Computed tomographic colonography versus colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer (SIGGAR): a multicentre randomised trial

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Lancet 2013; 381: 1194–202

Published Online February 14, 2013 http://dx.doi.org/10.1016/S0140-6736(12)62186-2

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Summary

Background Colonoscopy is the gold-standard test for investigation of symptoms suggestive of colorectal cancer; computed tomographic colonography (CTC) is an alternative, less invasive test. However, additional investigation after CTC is needed to confirm suspected colonic lesions, and this is an important factor in establishing the feasibility of CTC as an alternative to colonoscopy. We aimed to compare rates of additional colonic investigation after CTC or colonoscopy for detection of colorectal cancer or large (≥10 mm) polyps in symptomatic patients in clinical practice.

Methods This pragmatic multicentre randomised trial recruited patients with symptoms suggestive of colorectal cancer from 21 UK hospitals. Eligible patients were aged 55 years or older and regarded by their referring clinician as suitable for colonoscopy. Patients were randomly assigned (2:1) to colonoscopy or CTC by computer-generated random numbers, in blocks of six, stratified by trial centre and sex. We analysed the primary outcome—the rate of additional colonic investigation—by intention to treat. The trial is an International Standard Randomised Controlled Trial, number 95152621.

Findings 1610 patients were randomly assigned to receive either colonoscopy (n=1072) or CTC (n=538). 30 patients withdrew consent, leaving for analysis 1047 assigned to colonoscopy and 533 assigned to CTC. 160 (30·0%) patients in the CTC group had additional colonic investigation compared with 86 (8·2%) in the colonoscopy group (relative risk 3·65, 95% CI 2·87–4·65; p<0·0001). Almost half the referrals after CTC were for small (<10 mm) polyps or clinical uncertainty, with low predictive value for large polyps or cancer. Detection rates of colorectal cancer or large polyps in the trial cohort were 11% for both procedures. CTC missed 1 of 29 colorectal cancers and colonoscopy missed none (of 55). Serious adverse events were rare.

Interpretation Guidelines are needed to reduce the referral rate after CTC. For most patients, however, CTC provides a similarly sensitive, less invasive alternative to colonoscopy.

Funding NIHR Health Technology Assessment Programme, NIHR Biomedical Research Centres funding scheme, Cancer Research UK, EPSRC Multidisciplinary Assessment of Technology Centre for Healthcare, and NIHR Collaborations for Leadership in Applied Health Research and Care.

Introduction

Colonoscopy is the gold-standard investigation of the colon, offering a sensitive luminal examination that allows biopsy samples to be taken for definitive diagnosis. However, older patients and those with comorbidities are more likely to have an incomplete or difficult colonoscopy[1,2] and are at greater risk of adverse events than younger patients with no comorbidities.[3,4] Therefore, in some circumstances, it might be preferable to use an alternative first-line investigation for patients with symptoms suggestive of colorectal cancer.

One possibility is computed tomographic colonography (CTC), or virtual colonoscopy—a relatively new radiological technique for imaging the large bowel. CTC is less invasive than colonoscopy, and might be safer[5] and more acceptable[6–8] to patients. Most patients having colonoscopy need to be sedated, which is not necessary for CTC. However, if lesions needing biopsy or removal are detected at CTC, colonoscopy is usually needed. CTC also detects extracolonic lesions, which might explain symptoms but might also lead to additional investigations that ultimately bring no clinical benefit. So far, CTC and colonoscopy in symptomatic patients have never been compared in a randomised trial.

Systematic reviews suggest that CTC and colonoscopy have similar sensitivity for detection of colorectal cancer[9,10] and large polyps[10,11] if undertaken in accordance with best practice[12,13] by experienced practitioners. As a result, the sample size needed for a non-inferiority trial powered on detection rates would be unfeasibly large. Comparison of the benefits and costs of the two procedures will therefore depend on other factors. One of the most important is the need for additional investigation after CTC, which is likely to determine the practicality of more widespread use of CTC as a

diagnostic test. However, colonoscopy can also generate further tests because of incomplete examinations—a survey undertaken before our study reported a non-completion rate that exceeded 20% in routine UK practice.[14]

We have undertaken two pragmatic multicentre randomised trials in patients with symptoms suggestive of colorectal cancer. In a parallel trial,[15] we compared the relative sensitivity of CTC with that of barium enema in patients referred for radiological investigation of the colon. In this trial, we compared the need for additional diagnostic tests after CTC versus colonoscopy in patients regarded as suitable for colonoscopy by their referring clinician. Our studies of patient acceptability[16,17] and cost-effectiveness are reported elsewhere.[18]

