Missed Opportunities to Initiate Endoscopic Evaluation for Colorectal Cancer Diagnosis

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Abstract

Objectives—Delayed diagnosis of colorectal cancer (CRC) is among the most common reasons for ambulatory diagnostic malpractice claims in the United States. Our objective was to describe missed opportunities to diagnose CRC before endoscopic referral, in terms of patient characteristics, nature of clinical clues, and types of diagnostic-process breakdowns involved.

Methods—We conducted a retrospective cohort study of consecutive, newly diagnosed cases of CRC between February 1999 and June 2007 at a tertiary health-care system in Texas. Two reviewers independently evaluated the electronic record of each patient using a standardized pretested data collection instrument. Missed opportunities were defined as care episodes in which endoscopic evaluation was not initiated despite the presence of one or more clues that warrant a diagnostic workup for CRC. Predictors of missed opportunities were evaluated in logistic regression. The types of breakdowns involved in the diagnostic process were also determined and described.

Results—Of the 513 patients with CRC who met the inclusion criteria, both reviewers agreed on the presence of at least one missed opportunity in 161 patients. Among these patients there was a mean of 4.2 missed opportunities and 5.3 clues. The most common clues were suspected or confirmed iron deficiency anemia, positive fecal occult blood test, and hematochezia. The odds of a missed opportunity were increased in patients older than 75 years (odds ratio (OR) = 2.3; 95% confidence interval (CI) 1.3–4.1) or with iron deficiency anemia (OR = 2.2; 95% CI 1.3–3.6), whereas the odds of a missed opportunity were lower in patients with abnormal flexible sigmoidoscopy (OR = 0.06; 95% CI 0.01–0.51), or imaging suspicious for CRC (OR = 0.3; 95% CI 0.1–0.9). Anemia was the clue associated with the longest time to endoscopic referral (median = 393 days). Most process

breakdowns occurred in the provider–patient clinical encounter and in the follow-up of patients or abnormal diagnostic test results.

Conclusions—Missed opportunities to initiate workup for CRC are common despite the presence of many clues suggestive of CRC diagnosis. Future interventions are needed to reduce the process breakdowns identified.

Introduction

Delayed diagnosis of colorectal cancer (CRC) is among the most common reasons for ambulatory malpractice claims related to missed and delayed diagnosis in the United States (1,2). Several randomized controlled trials (3,4) have shown that survival in patients with CRC is significantly longer when the diagnosis is made at a more localized early stage, making a compelling case for early detection through screening programs (5). However, most patients with colorectal cancers are diagnosed after the onset of cancer-related symptoms (6) and it is imperative that frontline providers recognize clues to CRC diagnosis early.

Understanding and subsequently preventing delays in CRC diagnosis is consistent with high quality health care, but few contemporary studies describe the origins and characteristics of missed opportunities that lead to these delays (7). Limited endoscopic capacity (endoscopists, space, equipment) (8), and delays associated with patients completing their scheduled colonoscopy procedures can be responsible for delayed CRC diagnosis after a colonoscopy referral has been made (9,10). However, an important and potentially preventable determinant of delay in CRC diagnosis is a failure to pursue a workup for CRC in the presence of clues to its diagnosis. The breakdowns in the process of detecting and investigating clues represent potential missed opportunities that could lead to an earlier referral for colonoscopy, and an earlier diagnosis of CRC. This knowledge is important in guiding interventions to improve CRC diagnosis in primary care.

In this study, we identified patients diagnosed with a new CRC and evaluated episodes of care where opportunities for an earlier diagnosis of CRC were missed before initiation of an endoscopy consultation. Our objective is to describe missed opportunities to diagnose CRC before endoscopic referral, in terms of patient characteristics, the nature of the clues and the types of breakdowns involved in the diagnostic process.

Methods

Setting

We used a retrospective cohort design to identify and evaluate newly diagnosed cases of primary CRC at a tertiary care health system in Texas from February 1999 through June 2007. The system includes a large referral center with a multispecialty ambulatory care clinic and several satellite clinics. All patients are assigned a primary care provider and most patients continue to obtain their care within the system. Types of practitioners included both academic and non-academic practitioners and resident trainees, who are supervised closely by attending physicians. Using an integrated electronic medical record, we conducted a detailed review of care processes related to patient presentation, test ordering, referral, and follow-up procedures by obtaining data from progress notes, consultations menu, laboratory and radiology menus, discharge summaries, etc. The study was approved by the local Institutional Review Board.

Inclusion and exclusion criteria

We included all pathologically confirmed, newly diagnosed cases of primary CRC diagnosed between February 1999 and June 2007. After review of the electronic health record, we excluded patients who were diagnosed (or received their CRC diagnosis care) outside the

institution, were in the system for less than 30 days before diagnosis, and those with recurrent CRC (diagnosed with CRC within past 5 years).

