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Multicentre Study of 10,369 Symptomatic Patients Comparing the Diagnostic Accuracy of Colon Capsule Endoscopy, Colonoscopy and CT Colonography

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ABSTRACT

Background: During the COVID-19 pandemic, NHS England introduced colon capsule endoscopy (CCE) at scale to support the recovery of endoscopy. Symptomatic patients referred with suspected colorectal cancer (CRC) and a faecal immunochemical test (FIT) ≤ 100 μg Hb/g faeces were offered CCE.

Aims: To evaluate the safety, diagnostic accuracy and utility of CCE in this setting.

Methods: Consenting patients, referred on a suspected CRC pathway with FIT ≤ 100 μg Hb/g faeces, were offered CCE, colonoscopy or CT colonography. Each cohort was to be age-, sex-, symptom- and FIT-matched. We performed a paired comparison of findings in those who required colorectal endoscopy after CCE and recorded clinical outcomes.

Results: We recruited 4878 patients for CCE, 5025 for colonoscopy and 466 for CT colonography patients. CCE was safely tolerated by 98.4% of patients. CCE identified a matched mass lesion in all patients with CRC when the examination was complete and adequately prepared. More polyps ≥ 10 mm and 6–9 mm were detected by CCE than by colonoscopy or CT colonography. Per-patient sensitivities for polyps ≥ 10 mm and 6–9 mm were 97% in those with a paired, complete and adequately prepared CCE than colonoscopy. Completion (74%) and bowel preparation adequacy rates (74%) were poorer than those of colonoscopy and CTC (both 88%). However, CCE usefully performed a filter function in 86% of patients.

Conclusions: CCE is safe and accurate for the diagnosis of colorectal disease. In the suspected CRC pathway, its 'filter function' complements existing colorectal diagnostic services by creating additional capacity.

1 | Background

Colonoscopy is the accepted gold standard for colorectal investigation and diagnosis of suspected colorectal cancer (CRC), pre-malignant polyps and inflammation [1–3]. It is an invasive test, which carries small risks of bleeding, perforation and infection that are cumulative in patients who have lifetime surveillance procedures [4–7]. Sedo-analgesia is routinely offered to improve patient experience and allay anxiety, embarrassment and discomfort but has to be balanced against the risks

of cardiopulmonary and cerebrovascular complications [8–12]. It is a resource-intense procedure performed by highly trained endoscopists with support staff and facilities to monitor and recover patients. Yet most procedures are normal or identify incidental findings unrelated to the patients' symptoms [3, 13, 14]. Sometimes a colonoscopy cannot be adequately completed, and whilst quality and safety parameters in colonoscopy have been developed, significant disease can be missed [4].

Colonoscopy also delivers colorectal therapeutics, such as polypectomy; however, in the UK, the major demand for colonoscopy is as a diagnostic tool [3, 13, 14]. Since the COVID-19 pandemic, the demand for diagnostic colonoscopy has continued to increase and exceeds the capacity available to meet the targets for timeliness in CRC and inflammatory bowel disease (IBD) diagnosis [15–21]. This places patients at risk [15, 19, 20]. Computed tomography (CT) colonography is an alternative colorectal diagnostic providing additional capacity. It involves the use of low-dose ionising radiation and is generally reserved for frailer patients in whom colonoscopy cannot or should not be performed [22, 23].

Colon capsule endoscopy (CCE) is non-invasive, and some studies suggest that it causes less procedure-related distress than colonoscopy, is more acceptable to, and preferred by patients [24–26]. Patients do not require sedation or monitoring, and it can be performed in a community setting or in the home [23, 27–29]. It has a published sensitivity of 87%–88% in the detection of polyps ≥10 mm [30–32]. To date, no large population-based studies of symptomatic patients have been performed [33].

The UK National Institute for Health and Care Excellence recommends that symptomatic patients who have a faecal immunochemical test (FIT) ≥10 μg Hb/g faeces be referred for urgent colonoscopy or CT colonography [34]. However, practices introduced to minimise the risks of disease transmission during the COVID-19 pandemic put major constraints on access to colonoscopy and radiology services, with all but urgent and emergency procedures being suspended [19, 35]. During the recovery phase from the pandemic, NHS England recommended that urgent colonoscopy (and CT colonography) should be prioritised for those with a high CRC risk (FIT > 100 μg Hb/g). To minimise the risk of delayed CRC diagnoses in those with an intermediate risk (FIT 10-100 μg Hb/g) NHS England supported the development of CCE services to increase diagnostic capacity and mitigate pressures on colonoscopy units [35–37]. The widespread introduction of CCE across England permitted a large, observational diagnostic accuracy study to be conducted.

2 | Methods

2.1 | Patients and Study Design

The inclusion criteria were those patients aged 18 years and over, with a FIT ≤100 μg Hb/g faeces and who were referred for the investigation of suspected CRC by CCE, colonoscopy or CT colonography. The initial intermediate risk range was later extended to include patients with FIT <10 μg Hb/g faeces to allow flexibility for centres to offer CCE to lower-risk referred patients, least likely to need subsequent colonoscopy. There were no formal exclusion criteria. Instead, CCE selection guidance was provided to clinicians by an expert advisory group (EAG). This stated that patients with dysphagia, stricturing Crohn's disease, long-term daily use of non-steroidal anti-inflammatory drugs, prior abdominopelvic irradiation and during pregnancy may be more suitable for an alternative investigation. Pre-assessment using radiological imaging or a patency capsule was suggested for those at risk of capsule retention. The EAG also advised that patients with significant co-morbidity, the use of opioid or tricyclic antidepressant medication and impaired mobility may predict poor bowel preparation. However, the choice of test was entirely at the discretion and judgement of the responsible clinician and patient.

Noting the clinical context in which CCE was being introduced and the need to create additional colorectal diagnostic capacity, a pragmatic study design was developed permitting the diagnostic accuracy of CCE to be assessed in two ways (Figure 1). Initially, the diagnoses of three separate cohorts of patients undergoing CCE, colonoscopy or CT colonography as their index investigation were to be compared. Since the age, sex, symptomatology, and FIT were likely to be matched, it was argued that the prevalence of colorectal disease would similarly be matched. This is referred to as the comparative accuracy arm of the study [38]. Thereafter, a paired comparison of findings was undertaken in those who went on to colonoscopy (or flexible sigmoidoscopy) after CCE, for biopsy or polypectomy of pathology identified

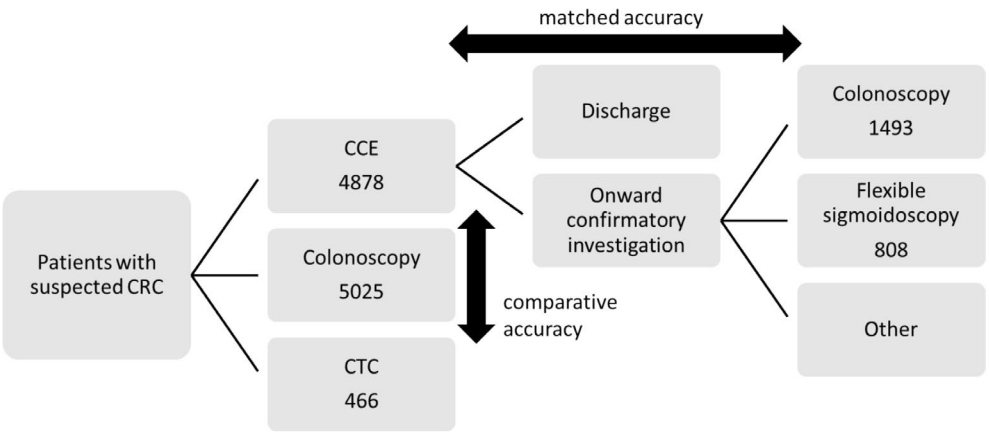

FIGURE 1 | Schematic of the comparative and matched accuracy design of the study.

or because the CCE examination was incomplete or the bowel preparation was inadequate. This is referred to as the matched accuracy arm. All patients provided written, informed consent to participate in the study. Ethical approval was obtained to conduct this evaluation: IRAS ID: 156515.