Methods

Study design and participants

The design and rationale of this multicentre randomised trial have been published previously.[19] The trial protocol can be found online. Research nurses at 21 UK National Health Service (NHS) teaching and general hospitals recruited patients referred by their family doctor for investigation of symptoms suggestive of colorectal cancer. Patients were eligible if they were aged 55 years or older, were fit to undergo full bowel preparation, had no known genetic predisposition to cancer, had no history of inflammatory bowel disease, had not had a whole-colon examination in the past 6 months, and were not in active follow-up for previous colorectal cancer. We obtained demographic and baseline clinical data such as age, sex, and symptoms for all potentially eligible patients. The consulting clinician then decided in line with usual practice whether to investigate the patient using colonoscopy or barium enema (the default examinations). We created two parallel trials and, within each, patients were randomly assigned to the default examination or CTC.[19] No patients were enrolled in both trials.

We obtained ethical approval from the Northern and Yorkshire Multicentre Research Ethics Committee and from all participating hospitals. The trials were supervised by independent data monitoring and trial steering committees. All patients gave informed written consent.

Randomisation

We randomly allocated patients (2:1) to receive either colonoscopy or CTC. A statistician (RE) generated the randomisation codes at a remote site, and codes were kept concealed until interventions were assigned. RE was involved in the design of both the trial and its database, but had no involvement in data collection or interpretation. Randomisation was done centrally by computer random number generation, in blocks of six, stratified by centre and patient sex. Participants and those administering the procedures were not masked to the assigned study intervention.

Procedures

CTC and colonoscopy were undertaken after full bowel preparation, and in accordance with contemporary guidelines on best practice.[20,21] For CTC, multidetector-row scanners (minimum four rows) were used with a maximum detector collimation of 2·5 mm and a pitch that allowed abdominal coverage (40 cm) within one breath-hold (20 s). Prone and supine scans were recommended. Readers used two-dimensional (2D) and three-dimensional (3D) visualisation as needed, but a minimum requirement was a primary 2D analysis with volume or surface rendering for problem solving. The reading platform was decided according to local preference, as was use of intravenous contrast and faecal tagging. Computer-assisted detection was available.

217 gastroenterologists or colorectal surgeons undertook the colonoscopies. 41 radiologists subspecialising in gastrointestinal radiology interpreted the CTC studies. All radiologists were familiar with interpreting the procedure, and those who had read fewer than 100 cases, or who desired additional training, attended a supplementary 2 day course.

For the **trial protocol** see http://www.hta.ac.uk/project/1366.asp

For each procedure, the radiologist or endoscopist issued a report as usual and completed a case report form. Flexible sigmoidoscopy (FS) was undertaken before CTC in some hospitals. Details of these FS examinations were recorded, including any lesions seen.

Adverse events within 24 h of the randomised procedure were recorded on the case report form, or on a questionnaire completed by patients the following morning. Details of unplanned hospital admissions within 30 days were collected by manually searching hospitals' patient administration systems.

Referrals for additional investigation were made at the discretion of local clinicians, and research nurses collected the reports from these procedures.

Outcomes

The primary outcome was the proportion of patients who had additional colonic investigation. Secondary outcomes were detection rates of colorectal cancer or large polyps, other colorectal diagnoses, miss rates for colorectal cancer, extracolonic cancer diagnoses, all-cause mortality, and serious adverse events. We also analysed extracolonic findings at CTC.

We defined additional colonic investigation as any subsequent examination of the colon until diagnosis (usually histological confirmation of a cancer or polyp), or until a patient was referred back to their family doctor.

Our definition of colorectal cancer included all cancers with International Statistical Classification of Diseases and Related Health Problems, revision 10 (ICD-10) site codes C18–C20. Polyp size was defined as the largest measurement at endoscopy, histology, or surgery. Details of cancer diagnoses (colonic and extracolonic) and deaths in the trial cohort were obtained from the NHS Information Centre (NHSIC). A colorectal cancer was defined as

