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ORIGINAL ARTICLE

COVID-19 Pandemic Had Minimal Impact on Colonoscopy Completion After Colorectal Cancer Red Flag Sign or Symptoms in US Veterans

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Abstract

Background Delays in colonoscopy work-up for red flag signs or symptoms of colorectal cancer (CRC) during the COVID-19 pandemic are not well characterized.

Aims To examine colonoscopy uptake and time to colonoscopy after red flag diagnosis, before and during the COVID-19 pandemic.

Methods Cohort study of adults ages 50–75 with iron deficiency anemia (IDA), hematochezia, or abnormal stool blood test receiving Veterans Health Administration (VHA) care from April 2019 to December 2020. Index date was first red flag diagnosis date, categorized into "pre" (April–December 2019) and "intra" (April–December 2020) policy implementation prioritizing diagnostic procedures, allowing for a 3-month "washout" (January–March 2020) period. Outcomes were colonoscopy completion and time to colonoscopy pre- vs. intra-COVID-19, examined using multivariable Cox models with hazard ratios (aHRs) and 95% confidence intervals (CIs).

Results There were 52,539 adults with red flag signs or symptoms (pre-COVID: 25,154; washout: 7527; intra-COVID: 19,858). Proportion completing colonoscopy was similar pre- vs. intra-COVID-19 (27.0% vs. 26.5%; $p=0.24$). Median time to colonoscopy among colonoscopy completers was similar for pre- vs. intra-COVID-19 (46 vs. 42 days), but longer for individuals with IDA (60 vs. 49 days). There was no association between time period and colonoscopy completion (aHR: 0.99, 95% CI 0.95–1.03).

Conclusions Colonoscopy work-up of CRC red flag signs and symptoms was not delayed within VHA during the COVID-19 pandemic, possibly due to VHA policies supporting prioritization and completion. Further work is needed to understand how COVID-19 policies on screening and surveillance impact CRC-related outcomes, and how to optimize colonoscopy completion after a red flag diagnosis.

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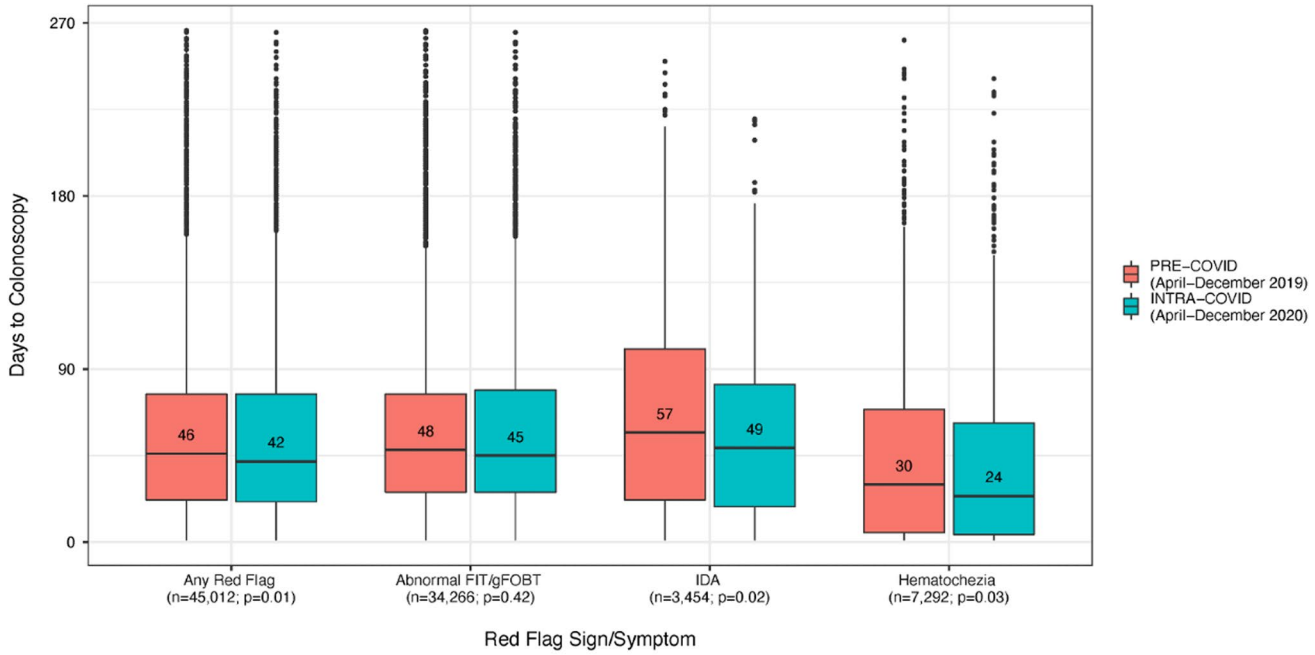
Graphical Abstract