2.2 | Colorectal Examination Techniques

Colonoscopy and CT colonography were performed and reported according to the practice of each individual centre with the Boston bowel preparation scale being applied [22, 23, 39, 40]. CCE was performed using the PillCamTM COLON 2 system (Medtronic.com). All CCE video reporters completed an approved online CCE training course (Imige Ltd) [41, 42]. This included an introductory webinar followed by five further hour-long webinars teaching broad aspects of CCE delivery, reading and reporting. A smartphone 'Image Recognition App' and a Rapid Reader simulator supported training. The App comprised 4 h of preparatory material split into 19 learning modules and included 100 illustrative video clips. It described the procedure, indications and contraindications, consent, bowel preparation, use of the DR3 video capture recording device, belt fitting instructions, tips and tricks to improve outcomes and advice on good reading practice. Formative assessments, requiring trainees to review 15 CCE videos in their entirety, locating, identifying and describing all landmarks and lesions, were delivered via the Rapid Reader simulator. Feedback was provided both online and by expert readers. The trainee then read five further full-length summative videos and a certificate of completion was awarded once all clinically significant pathology had been identified. The training course provided 50 h of training time.

All centres followed the guidelines of the European Society of Gastroenterological Endoscopy (ESGE) for bowel preparation for CCE [24]. This included a 3-day low-residue diet followed by two split doses of a polyethylene glycol-electrolyte solution (the evening before and the morning of the procedure), two directed 'boosters' comprising gastrografin and phosphosoda after swallowing the capsule and, if needed, a bisacodyl suppository at the end of the day. Moviprep (Norgine Ltd) or Plenvu (Norgine Ltd) when stocks were depleted, were used. Some centres were not able to access gastrografin and used phosphosoda boosters alone. Following the publication of a nested cohort within the CareForColon2015 trial suggesting that prucalopride might improve the CCE completion rate and with support from the EAG, 35 centres added this to their protocol during the evaluation [43].

In line with ESGE guidelines, the EAG recommended that patients with a normal CCE could be discharged and those with ≤ 3 polyps of < 6 mm could be discharged or have a repeat procedure in 3 years [24]. A complete CCE study was defined as one where the CCE was seen to be expelled or where the anal cushions were identified, and an adequate bowel preparation was defined as a score of ≥ 6 on the Colon Capsule Clear Score [44].

2.3 | Data Collection

Patient details were anonymised using a personal identification number assigned by the local centres. All data were entered by the local research team in each participating centre onto an electronic case report form. For all procedures, this included demographic data, presenting symptoms and signs, blood test results and FIT level. The FIT assays were those used by each participating site. Also required was a description of completeness and adequacy of examination, a description of all pathology identified and an estimation of size (< 6 mm, 6–9 mm and > 9 mm) and site (right, transverse or left colon or rectum) of any mass lesions. Complications and existing quality and safety standards for colonoscopy and CT colonography were reported [3]. Details of any subsequent procedures were also recorded so that findings could be matched endoscopically. 'Significant polyp disease' was defined as the presence of a single polyp of ≥ 6 mm or ≥ 3 polyps of any size [24].

2.4 | Powering and Analysis

Sample size calculation for the evaluation was based on the comparative diagnostic accuracy design. For 90% power to detect a difference in sensitivity at the 5% level of significance and with a prevalence of disease thought to be 30%, a sample size of 5000 patients would be required in each group. Disease prevalence for CRC, significant polyps and colitis was estimated from the findings of an earlier FIT diagnostic accuracy study involving patients referred with suspected CRC [38].

Data are presented descriptively as mean (with standard deviation [SD]) or median (with interquartile ranges [IQR]) for continuous variables and frequency (percentage) for categorical variables. T test and ANOVA were used to test for differences between the three cohorts. Polyp matching was undertaken in line with that described by Rex et al.; however, this had to be modified since each lesion identified was recorded based on size range (< 6 mm, 6–9 mm and > 9 mm) rather than absolute size [31]. In brief, for a polyp detected at CCE to be considered a true positive, it had to match a polyp found at endoscopy being (i) located within the same or adjacent colonic segment (right, transverse or left colon and rectum) and (ii) in the same or adjoining size range as found at endoscopy. Polyps reported by CCE but not matched at endoscopy were regarded as false positives. Polyps detected by endoscopy but not reported by CCE were regarded as false negatives. Matching was also reported on a per-patient basis. Here, the polyps were matched by the same size methods but without reference to the colonic segment and, when multiple polyps were present, patients were regarded as true positives only if they all were true positive polyps. If there were any false negative polyps, the patient was regarded as a false negative.

The term 'conclusivity' was used as a reflection of the filter function of CCE and was defined as whether it 'accurately informed the onward management of the patient'.

2.5 | Trial Monitoring Group

CCE had not previously been used as a first-line investigative tool for symptomatic patients. Funding by NHS England National Cancer Programme to support its introduction was a pragmatic response aimed at ameliorating pressures on endoscopy services

during and following the COVID-19 pandemic. Therefore, data submitted was regularly reviewed by the EAG to evaluate and compare progress in each participating centre, and monthly meetings were held with frontline staff to share best practice.

2.6 | Outcomes

The primary outcome was the diagnostic accuracy of CCE compared to colonoscopy in matched patients for the combined endpoint of CRC, significant polyps and colitis.

Secondary outcomes were

i. the comparative accuracy of CCE compared to the colonoscopy (and CT colonography) cohorts for a combined endpoint of CRC, significant polyps and colitis;
ii. the performance characteristics of CCE in terms of safety, completion and preparation adequacy;
iii. the utility of CCE to influence the onward management of the patient (conclusivity).

3 | Results

A total of 10,369 patients were recruited prospectively from 55 NHS Trusts in England during the period from April 2021 to March 2024, 4878 having CCE as the index investigation, 5025 a colonoscopy and 466 CTC. A median of 58 CCE patients (IQR 18–99) were recruited per site. The patient demographics, FIT, symptoms and signs and other laboratory results are presented by index investigation in Table 1 and Tables S1 and S2.

3.1 | Matched Diagnostic Accuracy

There were 2301 patients who had a CCE and then went on to colorectal endoscopy: 1493 (31% of patients) to colonoscopy and a further 808 (17%) to flexible sigmoidoscopy (Table 2 and Table S3). The main indication for referral was the pathology identified; however, the CCE was incomplete in 29% of patients. The subsequent endoscopy was normal in 23% of patients, with significant pathology being detected in 44%. Sixty-nine patients were diagnosed with CRC in the CCE cohort, 63 of whom went on to have a colonoscopy or flexible sigmoidoscopy. Of these patients, CCE identified 49 mass lesions. Twenty-four were reported as CRC, 21 as segmentally matched and 4 as non-segmentally matched large (≥ 10 mm) polyps. The 14 remaining patients diagnosed with CRC had either an incomplete CCE where the capsule did not fully examine the cancer segment or had an inadequately prepared bowel. No CRC was missed at the time of investigation on a per-patient match for those who had a complete and adequately prepared procedure. During the period of the study, however, one interval CRC was reported. The case was reviewed locally and by the EAG. The index procedure was an incomplete but well-prepared colonoscopy. It was abandoned at the distal

TABLE 1 | Participant demographics and symptoms at presentation.