Data collection procedures

Two reviewers (both physicians) independently reviewed each CRC case using a detailed data collection instrument. The purpose of two independent reviews was to evaluate agreement on the presence or absence of missed opportunities. Both reviewers evaluated all the relevant electronic data available (in most cases as far back as 1997) for presence of predefined clinical clues that warrant a diagnostic workup for CRC. Definitive clues were derived from expert opinion and current literature and included anemia (suspected iron deficiency (unexplained hemoglobin/hematocrit below lab norm, MCV below lab norm, absent iron studies) or confirmed iron deficiency), positive fecal occult blood test (FOBT), computerized tomographic (CT) imaging suspicious for CRC, suspected rectal or abdominal mass on physical exam, change in stool caliber, worsening constipation (recent (within 1 year) decrease in stool frequency), abdominal pain, weight loss, melena, intestinal obstruction, abnormal flexible sigmoidoscopy (showing polyp or mass), or abnormal double contrast barium enema (DCBE showing polyp, mass or filling defect) (11,12). Two other clues, positive family history of colon cancer (at least one first degree relative with CRC) and "other suspicious lower gastrointestinal symptoms" were categorized as possible prompts for a diagnostic workup.

Table 1 lists data items collected on chart review and illustrates how the data was used to make assessment on missed opportunities. We defined missed opportunities as episodes of care where endoscopic evaluation was not initiated in the presence of one or more predefined clinical clues. An episode of care was defined by a patient–provider interaction such as a clinic visit or hospitalization. A rigorous criteria was used to define missed opportunities. For example, if the provider was a subspecialist such as an ophthalmologist or dermatologist, he/she was not expected to follow-up on a hemoglobin level ordered by the primary care provider. We collected information on types of providers involved and the setting where missed opportunities occurred. Because our study was focused on understanding suboptimal care processes that cause diagnostic delays rather than their associated adverse outcomes, we collected data on all missed opportunities regardless of delay in diagnosis or potential harm.

In all cases with at least one missed opportunity, one of the reviewers was pre-assigned to perform additional chart review to evaluate process breakdowns. Elements from this portion of chart review were adapted from the data collection instrument used to study diagnostic claims in the Malpractice Insurers Medical Error Prevention Study (1) and a taxonomy proposed by Schiff *et al.* (13) to study diagnostic breakdowns. The data collection instrument allows categorization of identified missed opportunities according to provider encounter (history, physical examination, ordering non-endoscopic tests, or consultation for further workup), diagnostic tests (ordered tests either not performed or performed/interpreted incorrectly) or follow-up (abnormal diagnostic test results or visits). Each missed opportunity could be associated with several process breakdowns. Furthermore, we collected data on contributory factors associated with a specific process breakdown. The instrument was reviewed by multiple clinicians to ensure relevance and comprehensiveness.

The study team supervised and trained the reviewers during pilot testing to ensure reliable and consistent data collection. The reviewers were instructed not to designate opportunities as missed if there was insufficient documentation in the medical record to support them or when documentation supported an informed and intentional decision not to workup a particular clue. To reduce hindsight bias (14), we did not ask reviewers to make assessments of patient outcomes in terms of harm or stage of diagnosis. To ensure quality control of data entry about 10% of cases (*n* = 50 from each reviewer) were checked by a third investigator and found to be 98% accurate.

Data analysis

We evaluated the agreement between the two reviewers on the presence of at least one missed opportunity. We identified two groups of patients: (1) those for whom both reviewers agreed completely that at least one missed opportunity was present (i.e., endoscopic evaluation not initiated in the presence of at least one predefined clue) and (2) those for whom both reviewers agreed that there was no missed opportunity. We categorized the diagnostic clues according to the overall level of agreement between the two reviews on the presence of that clue into clues with "substantial" agreement ($\kappa = 0.60$–0.79) and clues with "fair to moderate" agreement ($\kappa < 0.60$).

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We compared the distribution (as proportions) of each clue as well as distributions of the referral times (from first appearance of a clue to endoscopy referral) between the two study groups with and without missed opportunities. We also compared the two groups with regards to patient related demographic (age, gender, race) and clinical (e.g., comorbid medical or psychologic/mental disorder) features. We used the Fisher's exact test for categorical variables and the nonparametric Wilcoxon's continuity-corrected normal approximation two-sample test for continuous variables. Multivariable logistic regression models were used, in which the outcome variable in these models was whether or not a patient had at least one missed opportunity, and predictor variables included age (< 65, 65–74, >75 years), race (white, black, Hispanic, other), comorbid medical and psychologic/mental conditions, and each of the clinical clues. The models were fit using maximum likelihood estimation, and odds ratios and 95% confidence intervals were calculated. All available covariates (demographic variables, medical and psychiatric comorbidities and clues) were initially entered into the logistic regression model, and only covariates with significant as well as stable risk estimates were kept in the final model. Data were analyzed using the SAS software (SAS Institute Inc., Cary, NC, version 9.1.3).

Results

Of 551 patients of CRC identified over the study period, 513 met the inclusion and exclusion criteria for our study. Both reviewers agreed on the presence of at least one missed opportunity in 161 patients and on the absence of any missed opportunities in 220 patients ($\kappa = 0.75$; also see Figure 1). The remaining 132 patients where one of the reviewers did not agree on the presence of a missed opportunity were excluded from further analysis on missed opportunities. Among the 161 patients with missed opportunities, there was a mean of 4.2 missed opportunities and 5.3 clues per patient.