Keywords COVID-19 · Colonoscopy · Colorectal cancer · Symptoms · Diagnosis

Introduction

In March 2020, the Coronavirus-2019 (COVID-19) pandemic dramatically impacted how patients interacted with healthcare providers and how they handled urgent and emergent medical conditions [1]. The Veterans Health Administration (VHA) postponed all non-urgent medical procedures to limit transmission and preserve personal protective equipment (PPE), personnel, and other hospital resources [2]. This included postponement and reprioritization of endoscopic procedures, including screening, surveillance, and diagnostic colonoscopies.

VHA facilities were directed to cease all non-urgent and elective procedures no later than March 18, 2020, with additional guidance for primary care providers to order colorectal (CRC) screening with fecal immunochemical tests (FIT), instead of average-risk screening colonoscopy [3]. On April 2, 2020, VHA provided guidance for prioritization of gastrointestinal (GI) endoscopic consults. To facilitate documentation of priorities as part of usual workflow for triage of procedure referrals, a "Consult Prioritization Toolbox" was implemented on April 20, 2020 at all VHA locations (Supplementary Table 1). This toolbox was embedded within the electronic health record (EHR) and allowed discrete selection of priority categories as part of routine review of consults for procedures.

Based on guidance from the National GI and Hepatology program, individuals were stratified into four different groups: Priority 1, indications for urgent procedures performed despite the COVID-19 pandemic; Priority 2, non-urgent procedures performed as soon as non-urgent procedures could be scheduled; Priority 3, routine cases more time sensitive than Priority 4; and Priority 4, routine cases that were not particularly time sensitive [3]. Examples of priority assignment included GI bleeding with symptoms and FIT-positive for ≥ 3 months to Priority 1, stable iron deficiency anemia (IDA) without symptoms and esophageal variceal banding to Priority 2, screening colonoscopy for persons at high risk for CRC and chronic diarrhea without alarm symptoms to Priority 3, and average-risk screening colonoscopy and endoscopic surveillance of pancreatic cysts to Priority 4 (Supplementary Table 1). On May 18, 2020, VHA provided additional guidance for how and when to resume endoscopic procedures deemed non-urgent or elective [3]. Throughout the pandemic, individual VHA sites had discretion to increase or decrease procedure access based on local issues, including COVID-19 incidence, availability of SARS-CoV-2 testing and PPE, and staffing. These postponements had

potential to significantly impact diagnostic work-up of persons presenting with CRC red flag signs or symptoms (signs/symptoms), including abnormal FIT or guaiac fecal occult blood test (gFOBT), IDA, or hematochezia.

Studies during the COVID-19 pandemic indicate that exposure to CRC screening tests has dramatically decreased [4, 5]; however, to our knowledge, no studies have examined how the pandemic impacted completion of diagnostic colonoscopies for CRC red flag signs/symptoms. Prior to the pandemic, studies found that longer wait times from abnormal FIT/gFOBT test or new symptom onset to diagnostic test could lead to adverse cancer outcomes [6–9]. Given the importance of timely work-up of alarm symptoms and to address current evidence gaps, we constructed and analyzed a cohort to identify whether there was a delay in colonoscopy for diagnostic work-up of new alarm signs/symptoms and, if appropriate, quantify differences between the periods before and after implementation of colonoscopy scheduling prioritization across the VHA nationally.

Methods

Study Design, Setting, and Data Sources

We conducted a retrospective cohort study among adults ages 50–75 years receiving VHA care to explore the association between red flag CRC signs/symptoms (pre-COVID-19 versus intra-COVID-19) and time to diagnostic colonoscopy. VHA is one of the largest integrated US healthcare providers, providing care to over 6 million individuals annually [10]. Since 1999, all VHA sites have utilized an integrated EHR for documentation of clinical encounters, which can be accessed for research. The VHA Corporate Data Warehouse (CDW) provides access to discrete EHR data, including demographic characteristics, administrative claims-based diagnosis and procedure codes, prescriptions, anthropometric measures (e.g., weight and height), and free-text data, including procedure notes and pathology reports.