	CCE ($n = 4878$)			Colonoscopy ($n = 5025$)			CTC ($n = 466$)		
		Sex			Sex			Sex	
Characteristic	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**
Age (years)									
N (%)	4859	2208 (45)	2651 (55)	5020	2457 (49)	2563 (51)	466	237 (51)	229 (49)
Mean (SD)	60 (14)	60 (13)	59 (14)	66 (13)	68 (12)	65 (13)	77 (9)	78 (9)	77 (9)
FIT μgHb/g faeces									
N	4671	2125	2546	4979	2437	2542	456	232	224
Mean (SD)	27 (48)	29 (51)	26 (45)	39 (65)	42 (68)	37 (61)	32 (24)	34 (26)	31 (21)
< 10 μgHb/g faeces (%)	998 (21)	392 (18)	606 (24)	873 (18)	398 (16)	475 (19)	8 (2)	2 (1)	6 (3)
10–100 (%)	3631 (78)	1715 (81)	1916 (75)	3892 (78)	1922 (79)	1970 (77)	444 (97)	226 (97)	218 (97)
> 100 (%)	42 (1)	18 (1)	24 (1)	214 (4)	117 (5)	97 (4)	4 (1)	4 (2)	0 (0)
Symptoms, *N* (%)									
Change of bowel habit	2784 (57)	1169 (53)	1615 (61)	3291 (65)	1507 (61)	1784 (70)	280 (60)	138 (58)	142 (62)
Rectal bleeding	1378 (28)	671 (30)	707 (27)	1625 (32)	790 (32)	835 (33)	73 (16)	37 (16)	36 (16)
Abdominal pain	1782 (37)	743 (34)	1039 (39)	2046 (41)	848 (34)	1198 (47)	170 (36)	78 (33)	92 (40)
Anaemia	680 (14)	291 (13)	389 (15)	1054 (21)	612 (25)	442 (17)	142 (30)	84 (35)	58 (25)

TABLE 2 | CCE findings paired with subsequent colorectal endoscopy findings presented on an 'intention to investigate' basis.

Characteristic	CCE, $n = 2301$ (%)	Colonoscopy, $n = 1493$ (%)	Flexible sigmoidoscopy, $n = 808$ (%)	Total, $n = 2301$ (%)
Indication for onward investigation				
Pathology identified at CCE		1050 (70)	428 (53)	1478 (64)
Incomplete CCE		317 (21)	348 (43)	665 (29)
Inadequate CCE prep		111 (7)	21 (3)	132 (6)
Continuing symptoms		6 (1)	3	9
Other/unknown		9 (1)	8 (1)	17 (1)
Investigative findings				
Normal	505 (22)	277 (19)	252 (31)	529 (23)
CRC	52 (2.3)	41 (3.4)	22 (4.0)	63 (3.6)
Right colon	(20%)			(16%)
Transverse colon	(28%)			(9%)
Left colon	(28%)			(34%)
Rectum	(24%)			(40%)
Patient with polyps				
All polyps	1357 (60)	943 (63)	318 (39)	1261 (55)
≥ 10 mm	593 (26)	345 (23)	100 (12)	445 (19)
6–9 mm	726 (32)	390 (26)	106 (13)	496 (22)
≥ 6 mm	1042 (42)	608 (41)	191 (24)	799 (35)
≥ 3 polyps	576 (25)	426 (29)	50 (6)	476 (21)
Polyp numbers and site				
All polyps	4006	2858	538	3396
≥ 10 mm	912 (23)	491 (17)	110 (20)	601 (18)
Right colon	267 (29)			165 (27)
Transverse colon	228 (24)			95 (16)
Left colon	313 (34)			244 (41)
Rectum	104 (11)			97 (16)
6–9 mm	1309 (33)	609 (21)	120 (22)	729 (21)
Right colon	330 (25)			203 (28)
Transverse colon	332 (25)			124 (17)
Left colon	531 (41)			335 (46)
Rectum	116 (9)			67 (9)
≥ 6 mm	2221 (55)	1100 (38)	230 (43)	1330 (39)
Polyp per-patient ratio				
≥ 10 mm	1.5			1.4
6–9 mm	1.8			1.5
Colitis	136 (6%)	105 (5%)	37 (2%)	142 (6%)

ascending colon, with views of the ileocaecal valve, because of patient intolerance. Pan-colonic diverticulosis was identified. A CCE was subsequently performed, being described as complete with adequate bowel preparation (Colon Capsule Clear Score of 8 [R2T3L3]). A small caecal polyp was identified in the caecum. The patient was offered a repeat colonoscopy under deep sedation at the time but never got back to the clinical team and then re-presented 18 months later with a 40 mm ascending colon cancer, pT3pN0M0. The CCE images were reviewed by an experienced reader and the site endoscopy lead. No pathology was detected. It is concluded that this was a post-colonoscopy and post-CCE CRC.

More polyps in absolute terms and on a per-patient basis (all, ≥10 mm and 6–9 mm) were diagnosed at CCE than at the subsequent colonoscopy or combined colorectal endoscopy. Significant polyps were identified in 42% of CCE patients, 41% of colonoscopy patients and 35% of colorectal endoscopy patients. The total prevalence of significant polyps was 55% compared to 38% and 39%, respectively. The polyp per-patient ratio was 1.5 for ≥10 mm at CCE compared to 1.4 at colorectal endoscopy and 1.8 compared to 1.5 for 6–9 mm polyps. The same prevalence of colitis was identified at CCE and colorectal endoscopy.

Paired polyp matching was undertaken in patients who had a complete and adequately prepared CCE and then went on to have a complete and adequately prepared therapeutic colonoscopy or, when appropriate, a flexible sigmoidoscopy (Table 3). Since true negative patients cannot be identified, the specificity of CCE cannot be calculated. Matching was determined on a per polyp and per-patient analysis. Whilst the per polyp matching was 75%–79% sensitive, the per-patient sensitivity was 97% for both ≥10 mm and 6–9 mm polyps.

3.2 | Comparative Diagnostic Accuracy of CCE, Colonoscopy and CTC, Each as a Separate Cohort

Patients in the CCE cohort had a median age of 61y (15–70) and were significantly younger than those in the colonoscopy 68y (58–76) and CT colonography 78y (73–83) cohorts ($p < 0.01$). They also had a lower FIT of 18 μg Hb/g faeces (10–34) than those having a colonoscopy 21 μg Hb/g faeces (11–45) and CT colonography 25 μg Hb/g faeces (14–41) ($p < 0.01$). The FIT was <10 μg Hb/g faeces in 21% of CCE patients. Symptom complexes tended to be different in the three cohorts. Table 4 summarises the comparative clinical outcomes from the initial investigation on an 'intention to investigate' basis. In total, there were 3498 CCE patients with a positive pathology (72%), 3833 (76%) colonoscopy patients and 341 (73%) CT colonography patients. A mass lesion, subsequently confirmed as CRC, was identified in 54 CCE patients (1.1%). This was fewer than in those having colonoscopy (151/5025 [3%]) and CT colonography (14/466 (3%)) as their index investigation. Polyps were identified in 43%, 40% and 23% of patients having CCE, colonoscopy and CT colonography, respectively. It was 26%, 19% and 18%, respectively, when diminutive polyps were excluded. Table 5 presents the comparative diagnostic accuracy for the combined end points of the 3035 (63%) CCE patients, 4405 (88%) colonoscopy and 411 (88%) CT colonography patients whose investigations were complete and adequate. Here the prevalence of mass lesions that were confirmed to be CRC was 1.6%, 2.8% and 3.2% in CCE, colonoscopy and CT colonography patients, respectively. Polyps were detected in 49% of CCE patients, 40% colonoscopy and 24% of CT colonography patients. For ≥10 mm polyps it was 16%, 10% and 9% of patients, respectively and for 6–9 mm polyps it was 20%, 11% and 12%, respectively. A higher proportion of transverse colonic polyps in CCE patients was noted. As expected, there was an age related variation in the prevalence of polyps in all three cohorts. For CCE patients, those aged ≥60y it was 64% compared to 56% in those <60y, whilst for colonoscopy patients it was 55% and 47%, respectively, and for CT colonography patients it was 32% and 8%, respectively. Males had a higher proportion of polyps than females in each cohort. It was 62% vs. 58% for CCE, 59% vs. 46% in colonoscopy and 32% vs. 29% for CT colonography. The increasing proportion of polyps detected at CCE and colonoscopy based on the stratification of the FIT value is presented in Figure 2. There was no variation in polyp prevalence by index of multiple deprivation decile (IMD). The distribution of polyps in right and transverse colonic segments was higher in CCE patients. A similar prevalence of colitis was identified between patients having CCE and colonoscopy and for the combined endpoint of CRC, significant polyps and colitis the prevalence was 32% for those having CCE, 22% for those having a colonoscopy and 19% at CT colonography. Accepting that the study was underpowered to assess CT colonography, CCE was not significantly less sensitive than the other diagnostic modalities.

