RESEARCH

Systematic analysis of missed colorectal cancer cases and common pitfalls in diagnosis

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/flgastro-2014-100513>).

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Previous communications (poster presentation) to Association of Coloproctology of GB & Ireland Annual Meeting 1–3 July 2013, Association of Surgeons of Great Britain and Ireland Annual Meeting 1–3 May and British Society of Gastroenterology Annual Meeting, 16–19 June 2013.

Received 11 August 2014
Revised 5 December 2014
Accepted 16 December 2014
Published Online First
28 January 2015

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To cite: Vaughan-Shaw PG, Aung M, Knight H, et al. *Frontline Gastroenterology* 2015;6:232–240.

ABSTRACT

Background Missed colorectal cancer on endoscopic or radiological investigations may delay diagnosis and impact outcome. This study audits incidence of previous investigations in patients with colorectal cancer, considers outcome in 'missed' cancer cases and examines the diagnostic pathway in the derived case series to identify common pitfalls in diagnosis.

Methods Patients diagnosed with colorectal cancer in 2011 at a single National Health Service (NHS) Trust were reviewed. Incidence of endoscopic and radiological investigations in the 3 years preceding diagnosis and outcome data were collected. Cases of prior investigation not leading to diagnosis were considered 'missed' cancers and survival compared with 'detected' cases. The diagnostic pathway in each 'missed' case was reviewed.

Results 395 colorectal cancer cases were studied. Eighteen (4.6%) patients underwent previous investigation including colonoscopy (n=4), flexible sigmoidoscopy (n=5), barium enema (n=5) and diagnostic abdominal CT scan (n=12), median 708 days prior to diagnosis. Previous investigation predicted reduced overall and disease-free survival (HR 2.07, p=0.04 and HR 2.66, p<0.0001), after age and gender adjustment. Ten different categories termed 'pitfalls' were derived from analysis of the diagnostic pathway. These included CT scanning for abdominal pain without further investigation (n=7), rectosigmoid cancer following a previous diagnosis of diverticular disease (n=4) and incomplete diagnostic investigations without adequate follow-up (n=3).

Conclusions A proportion of patients diagnosed with colorectal cancer have previously been investigated for gastrointestinal symptoms and survival appears reduced in these patients. Regular audit and analysis of previous investigations can identify common pitfalls in

diagnosis, which should be used to inform training and improve practice.

INTRODUCTION

Colorectal cancer (CRC) is the second commonest cause of cancer death in the UK. Large population-based studies have demonstrated higher mortality from CRC in the UK when compared to mean survival in Europe with later presentation and more advanced stage at diagnosis possible causative factors.^{1 2} While colonoscopy remains the gold standard diagnostic investigation for patients with lower gastrointestinal (GI) symptoms,^{3–6} other endoscopic or radiological investigations such as flexible sigmoidoscopy or CT scanning may be widely available and are increasingly utilised, particularly in the acute setting. Quoted false-negative rates for adenoma and CRC detection on colonoscopy vary widely in the international literature, yet approach 40% for small adenomas⁶ and 4–6% for CRCs.^{4 5} Reasons for missed lesions include incomplete colonoscopy, insufficient withdrawal time,^{7 8} poor bowel preparation⁹ or inadequate biopsy technique.⁴

While other endoscopic or radiological investigations may be more readily available, limitations exist; flexible sigmoidoscopy fails to visualise the proximal colon, while CT (in the absence of bowel preparation) will not reliably detect mucosal lesions <1.5 cm.¹⁰ It is important therefore that such investigations are not seen as an alternative to colonoscopy where CRC is considered. However, the choice of investigation in the path towards diagnosis is not always obvious, especially where failed investigations or equivocal results are encountered. Evidence on missed cancers

frequently comes from large population studies,^{5 11–13} yet patient-based studies may offer greater utility to the individual clinician in allowing case-by-case qualitative analysis, thereby identifying common pitfalls within the diagnostic pathway that may result in a missed cancer.

This study aims to identify the incidence of previous investigations in patients diagnosed with CRC in our trust and, using the derived case series, considers common scenarios resulting in delayed diagnosis.