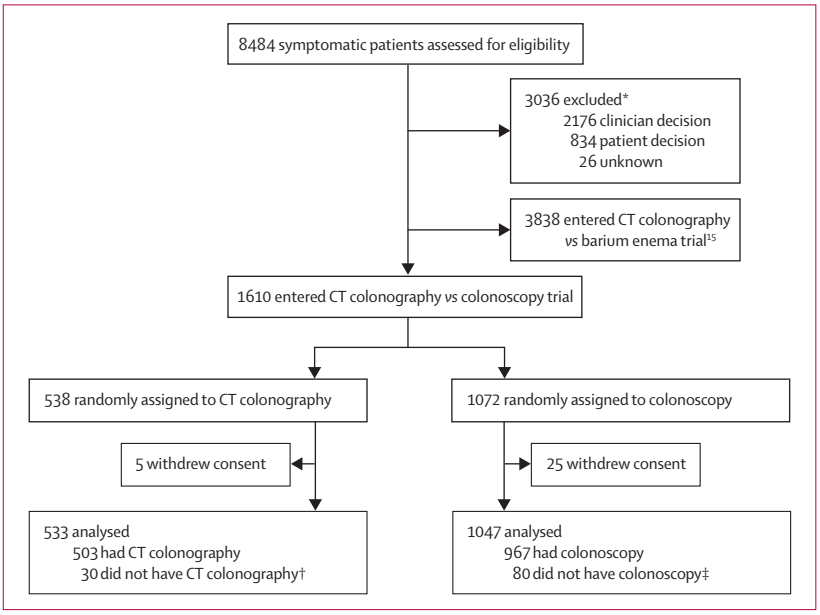

Figure 1: **Trial profile**
*Reasons why patients were not randomised can be found in the appendix. †11 had an alternative whole-colon examination; 19 did not have a whole-colon examination. ‡16 had an alternative whole-colon examination; 64 did not have a whole-colon examination.

	Patients included in CT colonography *vs* colonoscopy trial		Comparison of included and excluded patients		
	CT colonography (n=533)	Colonoscopy (n=1047)	Patients included in CT colonography *vs* colonoscopy trial (n=1580)	Excluded patients* (n=3036)	p value
Sex					0·0074
Male	240 (45%)	476 (45%)	716 (45%)	1251 (41%)	
Female	293 (55%)	571 (55%)	864 (55%)	1785 (59%)	
Age (years)					<0·0001
55–64	217 (41%)	384 (37%)	601 (38%)	802 (26%)	
65–74	186 (35%)	377 (36%)	563 (36%)	1045 (34%)	
75–84	113 (21%)	253 (24%)	366 (23%)	930 (31%)	
≥85	17 (3%)	33 (3%)	50 (3%)	259 (9%)	
Symptoms†					
Change in bowel habit	383 (72%)	772 (74%)	1155 (73%)	1926 (63%)	<0·0001
Harder, less frequent	66 (12%)	126 (12%)	192 (12%)	297 (10%)	..
Looser, more frequent	214 (40%)	410 (39%)	624 (39%)	1049 (35%)	..
Variable	54 (10%)	124 (12%)	178 (11%)	180 (6%)	..
Unspecified	49 (9%)	112 (11%)	161 (10%)	400 (13%)	..
Rectal bleeding	240 (45%)	432 (41%)	672 (43%)	1169 (39%)	0·0080
Abdominal pain	124 (23%)	227 (22%)	351 (22%)	574 (19%)	0·0077
Anaemia	60 (11%)	140 (13%)	200 (13%)	620 (20%)	<0·0001
Weight loss	82 (15%)	155 (15%)	237 (15%)	500 (16%)	0·19
Other symptoms	102 (19%)	172 (16%)	274 (17%)	585 (19%)	0·11

Data are number (%) unless otherwise specified. *Patients excluded from both this trial and the parallel CT colonography versus barium enema trial. †Some patients reported more than one symptom.

Table 1: **Characteristics of patients included in this trial versus excluded patients**

missed if it was identified through NHSIC as occurring within 36 months of randomisation, but was not detected by the randomised procedure or mentioned in the patient's discharge letter.

Extracolonic cancers included all reported primary malignant neoplasms, excluding colorectal cancers (C18–C20) and non-melanoma malignant neoplasms of the skin (C44).

A serious adverse event was defined as any incident causing hospital admission, death, threat to life, or permanent impairment.[22] An expert panel consisting of a radiologist, a gastroenterologist, and a colorectal surgeon reviewed reasons for unplanned hospital admissions and deaths within 30 days to decide whether any were attributable to a randomly assigned procedure (reviewers were masked to the assigned procedure). Panel members assessed cases independently and a consensus was reached when any disagreement arose.

Patients with extracolonic findings at CTC were followed up until either a diagnosis was given, the patient was put into regular surveillance, or a decision was made not to investigate further. The expert panel reviewed diagnoses resulting from extracolonic findings at CTC to establish whether these diagnoses could have explained patients' presenting symptoms.

Statistical analysis

We estimated that a sample size of 1430 would give 80% power to detect a significant difference in rates of additional colonic investigation at $\alpha=0\cdot05$ (two-tailed), assuming that 14% of patients after colonoscopy and 20% after CTC would need additional colonic investigation, and with 2:1 randomisation in favour of colonoscopy. The primary and secondary outcomes were analysed by intention to treat, except for colorectal cancer miss rates and adverse events, which were analysed only in patients who had their randomised procedure. The analysis of detection rates was per patient, using the most advanced colonic lesion diagnosed.