Study Sample and Selection Criteria

Our study population included Veterans ages 50–75 years with ≥ 1 documented red flag CRC sign/symptom identified between April 2019 and December 2020. The red flag signs/symptoms included were abnormal FIT/gFOBT, hematochezia, and IDA. Abnormal FIT/gFOBT was ascertained using structured lab data including the test date and result, using previously validated methodology [8]. Hematochezia diagnosis was identified using International Classification of Diseases, 9th (ICD-9: 569.3, 578.1) and 10th Revision (ICD-10: K62.5, K92.1) codes. IDA was identified by lab diagnosis using World Health Organization criteria [11]: a hemoglobin test identifying anemia (hemoglobin < 13.0 mg/dL in men, < 12.0 mg/dL in women) with a follow-up iron test within 3 months indicating iron deficiency (ferritin levels ≤ 15 ng/mL or transferrin saturation levels ≤ 16%), using previously tested methodology [12]. Individuals with red flag CRC signs/symptoms prior to the study period, prior colonoscopy, or prior diagnosis of inflammatory bowel disease or CRC through a lookback period extending to October 1999 were excluded.

Exposures, Outcomes, and Covariates

The primary exposure was the date of first red flag CRC sign/symptom, dichotomized into pre-COVID-19 and intra-COVID-19 periods. The pre-COVID-19 time window spanned from April 1, 2019, to December 31, 2019. The intra-COVID-19 time window spanned from April 1, 2020, to December 31, 2020. To account for potential unmeasurable effects near the start of the pandemic in the US, dates from January 1, 2020, to March 31, 2020, served as a washout period [13]. In primary analyses, we compared outcomes between the pre- and intra-COVID-19 periods.

The primary study outcomes were completion of any colonoscopy during the observation periods, and time to colonoscopy completion among adults who completed colonoscopy, defined as the number of days between date of red flag sign/symptom documentation and date of colonoscopy. Colonoscopy date was ascertained via CDW using Current Procedural Terminology codes (Supplementary Table 2).

Covariates included age, sex, race/ethnicity, red flag type (abnormal FIT/gFOBT, IDA or hematochezia), smoking status, Charlson Comorbidity Index (0, 1, 2+), and number of red flag signs/symptoms present (1, 2, or 3). We defined race/ethnicity in 7 mutually exclusive categories: non-Hispanic White (White); non-Hispanic Black (Black); Hispanic; Asian or Native Hawaiian/Pacific Islander; American Indian or Alaska Native; other (multiracial, and those designating "other" race); and missing, using race/ethnicity data within CDW. Smoking status was determined from the VHA Health Factors data domain, classifying based on terminology including "current smoker," "former smoker," "never smoker," or missing [14]. Charlson Comorbidity Index, a predictive measure of one-year mortality risk, was defined using National Cancer Institute (NCI) methodology based on ICD-9/10 claims data [15].

Statistical Analysis

We used univariable analyses to compare individuals pre- vs. intra-COVID-19 using Wilcoxon rank-sum tests or chi-square tests for continuous and categorical variables, respectively. Baseline variables different at a significance level of 0.05 were considered potential covariates in multivariable

models. Survival analyses were used to measure pre- vs. intra-COVID-19 policy on time to colonoscopy, treating colonoscopy completion as the primary event. Individuals were followed from date of red flag sign/symptom to (1) date of colonoscopy (outcome) or censored at (2) date of death identified using vital status or (3) end of follow-up, defined as December 31, 2019, for the pre-COVID group and December 31, 2020, for the intra-COVID group. Due to an anticipated low event rate causing Kaplan–Meier models to fail to reach a survival probability of 50%, we compared time to colonoscopy between two COVID-19 windows for subjects with colonoscopy completed using Wilcoxon rank-sum test. We conducted a secondary analysis where individuals could contribute up to 6 months of follow-up time, with individuals followed to (1) date of colonoscopy (outcome) or censored at (2) date of death or (3) end of 6 months. For the 6-month follow-up window, the time period was allowed to extend past the inclusion date windows for the pre- (April–December 2019) and intra-COVID-19 (April–December 2020) periods. Kaplan–Meier curves were created and log-rank tests used to compare differences in cumulative colonoscopy completion over time between pre-COVID-19 and intra-COVID-19 periods. Multivariable Cox proportional hazards models were used to measure the effect of COVID-19 policy period on time to colonoscopy. Hazard ratios (aHRs) and corresponding 95% confidence intervals (CIs) were derived from Cox models to summarize associations. To examine whether there were differential effects based on the first diagnosed red flag sign/symptom, we tested for interaction between red flag sign/symptom type and COVID-19 period and, since significant interactions were found ($p < 0.05$), conducted stratified analyses for each red flag. We also evaluated the effect of calendar date on the exposure-outcome relationship.