PATIENTS AND METHODS

A retrospective comparative cohort study was performed within a single National Health Service (NHS) Trust in order to derive a case series of missed CRC cases. All resection or biopsy specimens demonstrating colorectal adenocarcinoma for the 12-month period, January–December 2011, were identified. Patients with CRC were cross-referenced against endoscopic and radiological investigation for the preceding 3 years. Data on presenting symptoms, the diagnostic pathway and clinical outcomes were collected from endoscopy and picture archiving and communications systems, and clinical case notes. In patients who underwent multiple investigations, delay to diagnosis was calculated from date of latest investigation prior to diagnosis, to date of diagnosis. The study was approved by the local clinical audit department.

Sample size

The sample size was defined by the study duration, a 12-month period. A 3-year period prior to diagnosis was chosen, given the known history of colorectal polyps and adenoma-carcinoma sequence.

Quantitative outcomes and statistical analysis

The primary quantitative outcome of interest was incidence of ‘missed’ cancer. ‘Missed’ cancer cases were those who underwent previous investigations (including colonoscopy, barium enema, flexible sigmoidoscopy or prepared/unprepared abdominal CT scan) for GI symptoms that did not lead to a diagnosis of CRC. Incidence of patients undergoing previous colonoscopy and/or barium enema was also examined. Overall and disease-free survival was compared between ‘missed’ and ‘detected’ cancer cases. Disease-free survival was defined as survival in the absence of CRC local recurrence or metastasis. Unless otherwise stated, results are presented as median (IQR) with CIs for HRs given as (95% CI). Data were stored in Excel (Microsoft Inc, Seattle, Washington, USA) and analysed using Microsoft Excel, Prism 3.03 (GraphPad Software Inc, La Jolla, California, USA) and SPSS V22.0 (SPSS Inc, Chicago, Illinois, USA). Descriptive statistics were derived using Excel and PRISM. Univariate analysis using the Mann-Whitney test and χ^2 test without Yates correction was performed to identify significant variables between patients with or without previous investigations. Survival analysis to compare those with and

without previous investigations was undertaken using the Cox regression model and HRs derived. Adjustment for age and gender was undertaken using a multivariate Cox regression (step-wise forward) model.

Qualitative assessment

Data relating to symptoms and investigations were analysed separately by two authors (PGV-S, JMDW; see online supplementary table S1) through a systematic analysis by coding and categorising. No ‘a priori’ hypotheses or predetermined categories were applied to the analysis. An observation was made describing each diagnostic pathway, taking into account symptoms, age, investigation results and interval between investigations and these observations were categorised. An iterative approach was applied to derive new categories (in this study termed ‘pitfalls’), which were constantly compared to previously analysed data in a cyclical process until saturation (ie, if a new ‘pitfall’ is identified in one patient, all data previously analysed were reanalysed to identify further examples of this pitfall).¹⁴ Learning points were formulated to accompany each pitfall through discussion between two authors (JMDW and PGV-S) using recognised guidance from the British Society of Gastroenterology¹⁵ as well as the clinical experience of the two authors.

RESULTS

In total, 621 pathology specimens (biopsy or resection) with colorectal adenocarcinoma were identified from 434 patients. Thirty-three patients who were private patients or out of region for whom previous investigations could not be accessed were excluded. One patient had been diagnosed on a previous CT but had declined treatment and a further five patients with a new diagnosis of CRC and previous history of CRC were excluded. In total, 395 patients were included for analysis with follow-up of 702 (617–830.5) days.

‘Missed’ cancers

Eighteen patients (4.6%) had undergone previous investigations for GI symptoms over the preceding 3 years, a median 708 (353.5–921.25) days from diagnosis. In total, 27 investigations had been performed in these patients within 3 years with 4 colonoscopies (1%), 5 barium enemas (1%), 5 flexible sigmoidoscopies (1%) and 12 CT scans (3%; without bowel preparation). No patient in this cohort underwent CT colonography (CTC; ie, with bowel preparation). Details of each ‘missed’ case are given in [table 1](#).

Demographics, tumour site and stage, and routes to diagnosis, were compared between ‘missed’ and ‘detected’ cancer cases, and are displayed in [table 2](#).