We analysed all extracolonic cancers diagnosed within 36 months of randomisation, and calculated expected numbers by applying age-sex-specific cancer incidence for the general population to our cohort, having adjusted for reported mortality.[23] We compared incidence assuming a Poisson distribution.

Categorical outcomes were compared using Pearson's χ^2 test or Fisher's exact test, as appropriate. We calculated relative risks (RRs) with 95% CIs. We showed RRs for the primary outcome by age group (<65 years or ≥65 years) and sex using forest plots, and used tests of interaction (Mantel-Haenszel) to identify significant differences. To check whether clustering by trial centre affected results, we also analysed the primary outcome using random effects logistic models allowing for heterogeneity in the outcome and intervention effects by centre (odds ratios were compared).[24] All tests were two-tailed with significance assigned at 5%. We analysed the data using Stata 10.1.

The trial is an International Standard Randomised Controlled Trial, number 95152621.

Role of the funding source

The primary funder (the National Institute for Health Research) stipulated a randomised controlled design, but no funders or providers of equipment were involved in the collection, analysis, or interpretation of data, nor in the writing or submitting of the report. WA, ED, KW, IK-H, and SH had full access to study data, whereas CvW, GY, RJL, and JW had access to subsets of the data. All authors take responsibility for the decision to submit for publication.

Results

Recruitment for both trials began in March, 2004, and was completed in December, 2007. Of 8484 potentially eligible patients, 3036 were not included because either they or their clinician declined consent (for specific reasons, see appendix) and 3838 entered the accompanying CTC versus barium enema trial.[15] Of the remaining 1610 patients who entered the CTC versus colonoscopy trial, 30 subsequently withdrew consent (25 [2·3%] in the colonoscopy group and five [0·9%] in the CTC group), leaving 1580 for analysis (1047 assigned to colonoscopy and 533 to CTC; figure 1).

See Online for appendix

	CT colonography (n=533)	Colonoscopy (n=1047)	Relative risk (95% CI)	p value	CT colonography (n=533)		Colonoscopy (n=1047)	
					Men (n=240)	Women (n=293)	Men (n=476)	Women (n=571)
All referrals for additional colonic investigation	160* (30·0%)	86† (8·2%)	3·65 (2·87–4·65)	<0·0001	87 (36·2%)	73 (24·9%)	27 (5·7%)	59 (10·3%)
Colorectal cancer or polyp ≥10 mm suspected	83 (15·6%)	12‡ (1·1%)	13·59 (7·48–24·66)	<0·0001	45 (18·7%)	38 (13·0%)	4 (0·8%)	8 (1·4%)
Colorectal cancer	47	10	..	..	25	22	4	6
Polyp ≥10 mm	36	2	..	..	20	16	0	2
Smaller polyp suspected	49 (9·2%)	1§ (0·1%)	..	<0·0001	27 (11·2%)	22 (7·5%)	1 (0·2%)	0
8–9 mm	14	1	..	..	8	6	1	0
6–7 mm	22	0	..	..	14	8	0	0
≤5 mm	13	0	..	..	5	8	0	0
Clinical uncertainty (no lesions seen)	28 (5·3%)	73 (7·0%)	0·75 (0·49–1·15)	0·19	15 (6·3%)	13 (4·4%)	22 (4·6%)	51 (8·9%)
Inadequate examination	18	72	..	..	10	8	21	51
Adequate examination	10	1	..	..	5	5	1	0

Data are number, or number (%), unless otherwise specified. *150 patients were referred to endoscopy and ten directly to surgery. †16 patients were referred to endoscopy, 63 to radiology, and seven directly to surgery. ‡Comprises ten patients in whom biopsy samples were not taken at colonoscopy or were inconclusive, and two patients referred after an alternative procedure. §Patient referred after an alternative procedure.