We compared demographic and clinical characteristics of patients with and without at least one missed opportunity (see Table 2). Patients with missed opportunitites were significantly older than those without missed opportunities (median age of 71 vs. 67, respectively). Patients over 75 years of age had significantly more missed opportunities (42.9%) compared with < 65 years (29.2%) and 65–74 years (28% respectively; $P < 0.001$). African-American race, presence of congestive heart failure (CHF), and presence of coronary artery disease were also significantly associated with missed opportunities. Of those with missed opportunities, 12.4%

had CHF and 26.7% had coronary artery disease as compared with only 4.1% CHF and 17.3% coronary artery disease among patients without missed opportunities. On the other hand, presence of mental disorders was not associated with missed opportunities.

In Table 3, we compare the presence of predefined clinical clues and the associated referral times in CRC patients with and without missed opportunities. Suspected or confirmed iron deficiency anemia was the most common clue for which there was a high agreement between the two reviewers. It also was strongly associated with missed opportunities and had the longest referral time among clues with more than 10 cases. Hemoglobin values associated with missed opportunities were higher (mean = 11 gm/dl; median = 11.3 gm/dl) compared with those in cases without missed opportunity (mean = 9.9 gm/dl; median = 10.2 gm/dl). Patients with worsening constipation were more likely to have missed opportunities. On the other hand, clues that usually warrant hospitalization and/or urgent colonoscopy or surgery (e.g., obstruction, melena, abnormal flexible sigmoidoscopy or CT scan) were associated with no or few missed opportunities. Among those with a missed opportunity, the median time to referral for the six clues with at least 20 cases ranged from a low of 144 days for those with weight loss to 393 days for those with anemia.

In the final logistic regression analysis, patients with following characteristics were more likely to experience missed opportunities: age > 75 years (OR = 2.3 compared with those under the age of 65 years; 95% CI of 1.3–4.1) and anemia (OR = 2.2 compared to those without anemia; 95% CI of 1.3–3.6) whereas patients with abnormal flexible sigmoidoscopy (OR = 0.06 compared to those without the procedure; 95% CI of 0.01–0.51), and abnormal CT scan suspicious for CRC (OR = 0.3 compared to those without an abnormal CT scan; 95% CI of 0.1–0.9) were less likely to have missed opportunitites.

Tables 4–6 show the types of process breakdowns and their associated characteristics in terms of settings (such as outpatient clinic, inpatient), personnel (such as primary care physicians vs. other types of providers), diagnostic clues and key contributory factors discernable from record review. Of 937 total missed opportunities we identified, 54 (5.8%) were related to trainee physicians (residents and fellows). In Table 4, we show the characteristics of the diagnostic-process breakdowns related to the provider–patient encounter including history, physical examination, requesting diagnostic tests (non-endocopic tests) and consultations (gastroenterology for an endoscopy). Primary care physicians were most commonly involved. The most common diagnostic-process breakdown was the failure or delay to consult gastroenterology in the presence of a clinical clue most commonly anemia, positive FOBT, and hematochaezia. The other two frequent factors were not recording an adequate physical examination and a delay or failure to order a non-endoscopic diagnostic test including iron studies, barium enema, and complete blood count. The most common aspect of inadequate physical exam was an unrecorded rectal exam. The most common aspect for inadequate medical history was not documenting gastrointestinal bleeding in the presence of other clues (most commonly anemia).

In Table 5, we show diagnostic-process breakdowns associated with performance and/or interpretation of non-endoscopic diagnostic tests. The most common breakdown (68%) occurred when the diagnostic tests were requested but not performed. The reasons were mostly secondary to patients not appearing for appointments and apparent lack of requesting provider awareness about the non-performance of the test. Poor bowel preparation for barium enema accounted for most cases of inadequate performance of diagnostic tests. The types of diagnostic tests not interpreted correctly included complete blood count and iron studies (e.g., not interpreting anemia as iron deficiency). Table 6 shows process breakdowns associated with follow-up. In patients where non-endoscopic diagnostic test results were not acted upon, the most common tests included positive FOBT and complete blood count.

We also evaluated 132 patients who were excluded from the analysis due to disagreement on the presence of missed opportunities and explored the reasons for a disagreement between the two reviewers. First, we compared the baseline characteristics of the 132 patients who were excluded from analysis to all the other study patients. As shown in Table A1 in the Appendix, there were no significant differences between the two groups with regards to age, race, and comorbid medical and psychiatric diseases. Second, the mean number of clues per patient in the excluded group of 132 patients was 2.1 compared with 5.3 in the 161 study group patients in whom a missed opportunity was agreed upon. Thus in the 132 excluded patient group, there was less possibility that both reviewers would find at least one clue that they both agreed on that may have led to a missed opportunity. This we believe was the main factor responsible for disagreement. Third, we analyzed the type of clues present in these 132 cases. We found that among the 132 excluded patients, the reviewers' agreement (measured by kappa) was similar to those among the 381 study patients except for three clues (iron deficiency anemia, family history of colon cancer, and weight loss) in which the kappa dropped by more than 0.2 (Table A2 in Appendix). Because iron deficiency was one of the most common clues, it disproportionately affected assessment in the group.