3.3 | Safety of CCE

A patency capsule was used in 887 (18%) of the patients having CCE, 91% of whom were requested from 7 of the pilot sites. The overall complication rate for CCE was 1.6% (Table 6). The most common complications were the inability to swallow the capsule, vomiting and suspected retention. Three emergency laparotomies were performed on patients after CCE (0.06%).

TABLE 3 | Polyp matching accuracy in those with a complete and adequately prepared CCE and colorectal endoscopy.

	Polyp ≥10 mm		Polyp 6–9 mm	
	Per-patient	Per polyp	Per-patient	Per polyp
CCE true positives	252	507	382	744
CCE false positives	202	384	177	526
CCE false negatives	7	171	10	200
Sensitivity	97% (94–99)	75% (71–78)	97% (95–99)	79% (76–81)

TABLE 4 | Comparative accuracy: 'intention to investigate' prevalence of disease by each investigative cohort.

Characteristic	CCE, $n = 4878$ (%)	Colonoscopy, $n = 5025$ (%)	CTC, $n = 466$ (%)
CRC	54 (1.1)	151 (3.0)	14 (3.0)
Patients with polyps			
All polyps	2098 (43)	2025 (40)	107 (23)
≥ 10 mm	647 (13)	516 (10)	44 (9)
6–9 mm	899 (18)	568 (11)	53 (11)
≥ 6 mm	1247 (26)	959 (19)	84 (18)
≥ 3 polyps	757 (16)	497 (10)	12 (3)
Polyp numbers and site			
All polyps	5459	4185	163
≥ 10 mm	996 (18)	651 (16)	49 (30)
Right colon	292 (29)	214 (33)	21 (43)
Transverse colon	246 (24.5)	58 (9)	4 (8)
Left colon	344 (35.5)	241 (37)	18 (37)
Rectum	114 (11)	138 (21)	6 (12)
6–9 mm	1582 (30)	794 (19)	73 (45)
Right colon	413 (26)	225 (28)	18 (25)
Transverse colon	396 (25)	128 (16)	11 (15)
Left colon	628 (40)	314 (40)	28 (38)
Rectum	145 (9)	127 (16)	16 (22)
≥ 6 mm	2578 (47)	1445 (36)	122 (75)
Polyp to patient ratio			
≥ 10 mm	1.5	1.3	1.1
6–9 mm	1.8	1.4	1.4
Colitis	150 (3.1)	168 (3.3)	2 (0.4)
Diverticulosis	2050 (42)	2056 (41)	216 (46)
Diverticulitis	79 (1.6)	32 (0.6)	15 (3)
Angioectasia	321 (6.6)	40 (0.8)	1 (0.2)
Radiation proctopathy	6 (0.1)	22 (0.4)	0
Other gastrointestinal diseases	1111 (23)	267 (5)	58 (12)

Note: n (%) presented.

There was one death, and there were two perforations. Cases were reviewed by the local clinical team and by the EAG. It was concluded that each event was caused by the pathology detected by the CCE rather than the capsule itself. In addition, there were 64 (1.3%) technical failures with CCE, largely caused by a failure of the camera to capture right-sided colonic images.

3.4 | CCE Reading, Completion and Bowel Preparation Adequacy

The CCE was complete in 74% and adequately prepared in 74%, giving a composite for completion and adequacy in 63% of patients (66% for men and 60% for women). This is significantly poorer when compared to 88% (4405/5025) for those having a colonoscopy and CT Colonography (411/466) ($p < 0.01$). The performance of CCE was affected by the sex and age of the patient. The completion and adequacy rates were 77% and 76%, respectively, for men aged < 60y and 71% and 70% for those ≥ 60y. This compares to 69% each for completion and adequacy in women < 60y and 64% and 67%, respectively, for women ≥ 60y. The conclusivity of CCE was 77% for men < 60y and 74% for those ≥ 60y, whilst for women it was 70% and 68%, respectively. In 67% of the patients, the capsule was single read, mostly by a consultant gastroenterologist. The median (IQR) time to read was 50 (30–65) min (Table S3).

TABLE 5 | Comparative accuracy: Prevalence of disease in each investigative cohort for those with complete and adequately prepared procedures.

Characteristic	CCE, $n=3035$ (%)	Colonoscopy, $n=4405$ (%)	CTC, $n=411$ (%)
CRC	50 (1.6)	125 (2.8)	13 (3.2)
Patient with polyps			
All polyps	1475 (49)	1774 (40)	98 (24)
≥10 mm	471 (16)	455 (10)	39 (9)
6–9 mm	621 (20)	487 (11)	49 (12)
≥6 mm	881 (29)	831 (19)	75 (18)
≥3 polyps	536 (18)	433 (10)	12 (3)
Polyp numbers and site			
All polyps	3860	3658	152
≥10 mm	727 (19)	575 (16)	43 (28)
Right colon	203 (28)	191 (33)	17 (40)
Transverse colon	169 (23)	48 (8)	4 (9)
Left colon	254 (35)	214 (37)	17 (40)
Rectum	101 (14)	122 (21)	5 (12)
6–9 mm	1102 (29)	664 (18)	68 (45)
Right colon	250 (23)	200 (30)	16 (24)
Transverse colon	279 (25)	106 (16)	11 (16)
Left colon	457 (42)	271 (41)	26 (38)
Rectum	116 (11)	87 (13)	15 (22)
≥6 mm	1829 (47)	1257 (34)	111 (73)
Polyp per-patient ratio			
≥10 mm	1.5	1.3	1.2
6–9 mm	1.8	1.4	1.4
Colitis	105 (3.2)	142 (3.2)	2 (0.5)

Note: Bowel preparation adequacy was defined as a CCClear score of > 5 for CCE, a BBPS of > 5 (good or excellent) for colonoscopy and a CT colonography quality of bowel preparation and quality of bowel distension described as good or adequate.

3.5 | Utility

Onward investigation was prompted either by the identification of pathology or because of the incompleteness/inadequacy of the index test. The utility of CCE was explored in terms of its impact on the management of patients referred into the suspected CRC pathway (Figure 3). Here the observed sparing of urgent colorectal diagnostics was recorded. In total, 49% of patients continued to remain in a colorectal diagnostics pathway, with 31% requiring a colonoscopy and 16% a flexible sigmoidoscopy. However, 86% of patients were spared urgent colonoscopy for suspected CRC, being downgraded for a non-suspected CRC intervention.

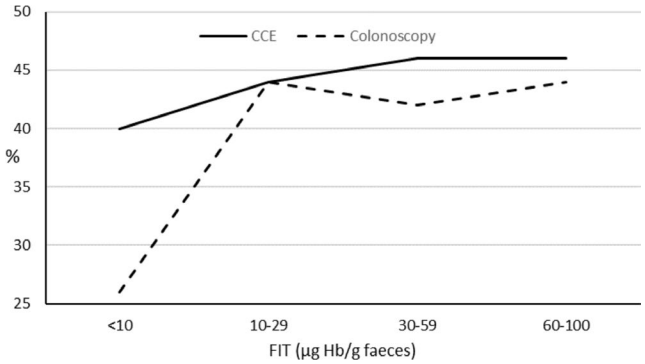

FIGURE 2 | The percentage of CCE and colonoscopy patients with colorectal polyps expressed by FIT value.

TABLE 6 | CCE procedural safety.

Characteristic	n = 4878 (%)
Patency capsule used	877 (18%)
Any complication at CCE	77 (1.6%)
Unable to cope with the prep	3
Inability to swallow	14 (0.3%)
Vomiting	18 (0.4%)
Aspiration	0
Oesophageal stricture	1
Suspected retention	32 (0.7%)
X-ray performed	14
Confirmed retention	10 (0.2%)
Retention cause by CRC	6
Required hospital admission	6
Perforation	2
Required laparotomy	3
Death	1
Ultra rapid transit of the capsule	8

Of the 14% of patients who required an urgent colonoscopy, it was for the pathology detected in over half the patients. Only 6% of patients who had a CCE for suspected CRC remained on that urgent pathway, needing a colonoscopy because of an incomplete procedure or an inadequately prepared bowel.

