

Emergency Room Becomes Critical Link in Detection of Early-Onset Colorectal Cancer

Emergency Department Visits for Anemia and Abdominal Pain Are Most Common Red Flags for Colorectal Cancer Diagnoses in Patients Under Age 35

KEY FINDINGS:

- Colorectal cancer diagnoses were preceded by a series of common red flag symptoms, which varied considerably based on the age of the patient.
- Younger colorectal cancer patients (under age 35) were most likely to first present with symptoms of anemia, muscle fatigue, and abdominal pain, and their first encounter was most commonly with the emergency department. Older patients were more likely to be diagnosed through routine screening or treatment for related disease through a gastroenterology specialist.
- The time-to-treat interval from first red flag symptom to colorectal cancer diagnosis and treatment was 230 days for patients under age 35, 203 days for those age 35–49, and 257 days for those age 50 and older. Following diagnosis, younger patients typically received surgery within 46 days. That interval was longer for patients aged 35–49 (59 days) and 50+ (56 days).
- Among the three age groups, patients ages 35–49 were most likely to present with symptoms of metastatic disease within 30 days of diagnosis.

EXECUTIVE SUMMARY:

Early-onset colorectal cancer (CRC) rates have been <u>increasing worldwide</u>, with roughly 18,000 people under the age of 50 <u>projected</u> to be diagnosed in the U.S. this year alone. Possible factors driving this trend include a combination of diet and lifestyle habits, lack of preventive screening among younger people, and a behavioral tendency among younger, healthier people to ignore symptoms until they become serious.

Several recent events have put a spotlight on these issues. Notably, the U.S. Preventive Services Task Force <u>lowered its</u> <u>recommended age</u> for routine CRC screening to 45 from 50. This brings the official U.S. guidance in line with recommendations from the American Cancer Society and should make it easier for younger Americans to receive preventive care. Mainstream awareness of colon cancer risk among younger generations also increased substantially following the death of acclaimed actor <u>Chadwick Boseman</u>, who succumbed to stage 4 colon cancer at age 43 in August 2020.

Despite this increased visibility and widespread accessibility of highly effective preventive screening, many people do not receive routine screening and many others ignore dangerous symptoms until the disease has already progressed. This has been a particularly challenging issue throughout the COVID-19 pandemic. According to an <u>analysis</u> published by Komodo Health and Fight Colorectal Cancer (Fight CRC) in May 2020, nationwide colonoscopy screenings and biopsies fell 90% during the height of the pandemic.



In order to dig deeper into patient behaviors and patterns of care associated with early-onset CRC, Komodo Health and Fight CRC evaluated the patient journeys of colorectal cancer patients in three distinct age groups: under age 35, 35–49, and 50+. The analysis identifies the most common red flag symptoms associated with a subsequent CRC diagnosis, the types of healthcare providers most likely to see first red flag symptoms, the total time-to-treatment from presentation of initial symptom to eventual CRC diagnosis and treatment, and the frequency of metastases between age groups. It also draws on anecdotal stories from Fight CRC's community of colorectal cancer patients to examine their first-hand experiences with the U.S. healthcare system.

METHODOLOGY:

This analysis used Komodo's Healthcare Map[™], the industry's largest and most complete database of de-identified, real-world patient data tracking U.S. patient journeys, to evaluate the "red flag" symptoms associated with CRC, broken out into three different age groups: younger than age 35; 35–49; and 50 and older. The analysis also examined, by age group, the medical specialties most often evaluating the first red flag symptoms seen in patients, the duration between symptoms and diagnosis to treatment, and the frequency of metastases.

In the population of patients who were ultimately diagnosed with CRC, this analysis examined ICD-10 codes in medical claims data for the top symptoms reported leading up to a CRC diagnosis. The research team then filtered for the symptoms most common and relevant to the disease, which included: anemia; constitutional symptoms (fatigue, generalized muscle weakness, abnormal weight loss); bleeding (hemorrhage of anus and rectum, melena, gastrointestinal hemorrhage); non-specific GI symptoms (unspecified abdominal pain, diarrhea, constipation, nausea with vomiting, generalized abdominal pain, right lower quadrant pain, epigastric pain, unspecified vomiting, unspecified lower abdominal pain); history of benign disease (polyp of colon, benign neoplasm of sigmoid colon, benign neoplasm of transverse colon, benign neoplasm of ascending colon); pre-existing intestinal disease (noninfective gastroenteritis and colitis, other specified diseases of intestine, diverticulosis of large intestine without perforation or abscess without bleeding). The analysis also pulled the rates of occurrence for the ICD-10 code for colonoscopy screening encounters for patients who were ultimately diagnosed with CRC across all three age groups.