Table 2: **Additional colonic investigation by reason for investigation, overall and by sex**

	CT colonography				Colonoscopy			
	Additional colonic procedure undertaken	Colorectal cancer detected	Polyp ≥10 mm detected	Colorectal cancer or polyp ≥10 mm detected	Additional colonic procedure undertaken	Colorectal cancer detected	Polyp ≥10 mm detected	Colorectal cancer or polyp ≥10 mm detected
All referrals for additional colonic investigation	160	29	26	55 (34%)	86	12	3	15 (17%)
Colorectal cancer or polyp ≥10 mm suspected	83	29	22	51 (61%)	12	9	2	11 (92%)
Colorectal cancer	47	27	3	30	10	9	1	10
Polyp ≥10 mm	36	2	19	21	2	0	1	1
Smaller polyp suspected	49	0	3	3 (6%)	1	0	0	0
8–9 mm	14	0	2	2	1	0	0	0
6–7 mm	22	0	0	0	0	0	0	0
≤5 mm	13	0	1*	1	0	0	0	0
Clinical uncertainty (no lesions seen)	28	0	1	1 (4%)	73	3	1	4 (5%)
Inadequate examination	18	0	1	1	72	3	1	4
Adequate examination	10	0	0	0	1	0	0	0

Data are number, or number (%). Only the most advanced lesion per patient is presented. *5 mm transverse colon polyp at CT colonography, and a 10 mm pedunculated sigmoid colon polyp at subsequent colonoscopy.

Table 3: **Results of additional colonic investigation, by reason for investigation**

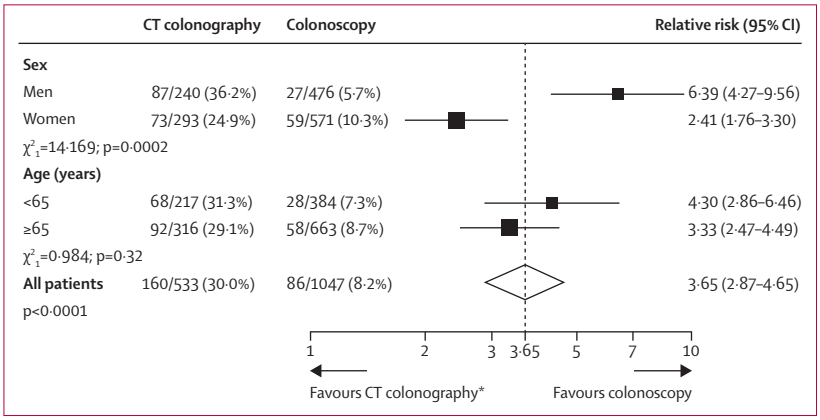

Figure 2: **Additional colonic investigation by sex and age group**
*Relative to the mean effect.

	CT colonography	Colonoscopy	Relative risk (95% CI)	p value
All patients, n	533	1047		
Colorectal cancer or polyp ≥10 mm	57 (10·7%)	119 (11·4%)	0·94 (0·70–1·27)	0·69
Colorectal cancer	30* (5·6%)	58† (5·5%)	1·02 (0·66–1·56)	0·94
Polyp ≥10 mm	27‡ (5·1%)	61§ (5·8%)	0·87 (0·56–1·35)	0·53
Patients who had their randomised procedure, n¶	503	967		
Colorectal cancer or polyp ≥10 mm	54 (10·7%)	116 (12·0%)	0·89 (0·66–1·21)	0·47
Colorectal cancer	28 (5·6%)	55 (5·7%)	0·98 (0·63–1·52)	0·92
Polyp ≥10 mm	26 (5·2%)	61 (6·3%)	0·82 (0·52–1·28)	0·38

Data are number, or number (%), unless otherwise specified. Only the most advanced lesion per patient is presented. *29 adenocarcinomas and one non-Hodgkin lymphoma. †55 adenocarcinomas, one carcinoid tumour, and two cancers that were not histologically confirmed. ‡24 adenomas and three hyperplastic polyps. §52 adenomas, four hyperplastic polyps, three serrated adenomas, one juvenile polyp, and one polyp excised but not retrieved. ¶Excludes lesions detected previously by flexible sigmoidoscopy.

Table 4: **Detection rates of colorectal cancer and large polyps**

The median age of participants in this trial was 68 years (IQR 61–75) and 864 (55%) were women. The most frequent presenting symptoms were change in bowel habit, rectal bleeding, and abdominal pain (table 1). Participants included in this trial were more likely to be male, younger, and to present with a change in bowel habit, rectal bleeding, or abdominal pain than were excluded patients. They were less likely to present with anaemia (table 1).

The proportion of patients who had their assigned procedure did not differ significantly between study groups (967 [92·4%] of 1047 in the colonoscopy group *vs* 503 [94·4%] of 533 in the CTC group; p=0·14). Reasons why patients did not have the procedure are outlined in the appendix. Of those patients who did not have the assigned procedure, 16 (20%) of 80 in the colonoscopy group and 11 (37%) of 30 in the CTC group had an alternative whole-colon examination (figure 1). FS was undertaken before the scheduled randomised procedure in eight patients assigned to CTC but none assigned to colonoscopy.