Discussion

Approximately one-third ($n = 161$) of 513 cases of colorectal cancer (CRC) might have had one or more missed opportunities to initiate an earlier diagnostic endoscopic test. All missed opportunities by definition were associated with the presence of a predefined clinical clue that would ideally warrant a diagnostic evaluation for CRC. There was a mean of 4.2 missed opportunities and 5.3 clues per patient with at least one missed opportunity. Patients who were older than 75 years, African American and those with congestive heart failure or coronary artery disease were more likely to experience missed opportunities. Suspected or confirmed iron deficiency anemia was the most common clue associated with missed opportunities, and had the longest lag time from first appearance to first endoscopy referral. Hemoglobin value in cases associated with missed opportunities was higher compared to those without, suggesting that mild iron deficiency anemia may be an under-recognized clue for CRC diagnosis. Breakdown in several steps of the diagnostic process was identified, most commonly in the provider–patient clinic encounter, but also in ordering, performance and interpretation of diagnostic tests and in follow-up of patients and abnormal diagnostic test results.

One advantage of this study is that it outlines a new approach to understand and reduce potentially preventable delays in CRC diagnosis. Previous studies, most of which are from outside the US, described the magnitude of delays and their association with both patient and physician factors (15–19), but did not present a comprehensive assessment of the types of care breakdowns associated with delays. We focused on missed opportunities in diagnostic care rather than delays in diagnosis because these opportunities precede most delays in care and can be targeted for improvement. For instance, if a clinician missed the presence of iron deficiency anemia on a patient visit and a month later the patient was diagnosed with CRC, we would still denote the first visit as a missed opportunity. We also minimized subjectivity by defining missed opportunities beforehand and the types of clinical clues that would warrant a CRC workup. The presence of an integrated electronic medical record provides valuable clinical information about signs and symptoms, diagnostic tests, consultations and follow-up, and is superior and more detailed than administrative data and paper record review.

Previous studies that addressed delays in CRC diagnosis have found 27–62% of these delays to be provider related (20–23). Multiple factors have been implicated in such delays, including misdiagnosis (20), lack of appropriate physical examination (21,24), observation of symptoms suggestive of CRC without subsequent investigation (20,25), lack of awareness of symptoms suggestive of CRC (7,24) and false-negative barium enema (21,26). Our study provides a more

comprehensive view of these factors and demonstrates that patients who experience diagnostic delays do so in the presence of multiple definitive clues and likely encounter multiple missed opportunities. In few patients, colonoscopy evaluation was delayed for many years despite the presence of an abnormal test (such as flexible sigmoidoscopy and DCBE) for which colonoscopy was indicated. However, most of these tests were performed before 1996, before the electronic medical record was universally used in the institution and well before notification procedures were put in place to inform providers of abnormal test results. This may explain why providers did not notice the tests on subsequent visits. Other reasons for this unusual delay include change in primary care providers and patients' reduced number of follow-up visits to the health-care system.

Disparities in CRC diagnosis have been described, with African Americans more likely to be diagnosed with more advanced CRC regardless of whether they have health insurance (27, 28). Our study further supports this phenomenon in terms of disparities in missed diagnostic opportunities. Although the elderly patients differ in their presentation from younger age groups and perhaps have screening related disparities (29), to our knowledge there is no previous published literature on this finding (22,30–33); in fact one study suggested the opposite (25).

The most common clue as well as the one most significantly associated with missed opportunities was suspected or confirmed iron deficiency anemia. We found failure to document, follow-up, or take an action on suspected or confirmed anemia in about half (52%) of the cases with missed opportunities. Given that most studies show approximately 10% prevalence of CRC among patients with iron deficiency anemia (34–37) and that the majority of patients with new CRC diagnosis are iron deficient at presentation of CRC, this is a potential area of improvement. Previous studies have described delays in CRC diagnosis in patients with anemia (26,31,34,35,38,39), but determinants and duration of such delays have not been comprehensively studied. In our study, suspected or confirmed iron deficiency anemia had the longest lag time to endoscopy referral (median of 393 days) and was the single most common clue across all types of diagnostic-process breakdowns, that is, those related to the clinical encounter, diagnostic test results and follow-up. We also found that milder cases were more likely to be missed, consistent with findings of a previous study from the United Kingdom (35).

Several missed opportunities are likely to have occurred in the clinical encounter. Both systems and cognitive factors have been recently proposed to explain diagnostic breakdowns due to inadequate documentation of history or physical exam or from not requesting certain tests such as for iron deficiency (1,40). Consistent with previous work in other types of diagnostic breakdowns in primary care (41), we found deficiencies in history or physical exam to be common in the medical encounter. However, retrospective reviews such as ours can only obtain limited information about the responsible systems and cognitive factors. Future studies are needed to understand and prevent process breakdowns related to the clinical encounter in CRC diagnosis (42,43).