For additional color on how the CRC patient journey progresses in younger populations, the team also analyzed the data for which specialties were first flagging symptoms for concern, and measured the number of days from first presentation of red flag symptoms to diagnosis and treatment.

The number of patients within each age group who had one or more codes for secondary malignancies indicative of metastatic disease within 30 days of the initial CRC diagnosis was also recorded. Patients with one or more claims with diagnostic codes for malignant neoplasm of the colon were identified in our data. Across the three age groups described above, the top 1,000 codes that occurred in a three-year timeframe prior to diagnosis were identified by frequency. These were manually reviewed by Komodo's clinical team to identify the most high-yield codes, which were included in our analysis.

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RESULTS:

Younger Patients More Likely to Present With Abdominal Pain as First "Red Flag"

The frequency of red flag symptoms differed greatly across the three age groups studied. Younger patients, under age 35 and between 35–49, were more likely than older patients to present first with vague abdominal symptoms, with "unspecified abdominal pain" being the most common presentation. The findings also point to higher rates of constipation, nausea, vomiting, and diarrhea in the younger age groups. By contrast, the most common red flag symptom in patients age 50 and over was associated with a screening encounter. Older patients were also more likely to present with diverticulosis of the large intestine, or with polyps, compared to the younger cohorts.

TOP SYMPTOMS BY AGE GROUP

Under 35	Age 35–49	50 and Over
1. Abdominal pain (31.98%*)	1. Abdominal pain (29.26%)	1. Encounter for screening for malignant
2. Anemia (25.32%)	2. Anemia (19.69%)	neoplasm of colon (28.86%)
3. Diarrhea (18.24%)	 Hemorrhage of anus and rectum (18.84%) Diarrhea (15.63%) Other fatigue (15.37%) Constipation (14.47%) 	2. Anemia (27.86%)
4. Constipation (17.98%)		3. Abdominal pain (22.13%)
5. Nausea with vomiting (16.37%)		4. Diverticulosis of large intestine without perforation or abscess without bleeding (20.83%)
6. Other fatigue (15.71%)		
7. Hemorrhage of anus and rectum (14.37%)		
	7. Melena (14.18%)	5. Other fatigue (16.87%)
8. Generalized abdominal pain (14.26%)	8. Generalized abdominal pain (13.69%) 9. Iron deficiency anemia (12.68%)	6. Polyp of colon (15.52%)
9. Iron deficiency anemia (13.86%)		7. Iron deficiency anemia, unspecified (15.06%)
10. Right lower quadrant pain (12.59%)	10. Nausea with vomiting (12.49%)	8. Constipation, unspecified (13.87%)
		9. Diarrhea, unspecified (12.72%)
		10. Other specified diseases of intestine (11.67%)

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*percentage of cohort reporting



Symptom Appearance by Age Group

Interestingly, pain in the lower right abdominal quadrant presented as a symptom for the youngest patient cohort much more frequently (12.59%) than in the 35–49 or 50+ cohorts (8.96% and 5.12%, respectively), suggesting these patients may be experiencing more irritation in the descending colon specifically. Physicians should, then, be paying attention to not only the presence of abdominal pain generally, but where that pain is localized.

Additionally, bleeding events occured at the highest rate among patients between 35–49, with 18.84% of patients exhibiting hemorrhaging of the anus or rectum, and at the lowest rate among patients 50 and over, with only 11.59% of patients exhibiting that symptom.



GASTROINTESTINAL HEMORRHAGE BY AGE GROUP

Of note, anemia rates in younger patients were comparable to those in older patients. However, for older patients, anemia generally triggers a colonoscopy, while in younger patients the symptom may be considered isolated or attributed to another cause.