4 | Discussion

This is the largest diagnostic accuracy study of CCE to have been undertaken. Set in clinical practice for the investigation of symptomatic patients at risk of CRC, the study first demonstrates the safety of CCE. Noting that guidance had been developed to support patient selection in line with existing capsule practice, CCE was complication-free in over 98% of patients. Retentions occurred in 0.2% of patients [45, 46]. The use of a large number of patency capsules by a few sites is probably unnecessary.

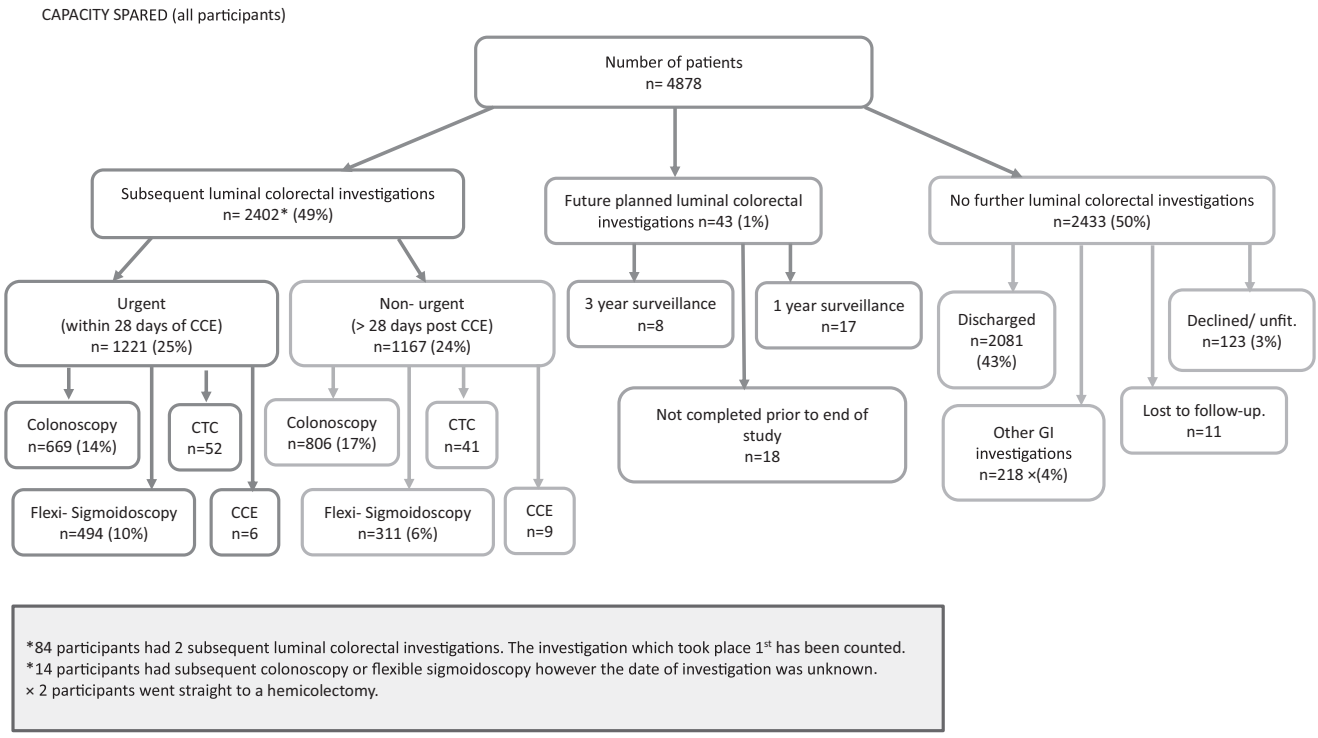

FIGURE 3 | Utility of CCE as a colonoscopy-sparing adjunct in the suspected CRC pathway.

The combined diagnostic accuracy endpoint of 53% in CCE patients exceeded the 44% of findings at colorectal endoscopy in paired patients, on an 'intention to investigate' basis (Table 2). The polyp matching of patients whose investigations were both complete and adequately prepared was 97% for ≥10 mm and 6–9 mm polyps. CRC or large (≥10 mm) polypoid lesions were reported in 52 of the 69 patients subsequently diagnosed with CRC. All of the remaining diagnoses were made at the subsequent flexible sigmoidoscopy or colonoscopy recommended in the CCE report because of an incomplete or inadequate examination. No CRC missed by complete CCE examinations in adequately prepared colons were identified. That a number of CRC were reported as large polyps is likely to have been a function of data entry of the study design. The electronic case reporting form used did not provide an option to include 'suspected cancer' as an outcome; neither did it request a specific lesion size (limiting the data entry of a large polyp to '≥10 mm'). If there was uncertainty, the default was to enter a mass lesion as a ≥10 mm polyp, which would prompt an urgent endoscopy. Our CRC detection finding is similar to that reported in clinical trials, most of which investigate screening or surveillance populations. Meta-analyses found that of 64 cancers, 54 were detected, 9 being missed in segments not reached by CCE (and detected at subsequent completion colonoscopy), only one being missed due to inaccurate sizing of a lesion assigning it to a low-risk category [47–50]. During the period of follow-up within the study, one patient who underwent both colonoscopy and CCE developed an interval CRC.

The cohort 2301 of patients who had both CCE and colorectal endoscopy is not necessarily representative of all patients who were recruited, since many did not require onward investigation. It is, however, free of the selection bias seen in the comparative arm of the study. Whilst the per-patient polyp sensitivity was 97%, the per-polyp sensitivity was less at 75%–79%. This likely reflects the difficulty in accurately localising the polyp within the colon. Matching required CCE to define a polyp as being in the same or adjacent colonic segment and the same or adjacent size bracket as was subsequently reported at colonoscopy or flexible sigmoidoscopy. This means that poor polyp localisation converts a true positive into a combined false negative and false positive. The differences in the relative proportions of polyps seen in the four colonic segments between CCE, colonoscopy and CT colonography in the comparative study are consistent with this. Although landmark recognition is a major focus in the training programme, reporters outside the context of a clinical trial may be less concerned about location and instead focus on criteria for onward colonoscopy or not. This and differences in definition may explain why the matched per polyp diagnostic accuracy does not meet the 87%–88% compared to colonoscopy in previous studies [30, 47, 48, 52,]. Whilst onward investigation was indicated because of the pathology identified at CCE in two thirds of patients, CCE was reported as normal in 22% of patients, similar to the finding at colorectal endoscopy (23%). Perhaps as reader experience develops, clinicians will become more confident in relying upon CCE.

The paired findings are supported by the larger comparative diagnostic accuracy arm. Here, the prevalence of CRC diagnoses in CCE patients was half that of those who had colonoscopy or CT colonography. However, more ≥10 mm polyps were detected at CCE. Noting that the three comparative accuracy cohorts were not absolutely risk matched, we conclude that the findings reflect the lower absolute prevalence of CRC amongst CCE patients [51]. Whilst all patients had been referred into a suspected CRC pathway, the mix of symptom

complexes, anaemia or palpable mass was different, and the FIT and age risk indicators were lower in the CCE cohort. It is likely that clinicians selected patients for CCE whom they perceived to be at lower risk of CRC in order to minimise the need for onward investigation and thus shorten their diagnostic pathway. This selection bias, a consequence of the limitations of the pragmatic study design, has not affected the combined outcome of CRC, significant polyps and colitis. Indeed, one might have anticipated less disease detection in the CCE cohort. Importantly, we observed that the effect of the risk factors—age, sex and FIT on—polyp detection at colonoscopy and CT colonography was mirrored at CCE. Accepting that a further analysis is required to determine whether patient symptomatology influenced the performance of CCE, we conclude that our findings are generalisable across the inclusion criteria. Few polyp false negative patients were detected in those patients whose CCE was paired, and no CRC has since been reported in those patients in the comparative arm of the study who were discharged after a normal CCE. A registry of long-term follow-up data for CCE patients is planned.