Our study findings should be interpreted with caution. Although the study was conducted in a single institution, it involved a large number of patients and providers. We did not collect identifiable information on providers and hence were unable to evaluate or adjust for providers' effects. However, patients are allocated to providers non-selectively at the institution (i.e., there is no specific provider assignment pattern for new patients), so it is reasonable to assume that cancer cases are distributed equally among most primary care providers. Subjects in the study do not represent the entire cohort of patients eligible for screening or the cohort of patients who present with signs or symptoms suggestive of CRC but no eventual CRC diagnosis. Hence, we could not account for the impact of false-positive tests, which may also compete for time

and resources for diagnostic evaluation. Several clues (signs, symptoms, lab test) that we used to define missed opportunities have unclear and probably low predictive value (and hence high false-positive results). Therefore, chasing these clues in every patient may not be cost-effective in most practice settings. However, the two most common clues (positive-screening FOBT and iron deficiency anemia) are hardly disagreed upon criteria for evaluating the presence of colon lesions (polyps or cancer). For policy makers, most benefit could be garnered by focusing on missed opportunities related to these two clues. We also may have missed clues or follow-up actions that were not documented in the chart. Because of recall bias, we did not interview providers to further analyze why opportunities were missed and what cognitive processes were involved; several were missed many years ago and some providers had since left the institution.

To overcome a methodological limitation of low reliability in studies of diagnostic breakdown (44), we used two independent reviewers and further analyzed cases only where both agreed with high reliability that missed opportunities were present. We could have added more reviews or provided a venue for increasing agreement but we opted to use only cases where complete agreement was achieved in the first round. Despite a low reproducibility agreement for certain clues, we were assured by the high agreement for several others and a substantial ($\kappa = 0.75$) agreement on the presence or absence of missed opportunities. This level of agreement is much higher than that achieved in previous studies using the similar methodology (41,44). Lastly, to address hindsight bias (14), we did not ask the reviewers to make judgements on outcomes such as stage at diagnosis and patient harm.

Conclusions

Missed opportunities to initiate an evaluation for CRC diagnosis are common in the ambulatory care setting and occur in the presence of several types of clues. Iron deficiency anemia is the most common clue in missed opportunities. Patients who were older than 75 years, African American, had coronary artery disease or CHF or had certain types of clues such as known or suspected iron deficiency anemia and worsening constipation, were more likely to experience missed opportunities. Future research is needed to address the systems and cognitive breakdowns (40) at the multiple diagnostic processes we identified to reduce delays in CRC diagnosis.

Study Highlights

What Is Current Knowledge

- Delayed diagnosis of colorectal cancer (CRC) is among the most common reasons for ambulatory diagnostic malpractice claims in the United States.

- Few contemporary studies describe the frequency, origins, and characteristics of missed opportunities in detecting and investigating CRC-related diagnostic clues.

What Is New Here

- Missed opportunities to initiate an earlier diagnostic endoscopic test are fairly common despite the presence of multiple clues to CRC diagnosis.

- Patients who are older than 75 years, African Americans, and those with congestive heart failure or coronary artery disease are more likely to experience missed opportunities.

- Suspected or confirmed iron deficiency anemia (especially mild) is the most common diagnostic clue associated with missed opportunities, having the longest lag time from first appearance to first endoscopy referral.

Acknowledgments

Appendix

The clinical and demographic characteristics of the colorectal cancer patients are summarized in Table A1. Table A2 shows the clues for which kappa values dropped by > 0.2.

Table A1

Demographic and clinical characteristics of 513 patients diagnosed with colorectal cancer categorized in two groups: those included in analyses and those excluded from subsequent analyses due to lack of consensus on a missed opportunity

	Patients included in analyses (n=381)		Patients excluded from analyses (n=132)		P value[a]
	n	*%*	*n*	*%*	
Age					
Median	69		68		0.36
< 65	143	37.5	56	42.4	0.50
65–74	115	30.2	40	30.3	
≥75	123	32.3	36	27.3	
Race					
White Caucasian	192	58.0	64	55.2	0.54
Black	106	32.0	43	37.1	
Hispanic and other race	33	10.0	9	7.8	
Comorbid medical diseases					
Congestive heart failure	29	7.7	8	6.1	0.55
Coronary artery disease	81	21.3	30	22.7	0.72
Hypertension	235	61.7	87	65.9	0.39
Diabetes	92	24.2	40	30.3	0.16

	Patients included in analyses (*n*=381)		Patients excluded from analyses (*n*=132)		*P* value[a]
	n	%	*n*	%	
Chronic obstructive pulmonary disease	49	12.9	19	14.4	0.65
Any of the above medical diseases	281	73.8	102	77.3	0.42
Comorbid psychological/mental disorders					
Depression	39	10.2	20	15.2	0.13
Anxiety	12	3.2	8	3.1	0.14
Dementia	10	2.6	4	3.0	0.81
Post-traumatic stress disorder (PTSD)	20	5.3	4	3.0	0.30
Schizophrenia	2	0.5	2	1.5	0.27
Bipolar	6	1.6	1	0.8	0.49
Alcohol	61	16.0	22	16.7	0.86
Any of the above psychological/mental disorders	116	30.5	46	34.9	0.35

[a]*P* value based on the nonparametric median two-sample test for median age, and on Pearson's χ^2 test for the rest of the variables.