Cancers and clinical outcome following negative colonoscopy or barium enema

Gender, age, cancer side (right or left), pT and pN were comparable between those with a previous

Table 1 Investigations and outcome in 'missed' cancer cases

Patient	Age	Investigations	Indication	Result	Days to diagnosis	Site	pT	pN	M	Outcome	Cause of death	Days from diagnosis to death/follow-up
1	81	Barium enema	RIF pain and abdominal mass	NAD	1081	Rectum	2	0	0	Died	Stroke	281
2	57	Flexible sigmoidoscopy	PR bleeding	NAD	1009	Ascending colon	4	0	0	Died	Metastatic CRC	271
3	84	Flexible sigmoidoscopy	PR bleeding	Poor views, DD	987	Sigmoid colon	4	2	0	Died	Metastatic CRC	502
4	59	CT	LUQ pain	NAD	977	Ascending colon	4	2	1	Metastatic cancer	—	761
5	67	Barium enema	CIBH	NAD	930	Sigmoid colon	NR	—	1	Died	Metastatic CRC	328
6	76	CT	RUQ pain	DD	895	Sigmoid colon	3	0	0	Disease-free	—	627
7	67	CT	RUQ pain	DD	832	Ascending colon	3	0	0	Disease-free	—	877
8	73	CT Barium enema	Abdominal pain CIBH	DD	773	Hepatic flexure	4	2	1	Died	Metastatic CRC	187
9	89	CT	LUQ pain	DD	770	Rectum	3	0	0	Progression	—	330
10	87	CT	RUQ pain	Cholecystitis	646	Sigmoid colon	3	0	0	Progression	—	422
11	77	Flexible sigmoidoscopy	PR bleeding	NAD	644	Rectum	NR	—	1	Metastatic cancer	—	740
12	84	CT then colonoscopy	Anaemia, weight loss, CIBH	DD stricture	532	Sigmoid colon	4	0	0	Died	Metastatic CRC	504
13	78	Colonoscopy then barium enema then CT	CIBH	Failed colonoscopy, caecal mass on barium enema. Caecal lipoma on CT	496	Ascending colon	2	0	0	Progression	—	627
14	76	Colonoscopy	Anaemia and CIBH	Polyyps on colonoscopy. CT NAD	306	Sigmoid colon	NR	—	1	Died	Metastatic CRC	648
15	61	Flexible sigmoidoscopy then CT	Abdominal pain	NAD	255	Ascending colon	2	0	0	Disease-free	—	668
16	91	Flexible sigmoidoscopy CT	Anaemia Abdominal pain	Flexible sigmoidoscopy performed instead of colonoscopy as oral preparation not tolerated. NAD	217	Ascending colon	4	0	0	Died	Unknown	111
17	77	CT	CIBH, anaemia	NAD	208	Caecum	4	0	1	Metastatic cancer	—	825
18	76	CT then colonoscopy then barium enema	CIBH and abdominal pain	CT NAD Colonoscopy and barium enema incomplete (not tolerated)	99	Splenic flexure	4	1	1	Died	Metastatic CRC	652

CIBH, change in bowel habit; CRC, colorectal cancer; DD, diverticular disease; NAD, no abnormality detected; LUQ, left upper quadrant; PR, per rectal; RIF, right iliac fossa; RUQ, right upper quadrant.

Table 2 Demographics and outcome in patients with 'missed' and 'detected' colorectal cancer

	All patients	Previous colon/BaE			Any previous investigation, 'missed' cases		
		No	Yes	p Value	No	Yes	p Value
n	395	387	8 (2.1%)	–	377	18 (4.6%)	–
Age (median)	72 (62.5–79)	72	76.5	0.15	72	76.5	0.07
Male	213 (54%)	211 (55%)	2 (25%)	0.15	209 (55%)	4 (22%)	0.007
Referral route							
2ww	208 (53%)	203 (52%)	5 (63%)	0.73	196 (52%)	12 (67%)	0.23
Emergency	67 (17%)	66 (17%)	1 (13%)	1.00	64 (17%)	3 (17%)	1.00
BCSP	47 (12%)	47 (12%)	0	0.60	47 (12%)	0	0.15
Routine referral	30 (8%)	30 (8%)	0	1.00	30 (8%)	0	0.38
Other	43 (11%)	41 (11%)	2 (25%)	0.21	40 (11%)	3 (17%)	0.43
Tumour site							
Right sided	131 (33%)	129 (33%)	2 (25%)	1.00	123 (33%)	8 (44%)	0.31
Tumour grade							
Well differentiated	26 (6%)	26 (7%)	0	1.00	26 (7%)	0	0.62
Moderately differentiated	312 (79%)	305 (79%)	7 (88%)	1.00	295 (76%)	17 (94%)	0.14
Poorly differentiated	56 (15%)	55 (14%)	1 (13%)	1.00	55 (14%)	1 (6%)	0.49
Not available	1 (<1%)	1 (<1%)	0	–	1 (<1%)	0	–
Tumour staging							
pT (median)	3	3	4	0.62	3	4	0.21
pN (median)	0	0	0	0.92	0	0	0.36
M1	63 (16%)	58 (15%)	5 (63%)	0.003	56 (15%)	7 (39%)	0.01
Disease-free survival at follow-up	253 (70%)	252 (65%)	1 (13%)	<0.001	250 (66%)	3 (17%)	<0.0001
Survival at follow-up	310 (78%)	308 (80%)	2 (25%)	0.001	301 (80%)	9 (50%)	0.007