For IDA patients, we conducted a sensitivity analysis where first date of either colonoscopy or esophagogastroduodenoscopy (EGD) served as the outcome, because in some cases, an upper endoscopy (i.e., diagnosing a peptic ulcer) would constitute appropriate completion of IDA clinical follow-up. To account for colonoscopies performed outside of VHA, we also conducted a sensitivity analysis that incorporated data from VA-paid community care colonoscopies during the pre-COVID-19 and intra-COVID-19 periods. For the study period, linked Medicare-VA claims data for colonoscopy were not available as of 8/3/2022. Analyses were performed using R version 4.0.2 [16]. The study was approved by San Diego Veterans Affairs Health System and UC San Diego Institutional Review Boards.

Results

There were 52,539 adults ages 50–75 with a diagnosis of abnormal FIT/gFOBT, IDA or hematochezia from April 1, 2019, to December 31, 2020 (pre-COVID-19: 25,154; washout: 7527; intra-COVID-19: 19,858) receiving VHA care (Table 1). Overall, the median follow-up was 85 days (Quartile 1–Quartile 3 [Q1-Q3]: 38–167 days; pre-COVID-19 median: 89 days; Q1–Q3: 39–175 days; intra-COVID-19 median: 83 days; Q1–Q3: 37–154 days). Abnormal FIT/gFOBT was the most common red flag (76%). Most participants were men (94%) and non-Hispanic white (67%). There were no clinically meaningful differences in red flag type, age, race/ethnicity, and Charlson Comorbidity Index score between pre-COVID-19 and intra-COVID-19 groups (Table 1).

Colonoscopy was completed by 6783 adults in the pre-COVID-19 period and 5256 adults in the intra-COVID-19 period, with similar proportions completing colonoscopy (pre vs. intra: 27.0% vs. 26.5%; $p = 0.24$). No significant difference in the cumulative proportion completing colonoscopy intra- vs pre-COVID-19 period was observed (Fig. 1). Among colonoscopy completers, median time to colonoscopy was similar for pre-COVID-19 vs. intra-COVID-19 (pre vs. intra, 46 days vs. 42 days; Fig. 2). There was similar time to colonoscopy pre-COVID-19 vs. intra-COVID-19 among adults with abnormal FIT/gFOBT (48 vs. 45 days) and hematochezia (30 vs. 24 days). There was shorter time to colonoscopy among adults with IDA (57 vs. 49 days).

There was no significant association between COVID-19 period and time to colonoscopy completion after adjusting for age, sex, race/ethnicity, and number of red flag signs/symptoms (aHR: 0.99, 95% CI 0.95–1.03) (Table 2). We found a significant interaction between red flag sign/symptom type and COVID-19 period (p's for interactions < 0.01). Notably, likelihood of colonoscopy completion intra-COVID-19 vs. pre-COVID-19 was increased among patients with IDA (aHR: 1.25, 95% CI 1.04–1.49) but was similar among patients with abnormal FIT/gFOBT (aHR: 0.99, 95% CI 0.95–1.03) or hematochezia (aHR: 0.99, 95% CI 0.91–1.08).

In a secondary analysis where all adults contribute up to 6 months follow-up time, the proportion completing colonoscopy was lower pre-COVID-19 vs. intra-COVID-19 (32% vs. 35%, respectively; $p < 0.01$). There was no

Table 1 Baseline characteristics of a national sample of adults with red flag signs or symptoms of CRC receiving VHA care, pre- (April–December 2019), washout (January–March 2020), and intra-COVID-19 (April–December 2020)

