New Hampshire Colonoscopy Registry. Am J Gastroenterol 2021; 116:171–179.
14. Gupta AK, Samadder J, Elliott E, et al. Prevalence of any size adenomas and advanced adenomas in 40-to 49-year-old individuals undergoing screening colonoscopy because of a family history of colorectal carcinoma in a first-degree relative. Gastrointest Endosc 2011; 74:110–118.
15. Imperiale TF, Wagner DR, Lin CY, et al. Results of screening colonoscopy among persons 40 to 49 years of age. N Engl J Med 2002;346:1781–1785.
16. Krigel A, Zhou M, Terry MB, et al. Symptoms and demographic factors associated with early-onset colorectal neoplasia among individuals undergoing diagnostic colonoscopy. Eur J Gastroenterol Hepatol 2020; 32:821–826.
17. Thoma MN, Castro F, Golawala M, et al. Detection of colorectal neoplasia by colonoscopy in average-risk patients age 40-49 versus 50-59 years. Dig Dis Sci 2011;56:1503–1508.
18. Yip B, Holub J, Lieberman D. Increasing prevalence of polyps $>$ 9 mm in young adults aged 40 to 59 years undergoing colonoscopy from 2002 to 2014. Gastroenterology 2021;160:1863–1865 e1.
19. Virostko J, Capasso A, Yankeelov TE, et al. Recent trends in the age at diagnosis of colorectal cancer in the US National Cancer Data Base, 2004-2015. Cancer 2019;125:3828–3835.
20. American Cancer Society. Cancer Facts & Figures 2017. Atlanta: American Cancer Society, 2017.
21. Jones WF, Ahnen DJ, Schroy PC 3rd. Improving on-time colorectal cancer screening through lead time messaging. Cancer 2020;126:247–252.
22. Guillem JG, Forde KA, Treat MR, et al. Colonoscopic screening for neoplasms in asymptomatic first-degree relatives of colon cancer patients. A controlled, prospective study. Dis Colon Rectum 1992;35:523–529.
23. Overholt BF, Brooks-Belli L, Grace MG, et al. Evaluating screening age for colonoscopy: a quality assurance assessment. J Clin Gastroenterol 2010; 44:e147–e153.
24. Imperiale TF, Kisiel JB, Itzkowitz SH, et al. Specificity of the multi-target stool DNA test for colorectal cancer screening in average-risk 45-49 year-olds: a cross-sectional study. Cancer Prev Res (Phila) 2021; 14:489–496.
25. Yen T, Scolaro J, Montminy E, et al. Spectrum of advanced colorectal neoplasia and anticipated yield of average-risk screening in veterans under age 50 [published online ahead of print November 18, 2021]. Clin Gastroenterol Hepatol https://doi.org/10.1016/j.cgh.2021.11.0172021.

26. Kolb JM, Hu J, DeSanto K, et al. Early-age onset colorectal neoplasia in average-risk individuals undergoing screening colonoscopy: a systematic review and meta-analysis. Gastroenterology 2021;161:1145–1155.e12.
27. Rutter CM, Knudsen AB, Lin JS, et al. Black and white differences in colorectal cancer screening and screening outcomes: a narrative review. Cancer Epidemiol Biomarkers Prev 2021;30:3–12.
28. Montminy EM, Zhou M, Maniscalco L, et al. Trends in the incidence of early-onset colorectal adenocarcinoma among black and white US residents aged 40 to 49 years, 2000-2017. JAMA Netw Open 2021;4:e2130433.
29. Imperiale TF, Abhyankar PR, Stump TE, et al. Prevalence of advanced, precancerous colorectal neoplasms in black and white populations: a systematic review and meta-analysis. Gastroenterology 2018;155:1776–1786e1.
30. **Low EE, Demb J**, Liu L, et al. Risk factors for early-onset colorectal cancer. Gastroenterology 2020;159:492–501 e7.
31. Meester RGS, Peterse EFP, Knudsen AB, et al. Optimizing colorectal cancer screening by race and sex: microsimulation analysis II to inform the American Cancer Society colorectal cancer screening guideline. Cancer 2018;124:2974–2985.
32. National Comprehensive Cancer Network. Colorectal Cancer Screening Version 2.2021. Published April 13, 2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf. Accessed June 5, 2021.

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Data Availability
Data will not be made available to other researchers. Detailed analytic methods are provided in the manuscript body and supplemental content.