Statistical tests used: χ^2 test and Fisher exact test for proportions, Mann-Whitney U test for continuous and categorical variables, Cox regression test used for survival outcomes.

2ww, two-week wait; BaE, barium enema; BCSP, bowel cancer screening programme.

negative colonoscopy or barium enema, and those with no previous colonic investigation (table 2). However, there was an increase in proportion of patients with metastases on presentation (63% vs 15%, $p=0.003$) and a reduced overall survival (25% vs 80%, HR 4.1 (1.8 to 9.3), $p=0.001$; table 3) and

disease-free survival from diagnosis (13% vs 65%, HR 3.7 (1.8 to 7.5), $p<0.0001$).

Cancers and clinical outcome following any abdominal investigation

Tumour stage and side were comparable between those with any previous investigation and those with no prior investigations (table 2), while cancers presenting following abdominal investigation were more common in females (78% vs 45%, $p=0.007$). Advanced disease (proportion of patients with metastases at presentation) was more common in previously investigated patients (39% vs 15%; $p=0.01$). Survival at follow-up was reduced in those with previous investigations (50% vs 80%, HR 2.6 (1.3 to 5.2), $p=0.007$; table 3) as was disease-free survival (17% vs 66%, HR 3.0 (1.8 to 5.1), $p<0.0001$).

Other variables associated with overall survival

Increased age, emergency presentation, patients not in the national screening programme, increasing pT or pN stage and presence of metastases at presentation were also associated with reduced overall survival on unadjusted analysis (table 3), yet gender, referral via the 2-week wait rule and cancer side were not.

Table 3 Factors predicting reduced overall survival

	Univariate hazard ratio (95% CI)	p Value
Previous colonoscopy/barium enema	4.05 (1.76 to 9.29)	0.001
Previous investigation	2.58 (1.29 to 5.15)	0.007
Increasing age	1.05 (1.03 to 1.07)	<0.0001
Male	0.99 (0.65 to 1.5)	0.96
Emergency presentation	2.58 (1.62 to 4.09)	<0.0001
BCSP	0.16 (0.04 to 0.66)	0.01
2ww	1.05 (0.69 to 1.61)	0.82
Right-sided cancer	1.30 (0.84 to 2.00)	0.24
pT	2.26 (1.51 to 3.29)	<0.0001
pN	1.63 (1.20 to 2.20)	0.002
Metastases at presentation	6.05 (3.91 to 9.37)	<0.0001
Tumour differentiation grade	1.81 (1.15 to 2.85)	0.01

Statistical tests used: Cox regression test.

2ww, two-week wait; BCSP, Bowel cancer screening programme.

Adjusted medium-term disease-free and overall survival

On adjustment for age and gender, previous colonoscopy or barium enema remained a significant predictor of survival (HR 3.24 (1.41 to 7.44), $p=0.006$) and disease-free survival (HR 3.08 (1.50 to 6.33), $p=0.002$). The presence of any previous investigation also remained a significant yet weaker predictor of survival (HR 2.07 (1.03 to 4.15), $p=0.04$) and disease-free survival (HR 2.66 (1.55 to 4.57), $p<0.0001$; figure 1A–D).