Additional diagnostic investigation of the colon was undertaken more than three times as often in patients assigned to CTC than assigned to colonoscopy (160 [30·0%] of 533 *vs* 86 [8·2%] of 1047; p<0·0001; table 2). We obtained similar results when we analysed rates only in patients who had their randomised procedure (data not shown). Models controlling for clustering by trial centre showed no attenuation of effect (data not shown).

In the colonoscopy group, 118 (11·3%) patients had a colonoscopy that was incomplete (did not reach the caecum), and 72 (6·9%) had an additional procedure for this reason. A further 13 (1·2%) patients were referred to confirm a suspected cancer or polyp (because biopsy samples were not taken or were inadequate for histological confirmation), and one patient was referred for an additional procedure because of persistent symptoms (table 2). By comparison, 83 patients (15·6%) in the CTC group were referred to investigate a suspected cancer or polyp of 10 mm or larger, 49 (9·2%) for smaller polyps, and 28 (5·3%) because of an inadequate examination or clinical uncertainty (table 2). All 29 cancers and 22 of the 26 large polyps identified at subsequent colonic investigations in the CTC group were in patients in whom a large lesion had been seen at the first examination; the yield in patients referred for small polyps or clinical uncertainty was low (table 3).

Relative referral rates differed significantly between men and women (p=0·0002). Men were more than six times as likely to have an additional colonic examination after CTC than after colonoscopy, whereas women were just over twice as likely to do so (figure 2). Results did not differ significantly by age group (p=0·32; figure 2).

Of 1047 patients assigned to colonoscopy, 119 (11·4%) were diagnosed with colorectal cancer or a large polyp: 116 (11·1%) at colonoscopy and three (0·3%) after an alternative procedure. By comparison, 57 (10·7%) of 533 patients assigned to CTC were diagnosed with colorectal cancer or a large polyp: 54 (10·1%) at CTC, two (0·4%) at previous FS, and one (0·2%) after an alternative procedure (see footnote to table 4 for histological diagnoses of cancers and large polyps). The overall detection rate of colorectal cancer or large polyps did not differ between groups (RR 0·94, 95% CI 0·70–1·27; p=0·69). Analysis of detection rates only in patients who had their randomised procedure (and excluding lesions detected at previous FS) gave similar results (table 4).[18]

We also analysed other colorectal findings. A significantly greater proportion of patients in the CTC group were diagnosed with diverticulosis than were those in the colonoscopy group (287 [54%] of 533 assigned to CTC *vs* 366 [35%] of 1047 assigned to colonoscopy; p<0·0001), whereas colitis (4 [1%] *vs* 34 [3%]; p=0·0022) and anal pathology (13 [2%] *vs* 73 [7%]; p=0·0002) were diagnosed more frequently in the colonoscopy group than in the CTC group. Other findings occurred in numbers too low to be analysed.

At least one previously unknown extracolonic finding was reported in 287 (60·4%) of the 475 patients who had CTC and did not have colorectal cancer diagnosed before discharge. A referral for additional investigation was made in 48 (10·1%) patients, leading to diagnosis of extracolonic malignancy in nine (see appendix). No patients had aortic aneurysms of 5·5 cm diameter or larger (the recommended threshold for surgical referral) but nine had aneurysms of 3·0–5·4 cm (recommended for surveillance).[25] Of 48 patients who had additional procedures to investigate an extracolonic finding, 17 (35%) were given a diagnosis that explained at least one of their presenting symptoms. A more detailed analysis will be published elsewhere.[18]

We analysed the data in June, 2012, when registration was reported to be 97% complete for cancers diagnosed until December, 2010[26] (at which point all patients had been followed up for at least 36 months), and all deaths until December, 2011, had been registered.[27] At the time of analysis (median follow-up for deaths 5·2 years, IQR 4·6–5·9), 154 (14·7%) patients assigned to colonoscopy and 63 (11·8%) assigned to CTC had died (p=0·11).

Of the 503 patients who had CTC, 28 (5·6%) received a colorectal cancer diagnosis as a result of the procedure (table 4), and one had an additional cancer that was diagnosed during the 3 year follow-up, giving a miss rate of one in 29 (3·4%). Of the 967 patients who had colonoscopy, 55 (5·7%) were diagnosed with colorectal cancer (table 4) and no cancers were missed.