Conflicts of interest
These authors disclose the following: Steven H. Itzkowitz and Lina Jandorf are on the Exact Science Corp advisory board and receive research support from Exact Sciences Corp and Freenome. No study sponsor or writing assistance was used for this study. The other authors disclose no conflicts.

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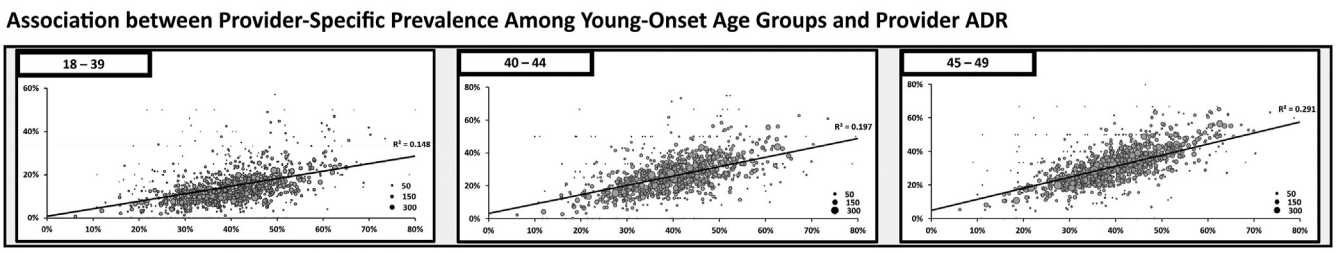
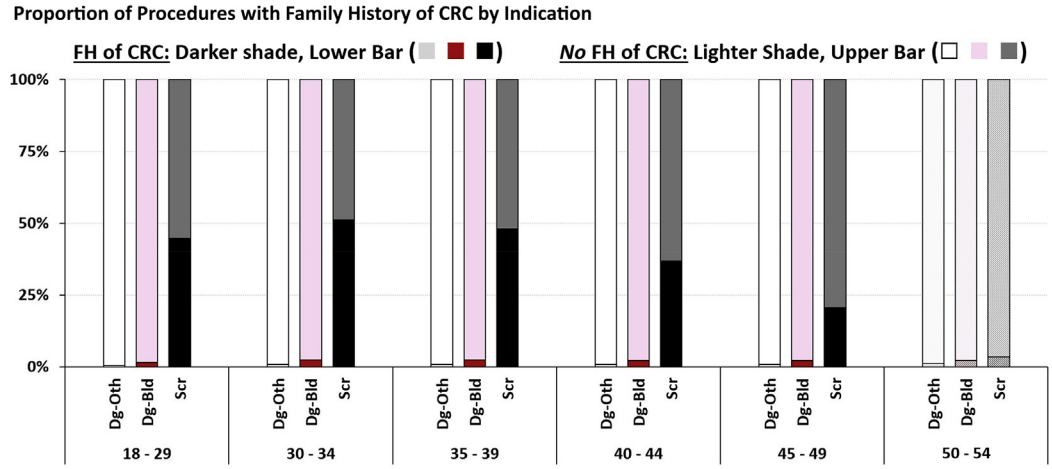


Supplementary Figure 1. Association between provider ADR and provider-specific neoplasia prevalence among young-onset age-groups. *Bubble plot* using linear regression analysis to determine the association between provider-specific any neoplasia prevalence (*y*-axis) and provider ADR (*x*-axis) by 3 age-groups: 18 to 39, 40 to 44, and 45 to 49. Provider-specific procedure counts are shown by *bubble size*. Ages 18 to 39 were grouped due to low procedure counts in this group. For each age-group, provider ADR was highly associated with prevalence (18–39: $P < .001$, regression coefficient [RC] $= 0.354$; 40–44: $P < .001$, RC $= 0.571$; 45–49: $P < 0.001$, RC $= 0.657$), whereas provider-specific procedure counts were not. For all 3 age-groups, provider ADR was not highly explanatory of variations in provider-specific any neoplasia prevalence.



Supplementary Figure 2. Proportion of procedures by indication and FH of CRC for each age-group. Each bar represents the total number of cases analyzed, regardless of neoplastic findings. *Dark shades* indicate positive FH of CRC; *light shades* indicate negative FH. Dg-Bld, diagnostic-bleeding; Dg-Oth, diagnostic-other; Scr, screening.