Table A2
Clues for which kappa values for agreement dropped by more than 0.2 in the 132 patients excluded for analysis compared with study patients

Clues	Kappa for presence of clue in 132 patients	Kappa for presence of clue in study patients
Suspected or confirmed iron deficiency anemia	0.60	0.82
Family history of colon cancer	0.47	0.75
Weight loss	0.41	0.64

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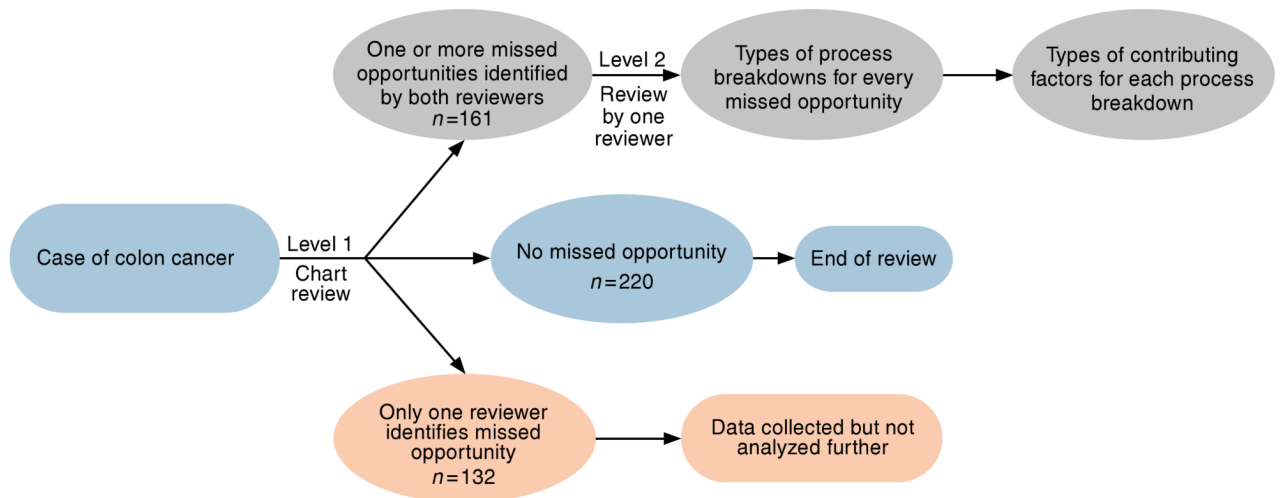
Figure 1.
Study flowchart.

Table 1

Types of data collected on medical record review

Data collection instrument categories	Details of data collected	An example of missed opportunity
Patient characteristics	Age, race/ethnicity, gender	68 Years, African American, male, none
	Medical and psychological comorbidities	
Type of clue Defined as predefined symptom and sign that should prompt an endoscopic evaluation for colorectal cancer	Suspected or confirmed iron deficiency anemia	Confirmed iron deficiency anemia with Hb=10.2 gm/dl
	Screen positive for FOBT	
	Screen positive for flex-sig	
	Screen positive for barium enema	
	Abnormal imaging suspicious for colon cancer (CT)	
	Suspected rectal or abdominal mass	
	BRBPR (in the absence of negative colonoscopy within previous 1-year period)	
	Change in stool caliber	
Date clue first appeared on medical record review	__/__/___	12 March 2004
Presence of missed opportunity? Defined as care episodes where endoscopic evaluation was not initiated despite the presence of one or more clues that warrant a diagnostic workup for CRC.	Did a missed opportunity occur?	Yes, twice
	Dates of missed opportunity	No mention of iron deficiency anemia on two subsequent primary care visits on 26 March 2004 and 12 August 2004
Process breakdown (adapted from Gandhi et al. (1))	Medical history deficient	Diagnostic/laboratory resultsnot followed up
	Physical examination deficient	
	Diagnostic/laboratory tests (delayed/not ordered)	
	Consult delayed or not requested	
	Diagnostic/laboratory test ordered but not performed	
	Diagnostic/laboratory test not performed correctly	
	Diagnostic/laboratory tests not interpreted correctly	
	Diagnostic/laboratory results not followed up	
	Problems with follow-up plans	
Contributory factors (reasons gleaned from chart review about why appropriate diagnostic workup was not performed)	Factors adapted from Gandhi *et al.* (1)	Inadequate test-result tracking system
Type of personnel involved	Codes for personnel adapted from Gandhi *et al.* (1)	Generalist/primary care physician
Setting of care	Codes for settings adapted from Gandhi *et al.* (1)	Primary care physician's office
Date of first colonoscopy referral	__/__/___	31 January 2005
Date of colonoscopy performance	__/__/___	15 February 2005
Date of CRC diagnosis	__/__/___	18 February 2005