Identification of pitfalls through qualitative analysis

The case series of 18 ‘missed’ cancers were systematically analysed. Ten different categories termed ‘pitfalls’ were derived from observations of the diagnostic pathway by the iterative quantitative analysis (see online supplementary table S1 and table 4). The commonest ‘pitfall’ was ‘CT performed for abdominal pain’ with further investigations performed in only one of these eight patients. The learning point derived from this ‘pitfall’ is that where CT is performed for abdominal pain, follow-up review or investigations may be indicated. A patient with acute abdominal

pain on a background of a persistent change in bowel habit (ie, diarrhoea or constipation), may require a CT of the abdomen and pelvis, yet colonoscopy would also be indicated. Another common ‘pitfall’ was rectal or sigmoid cancer was diagnosed following a finding of diverticular disease (DD) on previous investigations ($n=4$). The learning point derived was that DD may mask endoscopic or radiological appearances of CRC while CRC symptoms may be incorrectly blamed on DD. Therefore, in a patient with proven DD, it is important not to attribute all symptoms to the DD without appropriate investigations, for example, colonoscopy $\pm$ biopsies.

Given the small number of patients included, it was not possible to comparatively assess the effects of each pitfall in relation to clinical outcome.

DISCUSSION

This study demonstrates that a small proportion of patients (4.6%) diagnosed with CRC have been investigated for GI symptoms in the previous 3 years and that clinical outcome appears significantly reduced in such patients. A number of common ‘pitfalls’ occur

Figure 1 (A) Overall survival in patients with and without previous colonoscopy or barium enema. (B) Disease-free survival in patients with and without previous colonoscopy or barium enema. (C) Overall survival in patients with and without any abdominal investigations. (D) Disease-free survival in patients with and without any abdominal investigations.

Table 4 Categorisation of patients with previous investigations and outcome diagnosed within 3 years of that investigation

Pitfall	N	Days to diagnosis	Age	Site of tumour	Outcome	Learning point
Cancer diagnosed unlikely to reflect initial symptoms	2	1045	69	Rectum (n=1), ascending colon (n=1)	Died (n=2)	Patients should be reassured that their cancer is unlikely to be related to historical symptoms or missed by historical investigations where appropriate
Incomplete investigation, no further Ix	3	217	84	Sigmoid (n=1) Ascending (n=1) Splenic flexure (n=1)	Metastases on presentation (n=1), died (n=3)	If appropriate investigations are not tolerated or incomplete, repeat procedures with alternative preparation and/or general anaesthesia should be considered
CT performed for abdominal pain	8	708	73	Transverse (n=1) Ascending (n=4) Sigmoid (n=2) Rectum (n=1)	Metastases on presentation (n=2), died (n=2), disease progression (n=2), disease-free (n=4)	Where CT is performed for acute abdominal pain, follow-up investigation may be indicated (eg, colonoscopy is indicated if CIBH exists)
Normal barium enema, no further Ix	2	1005.5	74	Sigmoid (n=1) Rectum (n=1)	Metastases on presentation (n=1), died (n=2)	Barium enema is associated with a small miss-rate for CRC. Where symptoms persist, repeat or alternative investigations should be arranged
DD on investigation and sigmoid or rectal cancer	4	770	84	Sigmoid (n=3) Rectum (n=1)	Disease progression (n=1), disease-free (n=3)	DD may mask endoscopic or radiologic appearances of CRC while CRC symptoms may be incorrectly blamed on DD. Colonoscopy or barium enema is recommended after acute diverticulitis (ACPGBI position statement)
Rectosigmoid cancer after previous flexible sigmoidoscopy	2	644	77	Rectum	Metastases on presentation (n=1), died (n=1)	Flexible sigmoidoscopy is associated with a small miss-rate for CRC. Where symptoms persist, repeat or alternative investigations should be arranged
CT performed for CIBH	4	401	77	Caecum (n=1) Transverse (n=1) Sigmoid (n=2)	Metastases on presentation (n=2), died (n=3), disease-free (n=1)	Unprepared CT is not the first-line investigation in patients with CIBH
Equivocal endoscopic and/or radiological appearances	1	496	78	Caecum	Disease progression	Histological diagnosis should be sought wherever possible. If necessary, endoscopic procedure under GA or combined diagnostic endoscopic/laparoscopic procedure should be considered
Normal colonoscopy	2	507.5	80	Sigmoid (n=2)	Metastases on presentation (n=1), died (n=2)	Colonoscopy is associated with a small miss-rate for CRC. Where symptoms persist, repeat or alternative investigations should be arranged
Flexible sigmoidoscopy performed for abdominal pain	1	352	61	Ascending	Caecal cancer, disease-free	Flexible sigmoidoscopy is not indicated in isolated abdominal pain