Supplementary Table 1. Indication Grouping by Free-Text, Colonoscopy Type, and Indication

Indication categories, GIQuIC field	Criteria
Exclude	
Colonoscopy type	Surveillance
Colonoscopy indication	Surveillance due to prior colonic neoplasia
	Surveillance due to inflammatory bowel disease
	Inflammatory bowel disease of the intestine if more precise diagnosis or determination of the extent/severity of activity of disease will influence immediate/future management
	Intraoperative identification of a lesion not apparent/found at surgery
	Treatment of bleeding from such lesions as vascular malformation, ulceration, neoplasia, & polypectomy site
	Foreign body removal
	Excision of colonic polyp
	Decompression of an acute nontoxic megacolon or sigmoid volvulus
	Balloon dilation of stenotic lesions
	Palliative treatment of stenosing or bleeding neoplasms
	Marking a neoplasm for localization
Colorectal neoplasm risk assessment	High risk – genetic family cancer syndrome
	High risk – serrated polyposis syndrome
	High risk – inflammatory bowel disease
Free Text contains:	'surveillance'
	'ulcerative'
	'crohn'
	'personal history'
	'history of adenomatous'
	'h/o uc'
	'h/o cd'
Diagnostic-bleeding	
Colonoscopy Indication	Evaluation of unexplained GI bleeding
	Hematochezia
	Melena after an upper GI source has been excluded
	Presence of fecal occult blood
	Unexplained iron deficiency anemia
	Positive combined FIT-DNA test (eg, Cologuard)
	Positive Septin-9 test
Free Text contains:	'blood'
	'bleed'
	'anemia'
	'cologuard'
	'fobt'
	'fit'
Screening	
Colonoscopy type	Colon cancer screening
Colonoscopy indication	Screening for colonic neoplasia
Diagnostic - other	
Colonoscopy type	Diagnostic

Supplementary Table 2. Prevalence of Neoplasia by Age Group and Sex

Age group, indication	N_{tot}[a]	Non-adv adenoma	Sessile serrated	Adv adenoma	Adv sessile	Adenocarcinoma
18 – 29						
Female	22,929	876 (3.82%)	507 (2.21%)	148 (0.65%)	120 (0.52%)	22 (0.10%)
Male	14,267	780 (5.47%)	306 (2.14%)	120 (0.84%)	58 (0.41%)	15 (0.11%)
Total	37,196	1656 (4.45%)	813 (2.19%)	268 (0.72%)	178 (0.48%)	37 (0.10%)
30 – 34						
Female	14,093	1031 (7.32%)	444 (3.15%)	269 (1.91%)	109 (0.77%)	20 (0.14%)
Male	10,176	1141 (11.21%)	327 (3.21%)	255 (2.51%)	61 (0.60%)	34 (0.33%)
Total	24,269	2172 (8.95%)	771 (3.18%)	524 (2.16%)	170 (0.70%)	54 (0.22%)
35 – 39						
Female	19,725	2092 (10.61%)	654 (3.32%)	536 (2.72%)	179 (0.91%)	52 (0.26%)
Male	13,632	2016 (14.79%)	478 (3.51%)	594 (4.36%)	130 (0.95%)	68 (0.50%)
Total	33,357	4108 (12.32%)	1132 (3.39%)	1130 (3.39%)	309 (0.93%)	120 (0.36%)
40 – 44						
Female	30,306	4124 (13.61%)	1205 (3.98%)	1066 (3.52%)	311 (1.03%)	137 (0.45%)
Male	20,870	4227 (20.25%)	830 (3.98%)	1354 (6.49%)	216 (1.03%)	136 (0.65%)
Total	51,176	8351 (16.32%)	2035 (3.98%)	2420 (4.73%)	527 (1.03%)	273 (0.53%)
45 – 49						
Female	47,127	7877 (16.71%)	2033 (4.31%)	2232 (4.74%)	527 (1.12%)	229 (0.49%)
Male	32,807	7953 (24.24%)	1370 (4.18%)	2899 (8.84%)	334 (1.02%)	234 (0.71%)
Total	79,934	15830 (19.80%)	3403 (4.26%)	5131 (6.42%)	861 (1.08%)	463 (0.58%)
50 – 54						
Female	181,797	35879 (19.74%)	9034 (4.97%)	10553 (5.80%)	2549 (1.40%)	492 (0.27%)
Male	154,830	41754 (26.97%)	7334 (4.74%)	17006 (10.98%)	1814 (1.17%)	571 (0.37%)
Total	336,627	77633 (23.06%)	16368 (4.86%)	27559 (8.19%)	4363 (1.30%)	1063 (0.32%)

[a]Total number of procedures analyzed in the age and sex group.