	Overall *N* = 52,539	Pre-COVID-19 *N* = 25,154	Wash-out *N* = 7527	Intra-COVID-19 *N* = 19,858
Age, median [Q1–Q3]	68 [61–72]	68 [61–72]	68 [61–72]	68 [61–72]
Ages 50–59	10,873 (20.70%)	5102 (20.30%)	1578 (21.00%)	4193 (21.10%)
Ages 60–69	19,865 (37.80%)	9722 (38.60%)	2847 (37.80%)	7296 (36.70%)
Ages 70+	21,801 (41.50%)	10,330 (41.10%)	3102 (41.20%)	8369 (42.10%)
Sex:				
Female	3162 (6.02%)	1463 (5.82%)	426 (5.66%)	1273 (6.41%)
Male	49,377 (94.00%)	23,691 (94.20%)	7101 (94.30%)	18,585 (93.60%)
Race/ethnicity				
White	35,184 (67.00%)	17,056 (67.80%)	5012 (66.60%)	13,116 (66.00%)
Black	10,173 (19.40%)	4760 (18.90%)	1484 (19.70%)	3929 (19.80%)
Asian/Pacific Islander	726 (1.38%)	340 (1.35%)	119 (1.58%)	267 (1.34%)
American Indian	435 (0.83%)	194 (0.77%)	62 (0.82%)	179 (0.90%)
Multiracial/Other	804 (1.53%)	409 (1.63%)	108 (1.43%)	287 (1.45%)
Hispanic	2734 (5.20%)	1272 (5.06%)	380 (5.05%)	1082 (5.45%)
Missing	2483 (4.73%)	1123 (4.46%)	362 (4.81%)	998 (5.03%)
Charlson comorbidity index score				
0	15,981 (33.50%)	8191 (33.00%)	2614 (35.20%)	5176 (33.40%)
1	12,504 (26.20%)	6465 (26.00%)	1965 (26.40%)	4074 (26.30%)
2+	19,289 (40.40%)	10,195 (41.00%)	2854 (38.40%)	6240 (40.30%)
Red flag sign/symptom				
Abnormal FIT/gFOBT	40,117 (76.40%)	18,964 (75.40%)	5851 (77.70%)	15,302 (77.10%)
Hematochezia	8419 (16.00%)	3925 (15.60%)	1127 (15.00%)	3367 (17.00%)
Iron deficiency anemia	4003 (7.62%)	2265 (9.00%)	549 (7.29%)	1189 (5.99%)
Number of red flags				
1 Red Flag	48,670 (92.60%)	23,207 (92.30%)	6977 (92.70%)	18,486 (93.10%)
2 Red Flags	3798 (7.23%)	1907 (7.58%)	542 (7.20%)	1349 (6.79%)
3 Red Flags	71 (0.14%)	40 (0.16%)	8 (0.11%)	23 (0.12%)

Fecal immunochemical test/Guaiac fecal occult blood test, FIT/gFOBT; Quartile 1–Quartile 3, Q1–Q3

significant association between pre- vs. intra-COVID-19 period and time to colonoscopy completion, after adjusting for age, sex, race/ethnicity, and number of red flag signs/symptoms (aHR: 1.03, 95% CI 0.99–1.06) (Supplementary Table 3).

Sensitivity analyses accounting for diagnostic follow-up with EGD or colonoscopy among adults with IDA showed longer time to endoscopic evaluation pre-COVID-19 vs. intra-COVID-19 (54.5 days vs. 37 days, respectively; $p < 0.01$), with a qualitatively similar difference in days to evaluation between pre- and intra-COVID-19 groups for the analyses restricted to colonoscopy and examining any first endoscopic evaluation (Supplementary Fig. 1). There was no discernible difference in findings adjusting for calendar date. Sensitivity analyses incorporating VA-paid community care colonoscopies found similar proportions completing colonoscopy (pre- vs. intra-: 32.9% vs. 32.3%) and qualitatively similar times to colonoscopy and likelihood of colonoscopy completion (Supplementary Table 4).

Discussion

Although the COVID-19 pandemic has been associated with dramatic disruptions of healthcare delivery and postponement of elective and non-urgent procedures, this study of a national sample of adults with CRC red flag signs/symptoms demonstrated no clinically meaningful change in colonoscopy completion compared to a representative pre-pandemic time period. Moreover, the colonoscopy completion rates of 27.0% and 26.5% in the pre- and intra-COVID-19 periods, respectively, reflect soberingly low diagnostic work-up rates after identification of red flag signs/symptoms. Among colonoscopy completers, time to colonoscopy across all red flag indications combined did not markedly change between pre-COVID-19 and intra-COVID-19 procedural restrictions, though time to colonoscopy was shorter among individuals with IDA during the intra-COVID-19 period. These observations suggest overall colonoscopy uptake and timeliness among Veterans with CRC red flag signs/symptoms were not