ACPGBI, Association of Coloproctology of Great Britain and Ireland; CIBH, change in bowel habit; CRC, colorectal cancer; DD, diverticular disease; GA, general anaesthetic.

within these patients. The case-based approach applied here, which looks beyond purely quantitative outcomes, has enabled the derivation of relevant learning points that should be used to inform future management of patients with GI symptoms and reduce the incidence of missed cancer. This analysis highlights the advantage of audit and case-based analysis over population-based approaches in informing practice and training.

In our cohort, only 2% of patients had undergone previous colonoscopy *and/or* barium enema. A similar study by Somasekar *et al*,¹⁶ found that 56 (10%) patients with a diagnosis of CRC had undergone barium enema (5%) or colonoscopy (5%) in the preceding 5 years. Another study by Frenette and Strum¹⁷ reported a failure of diagnosis in 60 (16%) patients who had undergone colonoscopy, barium

enema or flexible sigmoidoscopy in the preceding 3 years. Our results are significantly lower than the cohorts of Somasekar and Frenette ($p < 0.005$, χ^2 test), and suggest a low 'miss-rate' for CRC with these investigations within our unit. While the sample size precludes firm conclusions to be drawn, such a finding may represent improved sensitivity of such investigations, perhaps due to an improvement in training, performance and equipment, over time. The reduction in 'missed' cancers may also reflect a decreasing threshold for repeating investigations¹⁸ or performing alternative investigations, and coincides with an increasing availability of endoscopic and radiological investigations over the last decade in the UK. Indeed, three of the four patients who had a colonoscopy in our study had a subsequent CT and/or barium enema within 2 months of that colonoscopy.

Unlike previous studies, we have considered abdominal CT scans for abdominal symptoms as a previous investigation of interest. We fully acknowledge that unprepared CT is not an appropriate investigation for suspected CRC, while abdominal pain is not a predicting feature of malignant disease.¹⁹ However, analysis of this cohort was undertaken to identify episodes of incorrect investigation choice or follow-up. In this study, 12 patients diagnosed with CRC had undergone an unprepared abdominal CT scan for abdominal symptoms in the preceding 3 years. Of these, four also underwent colonoscopy or barium enema. We acknowledge that the incidence of acute hospital admissions (eg, with diverticulitis) and the use of CT scanning is high in this age group, which may explain the high number of CT scans in this cohort. Nevertheless, the learning point derived from this observation is that unprepared CT is not the first-line investigation for patients with a change in bowel habit, while in patients with acute abdominal pain, follow-up investigations may be required (eg, in diverticulitis, as discussed below). CTC, although not encountered in our cohort, is now widely used for patients with GI symptoms and may have utility in patients with both abdominal pain and 'soft' GI symptoms in the acute and elective setting. Of note, colonic insufflation is not appropriate where luminal perforation is suspected, while the delay required for bowel preparation may preclude CTC in an acutely unwell patient.

This study highlights the role of audit in everyday practice. Auditing the incidence of lower GI or abdominal investigations preceding a final diagnosis of CRC has three roles: first, it should be used as a measure of quality assurance for the performance of individual investigations and overall management of patients with lower GI symptoms (eg, choice of investigation, multidisciplinary team (MDT) performance and level of follow-up). Such clinician or unit performance indicators may soon become available to patients and inform patient choices or perhaps even indemnity premiums. Second, the outcome in such patients should be used to emphasise findings and drive improvement through training or resource allocation. Finally, common pitfalls and learning points can be identified, and should be used to inform training and ultimately improve care.