Supplementary Table 3. Prevalence of Neoplasia by Age Group and Race/Ethnicity

Age group, race/ethnicity	N_{tot}[a]	Non-adv adenoma	Sessile serrated	Adv adenoma	Adv sessile	Adenocarcinoma
18 – 29						
White	24,898	1,126 (4.52%)	602 (2.42%)	190 (0.76%)	134 (0.54%)	23 (0.09%)
African American	2,497	91 (3.64%)	35 (1.40%)	22 (0.88%)	6 (0.24%)	2 (0.08%)
Hispanic or Latino[b]	2,454	135 (5.50%)	40 (1.63%)	18 (0.73%)	5 (0.20%)	0 (0.00%)
Asian	836	33 (3.95%)	12 (1.44%)	5 (0.60%)	2 (0.24%)	4 (0.48%)
American Indian/Alaska Native	70	2 (2.86%)	2 (2.86%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Other/unknown	8,895	404 (4.54%)	162 (1.82%)	51 (0.57%)	36 (0.40%)	8 (0.09%)
30 – 34						
White	15,605	1,478 (9.47%)	561 (3.60%)	375 (2.40%)	133 (0.85%)	38 (0.24%)
African American	2,134	143 (6.70%)	35 (1.64%)	39 (1.83%)	6 (0.28%)	2 (0.09%)
Hispanic or Latino[b]	1,825	165 (9.04%)	46 (2.52%)	50 (2.74%)	14 (0.77%)	0 (0.00%)
Asian	707	52 (7.36%)	14 (1.98%)	12 (1.70%)	2 (0.28%)	1 (0.14%)
American Indian/Alaska Native	82	4 (4.88%)	3 (3.66%)	2 (2.44%)	0 (0.00%)	0 (0.00%)
Other/unknown	4,740	495 (10.44%)	158 (3.33%)	96 (2.03%)	29 (0.61%)	12 (0.25%)
35 – 39						
White	20,761	2,583 (12.44%)	811 (3.91%)	778 (3.75%)	222 (1.07%)	74 (0.36%)
African American	3,102	323 (10.41%)	64 (2.06%)	78 (2.51%)	19 (0.61%)	12 (0.39%)
Hispanic or Latino[b]	2,721	325 (11.94%)	67 (2.46%)	106 (3.90%)	18 (0.66%)	10 (0.37%)
Asian	1,057	136 (12.87%)	25 (2.37%)	25 (2.37%)	7 (0.66%)	2 (0.19%)
American Indian/Alaska Native	119	14 (11.76%)	2 (1.68%)	5 (4.20%)	1 (0.84%)	0 (0.00%)
Other/unknown	8,318	1,052 (12.65%)	230 (2.77%)	244 (2.93%)	60 (0.72%)	32 (0.38%)
40 – 44						
White	31,647	5,258 (16.61%)	1,429 (4.52%)	1,672 (5.28%)	392 (1.24%)	185 (0.58%)
African American	5,028	683 (13.58%)	130 (2.59%)	183 (3.64%)	22 (0.44%)	23 (0.46%)
Hispanic or Latino[b]	4,356	673 (15.45%)	111 (2.55%)	225 (5.17%)	26 (0.60%)	34 (0.78%)
Asian	1,768	280 (15.84%)	60 (3.39%)	77 (4.36%)	10 (0.57%)	12 (0.68%)
American Indian/Alaska Native	140	26 (18.57%)	3 (2.14%)	9 (6.43%)	1 (0.71%)	0 (0.00%)
Other/unknown	12,593	2,104 (16.71%)	413 (3.28%)	479 (3.80%)	102 (0.81%)	53 (0.42%)
45 – 49						
White	47,694	9,480 (19.88%)	2,266 (4.75%)	3,425 (7.18%)	599 (1.26%)	289 (0.61%)
African American	10,042	1,752 (17.45%)	282 (2.81%)	521 (5.19%)	66 (0.66%)	56 (0.56%)
Hispanic or Latino[b]	6,141	1264 (20.58%)	179 (2.91%)	417 (6.79%)	54 (0.88%)	36 (0.59%)
Asian	2,457	504 (20.51%)	89 (3.62%)	150 (6.11%)	17 (0.69%)	23 (0.94%)
American Indian/Alaska Native	197	41 (20.81%)	5 (2.54%)	21 (10.66%)	1 (0.51%)	0 (0.00%)
Other/unknown	19,544	4,053 (20.74%)	761 (3.89%)	1,014 (5.19%)	178 (0.91%)	95 (0.49%)
50 – 54						
White	202,835	46,287 (22.82%)	11,033 (5.44%)	18,034 (8.89%)	3,009 (1.48%)	645 (0.32%)
African American	30,804	6,607 (21.45%)	902 (2.93%)	2,268 (7.36%)	162 (0.53%)	116 (0.38%)
Hispanic or Latino[b]	25,497	5914 (23.19%)	856 (3.36%)	2209 (8.66%)	228 (0.89%)	93 (0.36%)
Asian	11,093	2,611 (23.54%)	478 (4.31%)	843 (7.60%)	94 (0.85%)	38 (0.34%)
American Indian/Alaska Native	721	181 (25.10%)	25 (3.47%)	72 (9.99%)	7 (0.97%)	1 (0.14%)
Other/unknown	91,174	21,947 (24.07%)	3,930 (4.31%)	6,342 (6.96%)	1,091 (1.20%)	263 (0.29%)