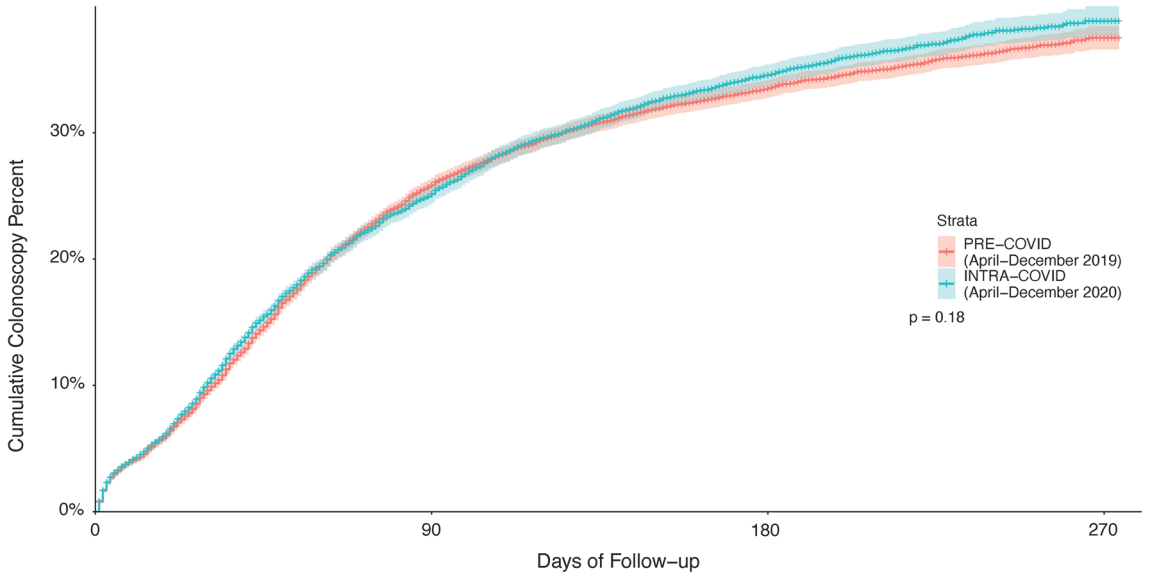


Fig. 1 Cumulative colonoscopy completion in a national sample of US Veterans with red flag signs and symptoms of CRC pre- vs. intra-COVID-19 pandemic. Survival curves, estimated via Kaplan–Meier approach for the outcome of time to colonoscopy completion, are shown for individuals with red flag signs or symptoms pre- vs. intra-COVID-19 pandemic. The curves demonstrate a similar cumulative proportion with colonoscopy completion for individuals with red flag signs/symptoms post vs. pre-COVID-19 pandemic. Red flags included abnormal FIT/gFOBT, iron deficiency anemia, and hematochezia