This study also demonstrates the role of case-based analysis. While population studies can report on large numbers and produce strong statistical evidence for a multitude of outcomes, patient-based studies may offer greater utility in allowing case-by-case analysis with a more formative approach, as has been performed here. This study is the first to apply a systematic qualitative and reflective approach to the CRC diagnostic pathway in order to identify common categories of scenario (termed here 'pitfalls'), and derive learning points. For example, this analysis found that cancers were most commonly diagnosed after a CT

performed for abdominal pain (n=8) or after any investigation reporting diverticular disease (n=4). This finding highlights the importance of eliciting all relevant symptoms when assessing an acute admission, and the need for caution when assessing and investigating potential CRC symptoms in patients with diverticulitis. While the incidence of DD in this age group may explain our finding, it has previously been shown that there is an increased incidence of CRC diagnosis within a year of diagnosing DD, indicating that the misclassification does occur.^{20 21} This finding therefore supports the current guidelines; the Association of Coloproctology of Great Britain and Ireland, and the American Society of Colon and Rectal Surgeons, both recommend that endoscopic evaluation be undertaken after resolution of acute diverticulitis to rule out alternative diagnoses or second pathologies,^{22 23} although some argue this as being unnecessary.²⁴

We acknowledge that the derived learning points may be considered obvious or onerous. The reinvestigation of every patient with a negative colonoscopy and persisting symptoms would require significant resources, and risks the complications associated with repeated invasive tests. Nevertheless, these findings should act to discourage the ignoring of symptoms in the light of a normal investigation. Furthermore, some of the learning points can be seen to reaffirm existing guidelines while others indicate the need for further guidance, for example, on follow-up of patients with acute abdominal pain and management of patients with equivocal biopsies.

This study achieved its aims: to identify the incidence of previous investigations in patients diagnosed with CRC in our trust, the impact of a potential delay on patient outcome and to identify common pitfalls that may lead to missed cancers. We acknowledge that the numbers of patients with previous investigations are small, introducing the possibility of type II statistical error and precluding a comparative analysis of individual tests. However, the size of this study has allowed case-by-case analysis, which is impossible in large population-based studies, and which has enabled the identification of common pitfalls and associated learning points that we believe are relevant to numerous patients across the UK and wider developed world. We also acknowledge that lead-time bias may account for a proportion of the reduced survival seen in those with previous investigations. Finally, the incidence of previous barium enema was investigated and discussed, yet is now rarely performed given the higher sensitivity²⁵ and increasing availability of CTC. While no patient in this series underwent CTC, it is now increasingly relevant to the elective investigation of lower GI symptoms, and may also have utility in patients with acute abdominal pain and 'soft' bowel symptoms. Future analysis should therefore consider

indications and performance of CTC, within the elective as well as acute setting.

CONCLUSIONS

This study demonstrates that a small proportion of patients diagnosed with CRC had been previously investigated for GI symptoms. Previous investigation predicts advanced disease at diagnosis and reduced survival. Common pitfalls that may lead to missed cancer should be recognised and approached with increased vigilance. Clinicians must ensure all symptoms are elicited to ensure appropriate investigations are undertaken, and consider repeat or alternative investigations and the input of the MDT where results are equivocal or symptoms persist. Finally, regular audit and qualitative analysis of previous investigations should be considered as a tool to inform training and improve practice.

Significance of this study

What is already known on this topic?

Some patients diagnosed with colorectal cancer have been previously investigated for lower gastrointestinal symptoms and may be considered 'missed cancers'.

What this study adds?

Many studies that investigate missed colorectal cancer are population-based approaches. This study is a case-based systematic analysis of previous investigations and the diagnostic pathway in missed cancer cases, and demonstrates the added value of patient-based studies in the investigation of this important topic.

How might it impact on clinical practice in the foreseeable future?

The framework and results from this study may be used alongside population-based approaches to identify pitfalls in colorectal cancer diagnosis and these should be used to inform training, practice and guidelines.

Acknowledgements The authors thank Professor JM Blazeby (Professor of Surgery, School of Social and Community Medicine, University of Bristol) for her critical appraisal of the manuscript and Lisa Richardson for administrative assistance in data collection.

Contributors PGV-S was involved in conception and design, acquisition of data, analysis and interpretation of data; drafting the article, revising it critically for important intellectual content. MA was involved in acquisition of data, or analysis and interpretation of data. HK and TW were involved in acquisition of data. NRB was involved in revising manuscript for important intellectual content. JMDW was involved in conception and design, analysis and interpretation of data; drafting the article and revising it.

Competing interests None.

Ethics approval Gloucestershire NHS Trust Clinical Audit Department.

Provenance and peer review Not commissioned; externally peer reviewed.

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