ANEMIA BY AGE GROUP

Colonoscopy Screenings Vary Widely by Age

As expected, the rate of colonoscopy screening in patients under age 35 was low, at only 5%. In the 35–49 age range, approximately 11% of patients had one or more encounters for screening colonoscopy prior to their diagnosis, potentially resulting from patients with a family history of CRC taking proactive screening steps as they approach 50.

The screening rate for patients age 50 and over was 28%. This is consistent with historic USPSTF recommendations, which encouraged patients to begin screening at 50.

Tied to this trend, the detected presence of benign disease and/or polyps was significantly higher in the 35–49 and 50+ age groups when compared to the <35 cohort. This is tied to older patients proactively undergoing colonoscopies; younger patients, unscreened, are unlikely to be screening for disease or polyps, both benign and malignant.



SCREENING AND BENIGN DISEASE DETECTION BY AGE GROUP



Symptoms in Younger Patients Most Likely to be Flagged By Emergency Medicine Practitioners

For patients under 35, the first CRC symptoms were most likely to be evaluated by emergency medicine practitioners. This is in contrast to the other two age brackets, in which gastroenterology specialists were most likely to be the first providers to flag CRC-related symptoms.

Emergency medicine was also fairly common among the 35–49 age group, but dropped to #4 in the 50+ group. These findings suggest that younger patients, less conscious of CRC as a concern for their demographic, are less likely to flag their symptoms to gastroenterology specialists and are more likely to wait until symptoms escalate to an emergency level before seeking care.

TOP SPECIALTIES BY AGE GROUP

Under 35	Age 35–49	50 and Over
1. Emergency Medicine	1. Gastroenterology	1. Gastroenterology
2. Internal Medicine	2. Emergency Medicine	2. Internal Medicine
3. Radiology, Diagnostic	3. Internal Medicine	3. Family Practice
4. Gastroenterology	4. Radiology, Diagnostic	4. Emergency Medicine
5. Family Practice	5. Family Practice	5. Radiology, Diagnostic

Notably, family practice and internal medicine specialties were highly ranked across all three groups, underscoring the importance of primary care in evaluating and identifying red flag symptoms and, in turn, referring the patient to a specialist.

The trend toward higher numbers of younger patients presenting in the emergency department does raise some important considerations, however. It may suggest a pattern of patients ignoring acute symptoms until they reach a level of urgency that requires immediate care. That may be partially due to the fact that many of the symptoms of early-onset CRC can often seem benign. Unspecified abdominal pain, fatigue, diarrhea, and a range of other symptoms that could be caused by any number of conditions in otherwise healthy, young people are among some of the most common symptoms linked to an eventual CRC diagnosis.

Younger CRC Patients Report Missing Early Warning Signs

Anecdotally, early-onset CRC patients reported a pattern of missed signals and – in some cases – a feeling that their physicians were relatively unconcerned about their early symptoms, given their young age and seemingly good health.

"I started having a lot of acid reflux and constipation in 2015. I decided to go to a GI doctor and asked her to do a colonoscopy and an endoscopy. When I woke up from the procedure, she said she found a couple of polyps and that they were removed,"



said a 33-year-old male who was diagnosed with CRC in 2018. "She never mentioned that they were that dangerous. I left the clinic with the feeling: 'OK, the doctor found these polyps, but they were removed, I'm fine now.'

"Fast forward two years later, and I am feeling extremely exhausted all the time. I thought I was just lazy and felt ashamed for being so sedentary.... A few months later I decided to find a GI doctor on my own. I woke up from the procedure, and he told me he had found a growth that looked like cancer," he explained.

Other CRC patients reported feeling incredulous at their diagnosis, wondering how they could possibly have such a serious condition when they felt so strong.

"I was shocked to be diagnosed with stage 3B colon cancer. I was 44 years old at the time and two classes away from completing my master's degree in public administration," said a female CRC patient who was diagnosed in 2011. "I felt healthy, on top of the world, and a little invincible. When I say a little invincible, it was because I was also serving as a Navy Reservist, entering my 8th year of service with a promotion in sight."