During the 3 year follow-up, 27 primary extracolonic cancers were diagnosed in the CTC group and 56 in the colonoscopy group (see appendix); incidence did not differ between groups (17·6 per 1000 person-years in the CTC group *vs* 18·7 per 1000 person-years in the colonoscopy group; incidence rate ratio [IRR] 0·94, 95% CI 0·59–1·49; p=0·79; appendix). In the first year, rates were more than twice as high as expected (IRR 2·33, 1·40–3·89; p=0·0007), but again rates did not differ significantly between the CTC and colonoscopy groups (IRR 0·95, 0·53–1·73; p=0·88). CTC detected nine (56%) of 16 extracolonic cancers diagnosed during the first year. Colonoscopy detected one extracolonic cancer: a lung primary diagnosed via a colonic metastasis.

Minor adverse effects are reported elsewhere;[17] we report more serious adverse events here. An unplanned hospital admission within 30 days occurred in 12 patients after colonoscopy and six after CTC. The expert panel judged four admissions as possibly attributable to a randomised procedure. Three occurred after colonoscopy (one abdominal pain, one rectal bleeding, one diarrhoea and vomiting); polypectomy was not undertaken at any of these examinations. Another patient had CTC followed by colonoscopy 22 days later for removal of two large lesions; the patient was then admitted immediately because of a suspected perforation but was discharged the following day. No confirmed perforations were reported. One patient died within 30 days, after surgery for colorectal cancer detected at CTC.

Discussion

This is the first randomised trial comparing CTC and colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer, and the first trial to compare rates of additional colonic investigation when the two tests are used in normal clinical practice (see panel). We report that 30% of patients had additional colonic investigation after CTC, compared with only 8% after colonoscopy. Almost half the referrals after CTC were for polyps smaller than 10 mm or because of clinical uncertainty, with low predictive value for colorectal cancer or large polyps. We also found a significant difference in relative referral rates by sex. Men were more likely than women to have a second examination after CTC, usually because a cancer or polyp was detected, whereas women were more likely than men to have a second examination after colonoscopy, usually because their colonoscopy was incomplete. This confirms results from other studies showing that women tolerate colonoscopy less well and have fewer polyps than men do.[1,28]

Most prospective studies of CTC have been within-patient comparisons in which all patients receive colonoscopy, irrespective of findings at CTC.[11] Such studies do not capture the uncertainties faced by radiologists and referring clinicians when dealing with a symptomatic population. If CTC is to become more widely used as an alternative to colonoscopy, the referral rate we report for subsequent endoscopic investigation is unacceptably high, particularly when it is considered that only a third of referred patients were found to have colorectal cancer or a large polyp, and concern has been expressed by endoscopists that colonoscopies after false-positive CTCs take significantly longer than routine examinations.[29]

Many of these referrals for colonoscopy might be avoidable. For example, small lesions rarely cause symptoms and carry a low risk of cancer. If, as we suggest,[15] the threshold for referral had been set at 8 mm, this would have reduced the referral rate to 23% with minimal loss of sensitivity. Further reductions could be made through the use of oral contrast to label residual fluid and stool (faecal tagging), which was rarely used in our study but is becoming widespread in clinical practice.[30] Faecal tagging might give radiologists greater confidence in the presence or absence of lesions,[31] potentially reducing referrals due to poor bowel preparation or to lesions identified with low certainty. Evidence-based referral guidelines are also needed, both for radiologists and referring clinicians.

In our trial, the unadjusted non-completion rate for colonoscopy was 11%, with 7% of patients having an additional examination for this reason. Although completion rates have increased substantially since the publication of a UK audit in 2004,[14] there might be a limit to what is achievable in symptomatic patients: one recent audit showed an unadjusted non-completion rate of 8% for

***Panel:* Research in context**

Systematic review

We searched the Medline database for reports on CT colonography (CTC), published between 1994 and 2003, using the terms "colonography", "colography", "CT colonoscopy", "CT pneumocolon", "virtual colonoscopy", and "virtual endoscopy". We did not apply any language restrictions. Additional searches using the Cochrane controlled trials register, Embase, Science Citation Index, and manual searches of key journals did not reveal any additional studies. 24 studies that met selection criteria were included in a meta-analysis, which showed that CTC has comparable sensitivity to colonoscopy for detection of colorectal cancer. However, we found no randomised trials comparing CTC with colonoscopy.

Interpretation

Our study is the first randomised trial to compare CTC and colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer. We report that CTC generated substantially more follow-up tests than colonoscopy. Almost half the referrals after CTC were for smaller polyps or clinical uncertainty, with a low probability of finding cancer or a large polyp. Many of these follow-up investigations might be avoided by the development of guidelines for patient referral and the use of techniques such as faecal tagging to increase specificity. Previous evidence suggests that CTC is a similarly sensitive, less invasive alternative to colonoscopy, and we found that it was preferred by patients. CTC might be a particularly suitable test in patients with low-risk symptoms, or in those who are older or have comorbidities. Women might also benefit from having CTC, as they have a higher rate of incomplete colonoscopy and generally have fewer polyps than men do. Our results suggest that more widespread use of CTC as an alternative to colonoscopy is justified, provided that guidelines on best practice and a system of training and audit are put in place.

all colonoscopies[32] and another showed a rate of 12% for non-screening colonoscopies;[33] similar to what we report.