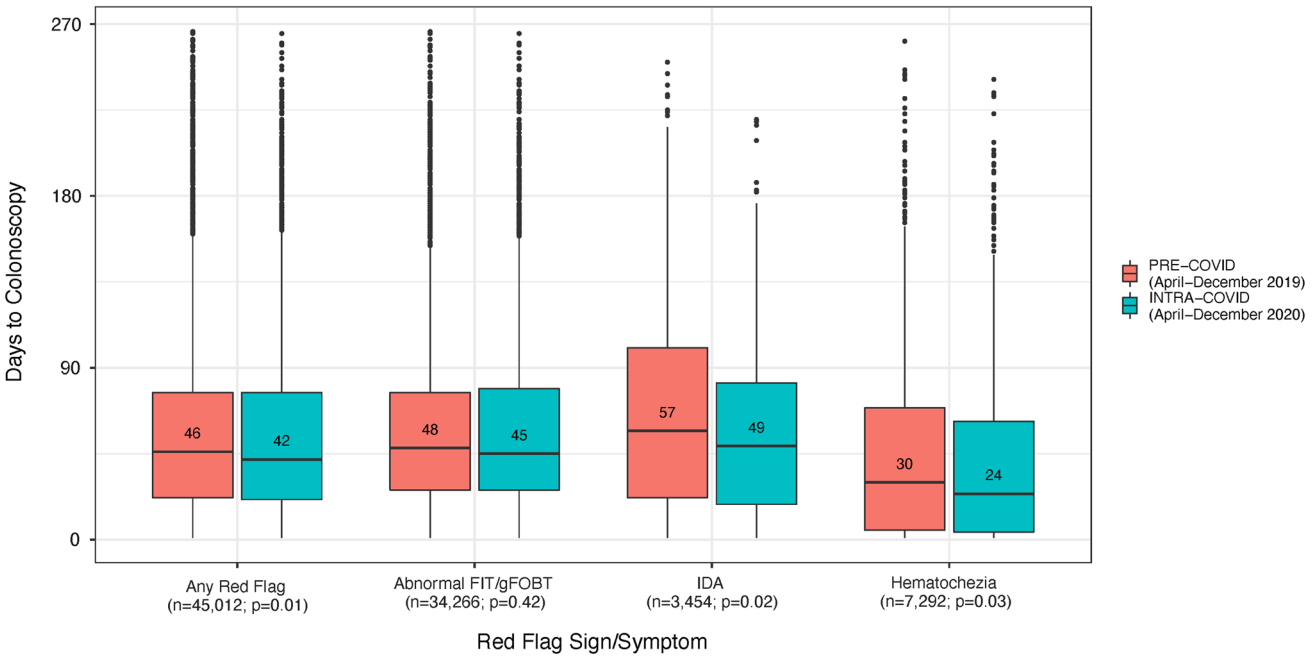


Fig. 2 Time to colonoscopy pre- and intra-COVID-19 pandemic, stratified by red flag sign/symptom of CRC, in a national sample of 45,012 individuals receiving VHA care. Median time to colonoscopy among colonoscopy completers with red flag signs and symptoms of CRC was shorter in the pre- vs. intra-COVID-19 pandemic period overall. In analyses stratified by red flag, individuals with iron deficiency anemia had significantly shorter time to colonoscopy in the intra- vs. pre-COVID-19 pandemic period. Abbreviation: Fecal immunochemical test/guaiac fecal occult blood test, FIT/gFOBT

Table 2 Colonoscopy completion and time to colonoscopy completion in a national sample of individuals with red flag signs or symptoms of CRC receiving VHA care, pre- (April–December 2019; $n = 25{,}154$) and intra-COVID-19 pandemic (April–December 2020; $n = 19{,}858$)

	COVID Time window	Time to colonoscopy, median days (Q1–Q3)**	Likelihood of colonoscopy receipt, intra vs pre* HR (95% CI)	
			Unadjusted HR (95% CI)	Adjusted*** HR (95% CI)
Overall	Pre-COVID-19	46 (22–77)	1.03 (0.99–1.06)	0.99 (0.95–1.03)
	Intra-COVID-19	42 (21–77)		
Stratified effects*				
Abnormal FIT/gFOBT	Pre-COVID-19	48 (26–77)	1.00 (0.96–1.04)	0.99 (0.95–1.03)
	Intra-COVID-19	45 (25–79)		
Hematochezia	Pre-COVID-19	30 (5–69)	1.00 (0.91–1.08)	0.99 (0.91–1.08)
	Intra-COVID-19	24 (4–62)		
Iron deficiency anemia	Pre-COVID-19	57 (22–101)	1.25 (1.04–1.49)	1.25 (1.04–1.49)
	Intra-COVID-19	49 (19–82)		

*The pre-COVID group represents the referent group;

**Median time to colonoscopy was calculated for only adults who completed colonoscopy

***Hazard models adjusted for age, sex, race/ethnicity, and number of red flag signs or symptoms

Confidence interval, CI; Fecal immunochemical test/Guaiac fecal occult blood test, FIT/gFOBT; Hazard Ratio, HR;

Quartile 1–Quartile 3, Q1–Q3

significantly impacted, as might have been feared. Indeed, in July 2020, the VA published findings showing colonoscopy volume decreases of 42% and 93% for March and April 2020, respectively [3]. Despite the significant drop in overall endoscopy volume for procedures with any indication described in that study, our findings indicate that colonoscopy uptake and time to colonoscopy were preserved among individuals needing diagnostic work-up for CRC red flag signs/symptoms.

We postulate that preservation of colonoscopy completion rates and time to colonoscopy was likely attributable to VHA guidance and policies implemented both before and during the pandemic to prioritize diagnostic colonoscopies over screening and surveillance colonoscopies. In April 2020, in addition to other policies to ensure safe continuation of healthcare delivery, guidance and policies were issued on colonoscopy prioritization based on presenting sign or symptom. Practical tools were provided for implementation, including the "Consult Prioritization Toolbox" applied by the National GI and Hepatology program within the EHR and bi-directional communication between and among local and national GI leaders to learn from best practices and ongoing challenges was available. We postulate that the overall impact of timely national guidance, practical tools for implementing guidance, and excellent communication between local and national GI leaders contributed to mitigation and prevention of pandemic-related delays in diagnostic colonoscopy completion. Nonetheless, the preservation of timely follow-up for diagnostic colonoscopy could have come at the expense of capacity to deliver screening and surveillance exams, which could lead to worse CRC-related outcomes across VHA.

Interestingly, time to colonoscopy completion stood out as markedly longer in the pre-COVID-19 period (median 57 days) compared to the intra-COVID-19 period (median 49 days) for patients with IDA. We postulate this is because of variation among clinicians in the knowledge that about 9% of individuals with IDA have CRC and that assignment of IDA as a Priority 2 condition reduced the impact of this variation in knowledge on recommendations and scheduling for colonoscopy [17]. As such, this observed outcome may suggest that providing scheduling priority guidance for common GI disease signs and symptoms, based on available literature on factors such as prevalence of malignancy or likelihood of needing immediate medical management, could improve timely diagnosis and treatment of individuals based on their disease risk. Such strategies have been successfully implemented on a national basis within the United Kingdom's National Health Service [18, 19].