Table 2

Demographic and clinical characteristics of 381 patients diagnosed with colorectal cancer categorized into two groups: with and without missed opportunities to initiate an earlier endoscopic referral

	Patients with at least one missed opportunity (n=161)		Patients with no missed opportunities (n=220)		P value[a]
	n	%	n	%	
Age					
Median	71		67		<0.001
<65	47	29.2	96	43.6	<0.001
65–74	45	28.0	70	31.8	
≥75	69	42.9	54	24.6	
Race					
White Caucasian	74	52.1	118	62.4	0.05
Black	56	39.4	50	26.5	
Hispanic and other races	12	8.2	21	11.1	
Comorbid medical diseases					
Congestive heart failure	20	12.4	9	4.1	0.003
Coronary artery disease	43	26.7	38	17.3	0.03
Hypertension	101	62.7	134	60.9	0.75
Diabetes	44	27.3	48	21.8	0.23

	Patients with at least one missed opportunity ($n=161$)		Patients with no missed opportunities ($n=220$)		P value[a]
	n	%	n	%	
Chronic obstructive pulmonary disease	21	13.0	28	12.7	1.00
Any of the above medical diseases	122	75.8	159	72.3	0.48
Comorbid psychological/mental disorders					
Depression	18	11.2	21	9.6	0.61
Anxiety	4	2.5	8	3.6	0.57
Dementia	5	3.1	5	2.3	0.75
Post-traumatic stress disorder (PTSD)	7	4.4	13	5.9	0.64
Schizophrenia	1	0.6	1	0.5	1.00
Bipolar	4	2.5	2	0.9	0.25
Alcohol	21	13.0	40	18.2	0.20
Any of the above psychological/mental disorders	42	26.1	74	33.6	0.12

[a] P value based on the nonparametric Wilcoxon's continuity-corrected normal approximation two-sample test for age, and on Fisher's exact test for the rest of the variables.

Table 3

A comparison of several clinical clues for colorectal cancer diagnosis and the associated median referral times in colorectal cancer patients with and without missed opportunities

Clues (κ)[a]	Patients with at least one missed opportunity (n=161)			Patients with no missed opportunities (n=220)		P value[b]
	Number of missed opportunities	Number of patients (Median days until first referral)	Percentage[c] (IQR[e])	Number of patients (Median days until first referral)	Percentage[d] (IQR[e])	
Clues with high agreement between reviewers (κ > 0.60)						
Screen positive for barium enema (κ = 0.86)	6	4	2.5	8	3.6	0.57
		2,514	1,470–3,676	0.5	0–1.5	0.007
Suspected or confirmed iron deficiency anemia (κ = 0.82)	357	83	51.6	58	26.4	<0.0001
		393	108–1114	2.5	0–12	<0.0001
Abnormal imaging suspicious for colon cancer (CT) (κ = 0.81)	8	5	3.1	22	10.0	0.01
		71	27–274	0.5	0–1	0.001
BRBPR (in the absence of colonoscopy within previous 1-year period) (κ = 0.80)	79	36	22.4	48	21.8	0.90
		161	63–321	0	0–1	<0.0001
Screen positive for flex-sig (κ = 0.78)	2	1	0.62	23	10.5	<0.0001
		1,246	1,246–1,246	0	0–0	<0.001
Screen positive for fecal occult blood test (κ = 0.76)	128	64	39.8	83	37.7	0.75
		146	51–528	1	0–7	<0.0001
Family history of colon cancer (κ = 0.75)	12	4	2.5	7	3.2	0.77
		441	210–686	0	0–0	0.003
Intestinal obstruction (κ = 0.72)	0	0	0	19	8.6	<0.0001
		n/a	n/a	1	0–2	—[f]

Clues (κ)[a]	Patients with at least one missed opportunity (n=161)			Patients with no missed opportunities (n=220)		P value[b]
	Number of missed opportunities	Number of patients / Median days until first referral	Percentage[c] / IQR[e]	Number of patients / Median days until first referral	Percentage[d] / IQR[e]	
Suspected rectal or abdominal mass (κ = 0.69)	8	6 / 14	3.7 / 2–44	7 / 0	3.2 / 0–1	0.78 / 0.01
Worsening constipation (κ = 0.66)	56	30 / 281	18.6 / 117–487	19 / 1	8.6 / 0–8	0.01 / <0.0001
Weight loss (κ = 0.64)	38	23 / 144	14.3 / 42–395	29 / 1	13.2 / 0–1	0.76 / <0.0001
Clues with fair or moderate agreement between reviewers (κ between 0.20 and 0.60)						
History of previous polyps (κ = 0.50)	61	10 / 663	6.2 / 277–977	11 / 0	5.0 / 0–8	0.65 / <0.001
Abdominal pain (κ = 0.49)	61	29 / 140	18.0 / 58–333	34 / 1	15.5 / 0–3	0.58 / <0.0001
Melena (κ = 0.48)	1	1 / 482	0.62 / 482–482	12 / 0	5.5 / 0–1	0.01 / 0.09
Other suspicious lower GI symptoms (κ = 0.45)	38	15 / 414	9.3 / 64–658	14 / 1	6.4 / 0–31	0.33 / 0.002
Change in stool caliber (κ = 0.39)	0	0 / n/a	0 / n/a	4 / 0	1.8 / 0–1	0.14 / —[f]

[a] Kappa (κ) is calculated using all 381 patients.