[a]Total number of procedures analyzed in the age and race/ethnicity group.
[b]For ease of comparison, "Hispanic or Latino" ethnicity was included alongside race. In this population, those with Hispanic or Latino ethnicity did not identify with one particular race group, so race and ethnicity were analyzed as two separate variables.

Supplementary Table 4. Prevalence of Neoplasia by Age Group and Indication

Age group, indication	N_{tot}[a]	Non-adv adenoma	Sessile serrated	Adv adenoma	Adv sessile	Adenocarcinoma
18 – 29						
Diagnostic-other	19,607	1,441 (7.35%)	207 (1.06%)	6 (0.03%)	836 (4.26%)	392 (2.00%)
Diagnostic-bleeding	15,955	1,321 (8.28%)	215 (1.35%)	28 (0.18%)	714 (4.48%)	364 (2.28%)
Screening	1,634	190 (11.63%)	24 (1.47%)	3 (0.18%)	106 (6.49%)	57 (3.49%)
30 – 34						
Diagnostic-other	11,597	1,561 (13.46%)	244 (2.10%)	7 (0.06%)	981 (8.46%)	329 (2.84%)
Diagnostic-bleeding	10,357	1,643 (15.86%)	358 (3.46%)	46 (0.44%)	919 (8.87%)	320 (3.09%)
Screening	2,315	487 (21.04%)	92 (3.97%)	1 (0.04%)	272 (11.75%)	122 (5.27%)
35 – 39						
Diagnostic-other	15,307	2,856 (18.66%)	547 (3.57%)	24 (0.16%)	1,805 (11.79%)	480 (3.14%)
Diagnostic-bleeding	13,338	2,712 (20.33%)	628 (4.71%)	88 (0.66%)	1,580 (11.85%)	416 (3.12%)
Screening	4,712	1,231 (26.12%)	264 (5.60%)	8 (0.17%)	723 (15.34%)	236 (5.01%)
40 – 44						
Diagnostic-other	20,124	4,751 (23.61%)	900 (4.47%)	50 (0.25%)	3,128 (15.54%)	673 (3.34%)
Diagnostic-bleeding	17,855	4,760 (26.66%)	1,143 (6.40%)	194 (1.09%)	2,779 (15.56%)	644 (3.61%)
Screening	13,197	4,095 (31.03%)	904 (6.85%)	29 (0.22%)	2,444 (18.52%)	718 (5.44%)
45 – 49						
Diagnostic-other	24,541	6,940 (28.28%)	1,495 (6.09%)	89 (0.36%)	4,451 (18.14%)	905 (3.69%)
Diagnostic-bleeding	22,295	7,232 (32.44%)	1,802 (8.08%)	311 (1.39%)	4,282 (19.21%)	837 (3.75%)
Screening	33,098	11,516 (34.79%)	2,695 (8.14%)	63 (0.19%)	7,097 (21.44%)	1,661 (5.02%)
50 – 54						
Diagnostic-other	16,250	4,777 (29.40%)	994 (6.12%)	60 (0.37%)	3,176 (19.54%)	547 (3.37%)
Diagnostic-bleeding	303,500	6,306 (37.36%)	1,924 (11.40%)	270 (1.60%)	3,529 (20.91%)	583 (3.45%)
Screening	303,500	115,903 (38.19%)	29,004 (9.56%)	733 (0.24%)	70,928 (23.37%)	15,238 (5.02%)

[a]Total number of procedures analyzed in the age and indication group.