There are several strengths of our study. We used a large, national sample of individuals receiving VHA care during the pre-COVID-19 and intra-COVID-19 time windows. Additionally, the use of national structured EHR and claims data provided up-to-date, complete patient information to examine our research questions throughout the course of the COVID-19 pandemic. Abnormal FIT/gFOBT and IDA were ascertained using laboratory codes, a more robust methodology than relying on billing diagnosis codes [12]. We also relied on commonly used diagnostic codes to inform ascertainment of hematochezia and prior laboratory criteria to identify abnormal FIT/gFOBT and IDA exposures. Our algorithms for ascertainment were based on those used in prior studies, one of which tested several different definitions of IDA and hematochezia, finding little to no difference in results [12].

A few limitations should also be considered. As Veterans can receive healthcare services outside of VHA, the results potentially underestimate the burden of abnormal FIT/gFOBT, IDA, and hematochezia in Veterans and may underestimate the proportion of individuals who completed colonoscopy after a red flag. Because of low colonoscopy uptake rate in our population, we compared median times to colonoscopy among all colonoscopy completers rather than among all subjects at risk, which does not account for censoring. Given restrictions on health care throughout the COVID-19 pandemic, it is possible individuals presenting with red flag signs/symptoms represent the more severe cases, potentially leading to increased urgency of care and overestimating the timeliness of colonoscopy uptake. This is also potentially reflected in the drop in number of individuals with red flag signs/symptoms from the pre-COVID-19 period to the intra-COVID-19 period. To account for this, our study examined clinical covariates, including Charlson Comorbidity Index and number of red flag signs/symptoms within 30 days of primary red flag presentation to ascertain if confounding existed. VHA facilities were given discretion to increase or decrease procedure access based on local COVID-19 conditions, which might lead to variability in findings across VHA sites. We were also unable to account for COVID-19 nucleic acid amplification test access and use, which might have provided more information about local VHA conditions. We also could not distinguish severity of hematochezia among patients, which might have justifiably led to marked differences in time to colonoscopy (e.g., for individuals with scant blood on toilet paper vs. more worrisome and persistent blood mixed in the stool). Our study did not examine the diagnostic yield of colonoscopies for red flag signs/symptoms pre- vs. intra-COVID-19, nor CRC stage at diagnosis or CRC-related mortality. With respect to the latter, studies allowing for longer follow-up time after a red flag diagnosis are needed and currently underway. In the sensitivity analysis that incorporated VA-paid community colonoscopies, we were unable to account for colonoscopies in Medicare patients performed outside of VHA, as these data were unavailable. Thus, our measurement of

colonoscopies performed outside of VHA reflects potentially incomplete data from outside of VHA. Finally, there was a nearly 12% decline in adults presenting with red flag signs/symptoms in the intra-COVID-19 period, potentially due to concerns about contracting COVID-19 by receiving care. This lower volume might have allowed for quicker work-up of adults with red flag signs/symptoms who did present, but also could lead to underestimation of the burden of red flag signs/symptoms in the VHA population.

Though the pandemic continues, evidence from our study indicates that, despite VHA recommendations to postpone and re-prioritize colonoscopies at the start of the pandemic, colonoscopy completion, and time to colonoscopy were preserved, and for some indications, improved, compared to the pre-pandemic timeframe among adults with select CRC red flag signs/symptoms. Our findings support the potential utility of prioritization strategies for endoscopy referral which were implemented during the pandemic by VHA, both in regular practice and during future pandemics. The impact of deferred care for lower priority indications is currently unknown. Future studies should examine whether diagnostic yield and CRC outcomes, such as stage at diagnosis or CRC-related mortality, differed pre- vs. post-COVID-19 related to these postponements and if certain colonoscopy prioritization strategies could be more broadly effective in diverse healthcare settings, as we continue to optimize care during and beyond the COVID-19 pandemic.

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Author's contribution JD, RB, JAD, AE, LL, SCS, AG, MEM, and SG contributed to concept and design and critical revision of the manuscript for important intellectual content . JD, RB, JAD, LL, AG, and SG contributed to analysis and interpretation of the data. JD and SG contributed to drafting of the manuscript and obtained funding. JD, RB, LL, and SG contributed to statistical analysis.

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Declarations

Competing interest We have read and understood the ICMJE policy on declaration of conflicts of interests and declare we have no conflict of interest. The contents of this work do not represent the views of the Department of Veterans Affairs or the United States Government.

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