The higher per-patient prevalence of polyps ≥ 10 mm at CCE even on an 'intention to investigate' provides significant reassurance, accepting that colonoscopy is the gold standard. Incomplete or inadequately prepared CCE may yet safely inform the onward management of patients. The observed prevalence of ≥ 10 mm polyps detected in the CCE cohort was 1.6–1.8 times higher than in the colonoscopy or CT colonography cohorts, when studies were complete and adequately prepared. It is likely that, for some, the CCE reader support over-estimated polyp size and double counting of polyps may occur [47]. This may explain the higher prevalence of transverse colonic polyps seen at CCE, consequent upon the capsule shuttling back and forth. Unnecessary over-investigation would result. It is, however, likely that CCE does detect more significant polyp disease since this observation is noted on both a per-patient and per-polyp basis. For example, for 6–9 mm polyps, 1.6 times more polyps and 1.8 times more patients with polyps were identified by CCE than by colonoscopy. Recent meta-analysis identified seven studies where significant pathology found at CCE and not detected by the index colonoscopy prompted a second unblinded colonoscopy. Additional polyps, initially missed, were recognised as being true positive findings, having been reported as false positives in the clinical trials [47]. Whilst CCE is a passive investigation, the extended period of mucosal examination over hours, compared to the average colonoscopic withdrawal time, being measured in minutes, may increase the opportunity for lesion detection. CCE may be better suited to polyp detection even in those studies not fulfilling the Colon Capsule Clear Score of ≥ 6. CT colonography only detected 3% of patients with ≥ 3 polyps compared to 10% at colonoscopy and 18% at CCE [53, 54].

The ScotCap study also recorded FIT and age in symptomatic patients referred for CCE with suspected CRC [27]. Here, the mean age was 59, but the distribution of FIT was likely to have been broader than in our evaluation. Of those whose FIT was recorded, it was < 10 μg Hb/g faeces in 55%, and for the remaining 45%, the upper end of the FIT range was set at > 100 μg Hb/g faeces. Nonetheless, using the composite of CRC, colitis and all polyps, a per-patient detection rate of 48% achieved in this study was similar to their experience of 51% [36].

Noting the overall polyp detection of CCE in both study arms, it seems likely that overall polyp detection by CCE does exceed that of colonoscopy and CT colonography. The evidence suggests that a number of false positive polyps will be true positives [55, 56]. However, for the future, more accurate characterisation of polyps and site localisation of polyps are challenges requiring technological support. Certainly, the findings from this evaluation do not suggest that right-sided lesions are missed at CCE [57]. Per-patient findings of colitis and diverticulosis had a comparable prevalence, accepting the limitations of CT colonography in suspected colitis diagnosis [58].

Integral to this study has been the placement of CCE as a filter test in the suspected CRC pathway. Its purpose was not only to identify those patients with a normal examination who could be spared a colonoscopy but also to appropriately inform the requirement and level of risk for onward endoscopic investigation. Accepting the high prevalence of disease in older patients with a FIT 10–100 μg Hb/g faeces, this prioritising role was a key element of its filter function. CCE informed the onward management of the majority of patients, with only 14% remaining on the suspected CRC pathway for colonoscopy, mostly because of the pathology detected. Whether this capacity-saving utility is sufficient to make CCE cost effective is beyond the remit of this observational study. Pragmatic guidance was produced by the EAG during the study intended to improve the completion rates and bowel preparation adequacy of CCE. Despite this, the performance of CCE was significantly less than that of colonoscopy and CT colonography. This may improve with more targeted guidance for patients and modified bowel preparation regimes [59–61]. Clearly, optimising completion and bowel preparation adequacy by appropriate patient selection remains key. The selection bias introduced by clinicians suggests that this was recognised during the study. Currently, we are unable to determine the degree to which the exclusion guidance was adhered to; however, a further assessment of patient factors affecting CCE performance is awaited. We do observe that filter function conclusivity, perhaps the more relevant metric, approached 80% in younger men and held around 75% across all ages. Only in older women did it fall below 70%.

We conclude that the pragmatic design of this large, multi-site English study, with matched and comparative arms, confirms that CCE is a safe diagnostic of colorectal disease, unlikely to miss significant disease and usefully to act as a filter test, appropriately informing the onward management of the patient in a resource-constrained healthcare system. It is likely to overdiagnose polyp disease, accepting colonoscopy as the gold standard. Long-term follow-up data do not yet exist. Because the conclusivity of CCE as a filter test, informing onward decision-making, is better than the combined completion and adequacy measure, it could be seen as offering 'patient choice' in the wider colorectal diagnostics pathway rather than being constrained to the concept of a low pathology prevalence-based 'sweet-spot' [28]. Lastly, as with CT colonography, CCE can provide diagnoses beyond the colorectum, which might enhance its utility for many. It is likely that the demand for colonoscopy will continue to exceed capacity. The ScotCap experience teaches us that CCE can be offered in a range of settings other than an endoscopy unit [27]. This may make it more attractive to some patients, and we are aware that some sites explored near to and at home CCE

during this study. The time to train in CCE reading is weeks rather than the years needed to become an expert colonoscopist [42]. Further, the availability of cloud technology provides new opportunities to bring in additional, accredited staff to support a CCE reading service. This large and comprehensive NHS E research evaluation of CCE provides the evidence base to explore the benefits that CCE could provide a future colorectal diagnostics service in its aim to diagnose 75% of (colorectal) cancers in the early stages by 2028 [62].

Author Contributions

James Turvill: conceptualization, writing – original draft, methodology, validation, writing – review and editing, formal analysis, supervision. **Monica Haritakis:** writing – review and editing, data curation, formal analysis, project administration, supervision. **Scott Pygall:** funding acquisition, project administration, supervision. **Emily Bryant:** conceptualization, funding acquisition, project administration, supervision. **Harriet Cox:** validation, project administration. **Greg Forshaw:** validation, project administration. **Crispin Musicha:** formal analysis. **Victoria Allgar:** formal analysis. **Robert Logan:** funding acquisition, writing – review and editing, conceptualization. **Mark McAlindon:** conceptualization, methodology, writing – review and editing.

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Disclosure

Patient and Public Involvement: The research design of this study, its conduct and oversight, and results dissemination were monitored by the NHS E colon capsule endoscopy pilot Expert Advisory Group, who were supported by the patient experience team within NHS England and the Public and Patient Voices (PPV) Forum.

Ethics Statement

The study gained NHS Ethics Approval (IRAS ID: 303921) and was sponsored by York and Scarborough Teaching Hospitals NHS Foundation Trust. Oversight was provided by an Expert Advisory Group.

Conflicts of Interest

M.M. has received a consultancy fee from Medtronic.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. M. D. Rutter, M. Brookes, T. J. Lee, P. Rogers, and L. Sharp, "Impact of the COVID-19 Pandemic on UK Endoscopic Activity and Cancer Detection: A National Endoscopy Database Analysis," *Gut* 70, no. 3 (2021): 537–543, https://doi.org/10.1136/gutjnl-2020-322179.

2. W. Hamilton, F. M. Walter, G. Rubin, and R. D. Neal, "Improving Early Diagnosis of Symptomatic Cancer," *Nature Reviews. Clinical Oncology* 13, no. 12 (2016): 740–749, https://doi.org/10.1038/nrclinonc.2016.109.

3. C. J. Rees, S. Thomas Gibson, M. D. Rutter, et al., "UK Key Performance Indicators and Quality Assurance Standards for Colonoscopy," *Gut* 65, no. 12 (2016): 1923–1929, https://doi.org/10.1136/gutjnl-2016-312044.

4. D. R. Gavin, R. M. Valori, J. T. Anderson, M. T. Donnelly, J. G. Williams, and E. T. Swarbrick, "The National Colonoscopy Audit: A Nationwide Assessment of the Quality and Safety of Colonoscopy in the UK," *Gut* 62, no. 2 (2013): 242–249, https://doi.org/10.1136/gutjnl-2011-301848.

5. E. Derbyshire, P. Hungin, C. Nickerson, et al., "Colonoscopic Perforations in the English NHS Bowel Cancer Screening Programme," *Endoscopy* 50, no. 9 (2018): 861–870, https://doi.org/10.1055/a-0584-7138.

6. Wang, et al., "Almost Threefold Risk of 30 Day Post Colonoscopy Unplanned Healthcare Consultation and Infection Compared to Screening Mammography," *Gut* 67 (2018): 1626–1636, https://doi.org/10.1136/gutjnl-2017-315308.