Faster Time to Treatment in Younger CRC Patients

When looking at the time from the first red flag symptom to diagnosis, data was similar across all three patient groups. Patients under age 35 and 35–49 showed slightly shorter intervals between diagnosis and chemotherapy treatment and between diagnosis and surgical treatment.



Though somewhat surprising, this may be because younger patients often wait until their condition has become more severe before seeking care, a hypothesis also supported by the findings reported above that the younger patient cohort is most likely to present in the emergency department first.

Time from diagnosis to a surgical treatment option was shortest in the youngest group, possibly because these patients are more medically fit for surgery and do not require extensive anesthesia evaluation.



TIME FROM DIAGNOSIS TO TREATMENT (DAYS)



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As other <u>recent studies</u> show a longer window between diagnosis and treatment in younger patients, this is an area that warrants further analysis.

Of patients with claims related to therapy, chemotherapy was the predominant initial therapy in patients across all age groups. Despite this, patients under 35 were 15% more likely to undergo surgery as their initial treatment compared to those 35–49 and 3% more likely than those 50 and over.

Higher Rate of Metastatic Disease at Time of Diagnosis for Patients Age 35-49

Among all new CRC diagnoses, roughly 20% of patients have metastatic disease at presentation and another 25% who present with localized disease will later develop metastases. In order to examine possible links between patient age and signals for metastases, the analysis tracked the total number of patients within each age group who had one or more codes for secondary malignancies indicative of metastatic disease within 30 days of the initial CRC diagnosis.

It found that 7.65% of patients under 35 had one or more claims for a secondary neoplasm indicative of metastatic disease within 30 days of their initial CRC diagnosis. That rate jumped to 13.70% among the 35–49 age group. For those in the 50 or older age group, 9.63% of CRC patients developed metastases within 30 days of initial diagnosis. These findings suggest a higher risk for metastatic CRC in patients between the ages of 35 and 49, which supports the decision by the U.S. Preventive Services Task Force to lower its recommended age for routine CRC screening and raises the question of whether it should be lowered further.

DISCUSSION:

This analysis illuminates many of the challenges and opportunities associated with early-onset CRC. Chief among these is the need for clear communication to providers and the general public about the importance of recognizing the red flags and taking them seriously. Young people are often conditioned to shrug off important symptoms as "just a stomachache from something I ate" or "overtiredness from a long day at work," when, in fact, they can be signals of something more serious. Likewise, physicians are taught from the first days of medical school: *If you hear hooves, think horse, not zebra* – which is sage advice meant to encourage young doctors to listen to their patients and observe the logical facts without jumping to extreme conclusions. However, despite best intentions, time-pressed healthcare providers may ignore critical warning signs in an otherwise healthy patient.

The recent decision by the U.S. Preventive Services Task Force to lower the recommended age for CRC screening is an important step toward recognizing CRC risk in younger populations and adopting measures to improve early detection. Our data showed that the rate of metastasis at the time of diagnosis, indicating later-stage disease, is highest among patients age 35–49. Lowering the age for preventive screening would specifically target this group and help improve early detection. When CRC is found at an early stage, the five-year survival rate is roughly 90%. For that reason, efforts to increase preventive screening have helped the overall CRC death rate decline 51% over the last 40 years. That same focus on early detection and treatment needs to extend to younger populations who are, unfortunately, experiencing the opposite trend line in CRC death rates.

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About Fight CRC

Fight Colorectal Cancer (Fight CRC) is the leading patient-empowerment and advocacy organization in the United States, providing balanced and objective information on colon and rectal cancer research, treatment, and policy. We are relentless champions of hope, focused on funding promising, high-impact research endeavors, while equipping advocates to influence legislation and policy for the collective good.

About Komodo Health

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Komodo Health believes that smarter, more innovative use of data and analytics is essential for reducing disease burden. We apply artificial intelligence and other advanced data science techniques to our first-of-its-kind Healthcare Map[™], which tracks the unique patient journeys of over 325 million patients. We empower a multitude of healthcare stakeholders – life sciences companies, healthcare payers and providers, patient advocacy groups, and others – to create a more cost-effective, value-driven healthcare system. For more information, visit <u>www.komodohealth.com</u>.

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