[b] Fisher's exact test was used to test for differences in proportions of patients with a given clue. The nonparametric Wilcoxon's continuity-corrected normal approximation two-sample test was used to test for differences in days until first referral.

[c] The percentage of the 161 patients with a missed opportunity who had the given clue.

[d] The percentage of 220 patients without a missed opportunity who had the given clue.

[e] IQR: interquartile range.

[f] Median times could not be compared because there were no patients with missed opportunities.

Table 4

Characteristics and number of missed opportunities that arose directly from provider–patient encounters

Level of process breakdown	Number of patients	Number of missed opportunities	Most common settings	Most common clinical clues involved	Most common personnel involved	Most common contributory factors
Medical history deficient	50	100	Provider Office (90), Inpatient (7), Emergency Room (3)	Anemia (65), FOBT + (18), Hematochezia (12)	Primary care (58), Physician assistant (20)	*Provider:* Deficient recording of critical history data (101) *Patient:* None
Physical examination deficient	64	125	Provider office (107), Inpatient (15), Emergency room (3)	Anemia (73), Worsening constipation (20), Hematochezia (9)	Primary care (67), Physician assistant (24)	*Provider:* Deficient recording of critical examination data (126) *Patient:* Declined (8)
Diagnostic/laboratory tests (delayed/not ordered)	59	116	Provider office (90), Inpatient (20), Emergency room (4), Radiology (2)	Anemia (80), Hematochezia (12), FOBT + (8)	Primary care (63), Physician assistant (19)	*Provider:* Apparent lack of awareness that subsequent diagnostic testing was required (115), Apparent lack of knowledge (35) *Patient:* Patient declined (3)
Consult delayed or not requested	130	389	Provider office (320), Inpatient (41), Emergency Room (17)	Anemia (187), FOBT + (74), Previous polyps (58), Hematochezia (49), Worsening constipation (40)	Primary Care (203), Physician Assistant (77), Patient (23), Geriatrics (18), Emergency Medicine (11)	*Provider:* Apparent lack of awareness that subsequent referral was required (341) *Patient:* Declined (68), Cancelled appt (39), Missed appt (12)

Table 5

Characteristics and number of missed opportunities that arose directly from diagnostic test result–related factors

Level of process breakdown	Number of patients	Number of missed opportunities	Most common setting	Most common clues	Most common personnel involved	Most common contributory factors
Diagnostic/ laboratory test ordered but not performed	36	53	Provider office (33)	Anemia (29)	Nurse (17)	*Provider:*
			Radiology (14)	Abdominal pain (9)	Primary Care (12)	No tracking mechanism for orders (26)
			Patient's home (3)	Hematochezia (8)	Radiology (11)	Provider unaware test not performed (18)
				FOBT + (7)	Patient (8)	*Patient:*
			Inpatient (2)			Cancelled appt (5)
						Missed appt (4)
Diagnostic/ laboratory test not performed correctly	6	7	Radiology (3)	Anemia (2)	Radiology (4)	*Provider:*
			Provider office (2)	FOBT + (2)		Incomplete test due to poor bowel prep (11)
				Rectal mass (2)		*Patient:*
			Inpatient (1)	Hematochezia (1)		None
Diagnostic/ laboratory tests not interpreted correctly	11	13	Provider office (10)	Anemia (8)	Physician assistant (5)	*Provider:*
			Inpatient (2)	FOBT + (3)	Primary care (4)	Misinterpretation of test results (10)
			Radiology (1)	Barium enema + (1)		*Patient:*
						None

Table 6

Characteristics and number of missed opportunities that arose directly from follow-up-related factors

Level of process breakdown	Number of patients	Number of missed opportunities	Most common setting	Most common clues	Most common personnel involved	Most common contributory factors
Diagnostic/ laboratory results not followed up	60	97	Provider office (91)	Anemia (62)	Primary care (38)	*Provider:* No evidence of follow-up despite post-test visit (81)
			Emergency room (3)	FOBT + (28)	Physician assistant (22)	Failed transmission of result to clinician (16)
						Inadequate test-result tracking system (14)
			Inpatient (3)			*Patient:* Missed/cancelled appt (4)
Problems with follow-up plans	27	37	Provider office (26)	Anemia (14)	Patient (11)	*Provider:* Provider selected wrong interval for follow-up (13)
			Patient (9)	FOBT + (8)	Primary Care (10)	Follow-up appt not scheduled (11)
			Emergency room (1)	Abdominal pain (7)	Physician assistant (7)	*Patient:* Missed/cancelled appt (18)