7. J. Jason Ferreira, M. Akbari, L. Gashin, et al., "Prevalence and Lifetime Risk of Endoscopy-Related Complications Among Patients With Inflammatory Bowel Disease," *Clinical Gastroenterology and Hepatology* 11, no. 10 (2013): 1288–1293, https://doi.org/10.1016/j.cgh.2013.04.047.

8. A. J. Ball, C. J. Rees, B. M. Corfe, and S. A. Riley, "Sedation Practice and Comfort During Colonoscopy: Lessons Learnt From a National Screening Programme," *European Journal of Gastroenterology & Hepatology* 27, no. 6 (2015): 741–746, https://doi.org/10.1097/MEG.0000000000000360.

9. S. Bond, C. Kyfonidis, M. Jamieson, et al., "Evaluation of an Innovative Colon Capsule Endoscopy Service in Scotland From the Perspective

of Patients: Mixed Methods Study," *Journal of Medical Internet Research* 14, no. 25 (2023): e45181, https://doi.org/10.2196/45181.

10. R. Sidhu, D. Turnbull, H. Haboubi, et al., "British Society of Gastroenterology Guidelines on Sedation in Gastrointestinal Endoscopy," *Gut* 0 (2023): 1–27, https://doi.org/10.1136/gutjnl-2023-330396.

11. L. Fuccio, C. J. Rees, L. Frazzoni, et al., "Patient- Reported Experience of Colonoscopy in Italy: A Multicentre Prospective Observational Study," *Gut* 72 (2023): 2227–2230, https://doi.org/10.1136/gutjnl-2023-330415.

12. M. K. Thygesen, G. Baatrup, C. Petersen, N. Qvist, R. Kroijer, and M. Kobaek-Larsen, "Screening Individuals' Experiences of Colonoscopy and Colon Capsule Endoscopy; a Mixed Methods Study," *Acta Oncologica* 58, no. sup1 (2019): S71–S76, https://doi.org/10.1080/0284186X.2019.1581372.

13. L. Shenbagaraj, S. Thomas-Gibson, J. Stebbing, et al., "Endoscopy in 2017: A National Survey of Practice in the UK," *Frontline Gastroenterology* 10 (2019): 7–15, https://doi.org/10.1136/flgastro-2018-100970.

14. S. E. R. Bailey, G. A. Abel, A. Atkins, et al., "Diagnostic Performance of a Faecal Immunochemical Test for Patients With Low-Risk Symptoms of Colorectal Cancer in Primary Care: An Evaluation in the South West of England," *British Journal of Cancer* 124 (2021): 1231–1236, https://doi.org/10.1038/s41416-020-01221-9.

15. A. Sud, B. Torr, M. E. Jones, et al., "Effect of Delays in the 2-Week-Wait Cancer Referral Pathway During the COVID-19 Pandemic on Cancer Survival in the UK: A Modelling Study," *Lancet Oncology* 21, no. 8 (2020): 1035–1044, https://doi.org/10.1016/S1470-2045(20)30392-2.

16. https://www.england.nhs.uk/statistics/statistical-work-areas/cancer-waiting-times/.

17. https://www.nice.org.uk/news/article/nice-recommends-extending-use-of-tests-for-colorectal-cancer-which-could-reduce-waiting-time-for-colonoscopies.

18. S. Ravindran, S. Thomas-Gibson, M. Bano, et al., "National Census of UK Endoscopy Services 2021," *Frontline Gastroenterology* 13, no. 6 (2022): 463–470, https://doi.org/10.1136/flgastro-2022-102157.

19. E. Morris, R. Goldacre, E. Spata, et al., "Impact of the COVID-19 Pandemic on the Detection and Management of Colorectal Cancer in England: A Population-Based Study," *Lancet Gastroenterology & Hepatology* 6, no. 3 (2021): 199–208, https://doi.org/10.1016/S2468-1253(21)00005-4.

20. COVIDSurg Collaborative, "The Impact of Surgical Delay on Resectability of Colorectal Cancer: An International Prospective Cohort Study," *Colorectal Disease* 24, no. 6 (2022): 708–726, https://doi.org/10.1111/codi.16117.

21. Public Health Scotland, "Diagnostic Waiting Times—Quarter Ending, 2023".

22. National Institute for Health and Care Excellence (NICE), "Computed Tomographic Colonography (Virtual Colonoscopy)," *Interventional Procedures Guidance* (2005): IPG129, https://www.nice.org.uk/guidance/ipg129.

23. C. Spada, C. Hassan, D. Bellini, et al., "Imaging Alternatives to Colonoscopy: CT Colonography and Colon Capsule. ESGE and ESGAR Guideline—Update 2020," *Endoscopy* 52 (2020): 1022–1036, https://doi.org/10.1055/a-1258-4819.

24. C. Spada, C. Hassan, J. P. Galmiche, et al., "Colon Capsule Endoscopy: ESGE Guideline," *Endoscopy* 44, no. 527–536 (2012): 527–536, https://doi.org/10.1055/s-0031-1291717.

25. H. Y. Shi, F. K. L. Chan, A. Higashimori, et al., "A Prospective Study on Second-Generation Colon Capsule Endoscopy to Detect Mucosal Lesions and Disease Activity in Ulcerative Colitis (With Video)," *Gastrointestinal Endoscopy* 86 (2017): 1139–1146, https://doi.org/10.1016/j.gie.2017.07.007.

26. H. Ojidu, H. Palmer, J. Lewandowski, et al., "Patient Tolerance and Acceptance of Different Colonic Imaging Modalities: An Observational Cohort Study," *European Journal of Gastroenterology & Hepatology* 30, no. 5 (2018): 520–525, https://doi.org/10.1097/MEG.0000000000001090.

27. C. MacLeod, J. Hudson, M. Brogan, et al., "ScotCap—A Large Observational Cohort Study," *Colorectal Disease* 24, no. 4 (2022): 411–421, https://doi.org/10.1111/codi.16029.

28. M. Ismail, G. Murphy, and S. Semenov, "Comparing Colon Capsule Endoscopy to Colonoscopy; a Symptomatic patient's Perspective," *BMC Gastroenterology* 22, no. 1 (2022): 31, https://doi.org/10.1186/s12876-021-02081-0.

29. U. Deding, P. Cortegoso Valdivia, A. Koulaouzidis, et al., "Patient-Reported Outcomes and Preferences for Colon Capsule Endoscopy and Colonoscopy: A Systematic Review With Meta-Analysis," *Diagnostics (Basel)* 11, no. 9 (2021): 1730, https://doi.org/10.3390/diagnostics11091730.

30. S. Pecere, C. Senore, C. Hassan, et al., "Accuracy of Colon Capsule Endoscopy for Advanced Neoplasia," *Gastrointestinal Endoscopy* 91 (2020): 406–414.e1, https://doi.org/10.1016/j.gie.2019.09.041.

31. D. Rex, S. Adler, J. Aisenberg, et al., "Accuracy of Capsule Colonoscopy in Detecting Colorectal Polyps in a Screening Population," *Gastroenterology* 148 (2015): 948–967, https://doi.org/10.1053/j.gastro.2015.01.025.

32. A. Parodi, G. Vanbiervliet, C. Hassan, et al., "Colon Capsule Endoscopy to Screen for Colorectal Neoplasia in Those With Family Histories of Colorectal Cancer," *Gastrointestinal Endoscopy* 87, no. 3 (2018): 695–704, https://doi.org/10.1016/j.gie.2017.05.023.

33. Scottish Health Technologies Group (SHTG), "Second-Generation Colon Capsule Endoscopy (CCE-2) for the Detection of Colorectal Polyps: SHTG Recommendation, 2020," https://shtg.scot/media/1888/second-generation-colon-capsule-endoscopy-cce-2-for-the-detection-of-colorectal-polyps-shtg-recommendation-01-20-gastro.pdf.

34. "Suspected Cancer Guidance," published June 2015 later update October 2023, http://www.nice.org.uk/guidance/ng12.

35. nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/triaging-patients-with-lower-gi-symptoms.pdf.

36. C. Loveday, A. Sud, M. E. Jones, et al., "Prioritisation by FIT to Mitigate the Impact of Delays in the 2-Week Wait Colorectal Cancer Referral Pathway During the COVID-19 Pandemic: A UK Modelling Study," *Gut* 70 (2020): 1053–1060, https://gut.bmj.com/content/early/2020/08/24/gutjnl-2020-321650.

37. NHS England, "NHS Rolls out Capsule Cameras to Test for Cancer," https://www.england.nhs.uk/2021/03/nhs-rolls-out-capsule-cameras-to-test-for-cancer/.

38. J. L. Turvill, D. Turnock, D. Cottingham, et al., "Diagnostic Accuracy of Faecal Immunochemical Test for Haemoglobin in Patients With Suspected Colorectal Cancer," *British Journal of General Practice* 71, no. 709 (2021): e643–e651, https://doi.org/10.3399/BJGP.2020.1098.

39. BSGAR and the Royal College of Radiologists, "Guidance on the Use of CT Colonography for Suspected Colorectal Cancer," https://www.rcr.ac.uk/our-services/all-our-publications/clinical-radiology-publications/guidance-on-the-use-of-ct-colonography-for-suspected-colorectal-cancer/.

40. E. J. Lai, A. H. Calderwood, G. Doros, O. K. Fix, and B. C. Jacobson, "The Boston Bowel Preparation Scale: A Valid and Reliable Instrument for Colonoscopy-Oriented Research," *Gastrointestinal Endoscopy* 69 (2009): 620–625, https://doi.org/10.1016/j.gie.2008.05.057.

41. https://www.thejag.org.uk/Downloads/JAG/JAG%20certification/Colon%20Capsule%20certification%20-%20JAG%20position%20statement%20-%20%20Jan%202022.pdf.

42. https://imige.co.uk/our-professional-courses/.

43. U. Deding, L. Kaalby, G. Baatrup, et al., "The Effect of Prucalopride on the Completion Rate and Polyp Detection Rate of Colon Capsule

Endoscopies," *Clinical Epidemiology* 14 (2022): 437–444, https://doi.org/10.2147/CLEP.S353527.

44. M. R. de Sousa, C. Arieira, P. Carvalho, et al., "Colon Capsule CLEansing Assessment and Report (CC-CLEAR): A New Approach for Evaluation of the Quality of Bowel Preparation in Capsule Colonoscopy," *Gastrointestinal Endoscopy* 93, no. 1 (2021): 212–223, https://doi.org/10.1016/j.gie.2020.05.062.

45. Y.-C. Wang, J. Pan, Y.-W. Liu, et al., "Adverse Events of Video Capsule Endoscopy Over the Past Two Decades: A Systematic Review and Proportion Meta-Analysis," *BMC Gastroenterology* 20 (2020): 364, https://doi.org/10.1186/s12876-020-01491-w.

46. A. Reumkens, E. J. A. Rondagh, C. M. Bakker, et al., "Post-Colonoscopy Complications: A Systematic Review, Time Trends, and Meta-Analysis of Population-Based Studies," *American Journal of Gastroenterology* 111 (2016): 1092–1101, https://doi.org/10.1038/ajg.2016.234.

47. M. Sulbaran, L. Bustamante-Lopez, W. Bernardo, et al., "Systematic Review and Meta-Analysis of Colon Capsule Endoscopy Accuracy for Colorectal Cancer Screening. An Alternative During the Covid-19 Pandemic?," *Journal of Medical Screening* 29, no. 3 (2022): 148–155, https://doi.org/10.1177/09691413221074803.

48. H. Ali, R. Pamarthy, S. Sarfraz, and E. Ali, "Diagnostic Accuracy for per-Patient Polyp Detection of Second-Generation Capsule Endoscopy Compared to Colonoscopy: A Meta-Analysis of Multicenter Studies," *Cureus* 13, no. 8 (2021): e17560, https://doi.org/10.7759/cureus.17560.

49. P. Cortegoso Valdivia, U. Deding, T. Bjørsum-Meyer, et al., "Inter/Intra-Observer Agreement in Video-Capsule Endoscopy: Are we Getting It all Wrong? A Systematic Review and Meta-Analysis," *Diagnostics* 12, no. 10 (2022): 2400, https://doi.org/10.3390/diagnostics12102400.

50. T. Kjølhede, A. M. Ølholm, L. Kaalby, K. Kidholm, N. Qvist, and G. Baatrup, "Diagnostic Accuracy of Capsule Endoscopy Compared With Colonoscopy for Polyp Detection: Systematic Review and Meta-Analyses," *Endoscopy* 53, no. 7 (2021): 713–721, https://doi.org/10.1055/a-1249-3938.

51. I. Al-Najami, C. P. Rancinger, M. K. Larsen, et al., "The Diagnostic Yield of Colonoscopy Stratified by Indications," *Gastroenterology Research and Practice* 2017 (2017): 1–5, https://doi.org/10.1155/2017/4910143.

52. T. Möllers, M. Schwab, L. Gildein, et al., "Second-Generation Colon Capsule Endoscopy for Detection of Colorectal Polyps: Systematic Review and Meta-Analysis of Clinical Trials," *Endoscopy International Open* 9, no. 4 (2021): E562.e71, https://doi.org/10.1055/a-1353-4849.

53. B. Cash, M. Fleisher, S. Fern, et al., "Multicentre, Prospective, Randomised Study Comparing the Diagnostic Yield of Colon Capsule Endoscopy Versus CT Colonography in a Screening Population (The TOPAZ Study)," *Gut* 70, no. 11 (2021): 2115–2122, https://doi.org/10.1136/gutjnl-2020-322578.

54. B. González-Suárez, M. Pagés, I. K. Araujo, et al., "Colon Capsule Endoscopy Versus CT Colonography in FIT-Positive Colorectal Cancer Screening Subjects: A Prospective Randomised Trial—The VICOCA Study," *BMC Medicine* 18 (2020): 255, https://doi.org/10.1186/s12916-020-01717-4.

55. N. E. Burr, E. Derbyshire, J. Taylor, et al., "Variation in Post-Colonoscopy Colorectal Cancer Across Colonoscopy Providers in English National Health Service: Population Based Cohort Study," *BMJ* 367 (2019): l6090, https://doi.org/10.1136/bmj.l6090.

56. P. J. Pickhardt, B. D. Pooler, D. H. Kim, C. Hassan, K. A. Matkowskyj, and R. B. Halberg, "The Natural History of Colorectal Polyps: Overview of Predictive Static and Dynamic Features," *Gastroenterology Clinics of North America* 47, no. 3 (2018): 515–536, https://doi.org/10.1016/j.gtc.2018.04.004.

57. I. Otani, S. Oka, S. Tanaka, et al., "Diagnostic Yield of Colon Capsule Endoscopy in Detection of Superficial Colorectal Lesions," *Digestion* 101, no. 3 (2020): 262–269, https://doi.org/10.1159/000499332.

58. W. Halder, F. M. Laskaratos, H. El-Mileik, et al., "Review: Colon Capsule Endoscopy in Inflammatory Bowel Disease," *Diagnostics (Basel)* 12, no. 1 (2022): 149, https://doi.org/10.3390/diagnostics12010149.

59. P. Cortegoso Valdivia, K. Skonieczna-Żydecka, A. Elosua, et al., "Indications, Detection, Completion and Retention Rates of Capsule Endoscopy in Two Decades of Use: A Systematic Review and Meta-Analysis," *Diagnostics (Basel)* 12, no. 5 (2022): 1105, https://doi.org/10.3390/diagnostics12051105.

60. A. I. Ferreira, T. Lima Capela, M. Freitas, et al., "Colon Capsule Endoscopy: Predictors of Inadequate Bowel Preparation," *United European Gastroenterology Journal* 10, no. Suppl. 8 (2022): 1048–1049.

61. A. Gimeno-Garcia, B. Gonzalez-Suarez, Z. Ganzo, et al., "Predictive Factors for Inadequate Bowel Cleansing in Colon Capsule Endoscopy," *Gastroenterología y Hepatología* 45, no. 8 (2022): 605–613, https://doi.org/10.1016/j.gastrohep.2022.01.003.

62. https://www.england.nhs.uk/cancer/early-diagnosis/.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.