Meta-analysis shows that CTC has a sensitivity for colorectal cancer of 96% when compared with colonoscopy as the reference standard.[9] Several audits have shown a cancer miss rate by colonoscopy of 5%.[34–36] In our trial, CTC missed one cancer (of 29) whereas colonoscopy missed none (of 55). For large polyps, the sensitivity of CTC relative to colonoscopy in our trial was in broad agreement with average sensitivities reported in meta-analyses: 85%[11] and 93%.[10] However, results of studies vary widely, which has been attributed mainly to differences in the equipment used[11] and in the skill of radiologists.[37] If diagnostic standards are to be maintained as use of CTC becomes more widespread, formal training and testing will be needed, with retraining for those who do not achieve a suitable level.[38] Minimum standards for reporting and regular audit are also needed, as exist for colonoscopy.[39]

Our analysis of colonic findings showed that colitis was diagnosed significantly more frequently in patients having colonoscopy than in those having CTC, making CTC an unsuitable test when colitis is suspected.

Extracolonic abnormalities were reported in around 60% of patients who had CTC in both this and the parallel trial;[15] a rate similar to that seen in screening populations.[40,41] Most extracolonic findings were judged to be clinically unimportant, and rates of additional extracolonic investigation after CTC (10% in this trial and 7% in the parallel trial) were similar to those reported in two retrospective UK studies of symptomatic patients, and in an older asymptomatic US cohort.[41–43] In patients who were investigated, only a third received a diagnosis that explained at least one of their presenting symptoms.

The proportion of patients with an extracolonic cancer diagnosed within 3 years was similar after CTC and colonoscopy (around 5%), and time to diagnosis was not shorter in the CTC group (appendix). Around 60% of diagnoses were made during the first year, suggesting that they resulted from ongoing investigation of patients' original symptoms. Clearly, when symptoms are vague but colorectal cancer is suspected, clinicians are faced with a choice: to undertake a specific colonic examination such as colonoscopy and refer for additional investigation only in patients for whom there is persistent concern about symptoms, or to refer for CTC, which allows imaging of both colonic and extracolonic regions of the abdomen and pelvis in one examination, but does not detect all extracolonic cancers and might offer false reassurance that an extracolonic cause of symptoms has been ruled out. It is not clear which is the best strategy, and both could result in patients undergoing additional investigation without clinical benefit.

Previous studies suggest that adverse events are more frequent after colonoscopy than after CTC;[3–5] we were unable to corroborate this finding because serious adverse events were rare in both groups. However, in a report published elsewhere,[17] we have confirmed results from previous studies[6–8] showing that patients find CTC more acceptable than colonoscopy. Patients allocated colonoscopy in our trial were more satisfied with the way results were delivered (since this was more likely to happen immediately and via a face-to-face conversation), but reported more physical discomfort and worry, and were significantly less satisfied with the test than were patients in the CTC group.[17]

The health economic analysis of the trial is reported elsewhere.[18] The higher unit cost of colonoscopy was largely offset by the greater number of additional procedures needed to investigate suspected colonic lesions in the CTC group. The mean difference in net costs at 2010–11 prices was a statistically insignificant £65 per patient in favour of CTC. The detection rate of colonic lesions by colonoscopy was only slightly higher than the detection rate for CTC, with an incremental cost of £9270 per case detected. As a result, neither method shows clear superiority in terms of cost-effectiveness for detecting colonic lesions.

In conclusion, in our pragmatic trial of symptomatic patients, CTC was associated with a high referral rate for additional tests. These referrals have the potential to increase anxiety and overall cost, and—in patients referred for colonoscopy—mitigate the advantage of avoiding an endoscopic examination. For most patients, however, CTC offers a similarly sensitive, less invasive alternative to colonoscopy. With wider implementation,

there will be a need for protocols to improve specificity, along with attention to referral criteria and an emphasis on radiologist training and assessment. With these in place, our results suggest that CTC should be considered as an alternative first-line investigation for patients with symptoms suggestive of colorectal cancer.

Contributors

WA and SH were joint principal investigators. They designed the study and wrote the grant application, assisted by CvW, RE, CK, RJL, DM, and JW. RE generated the randomisation codes and designed the study database. WA, ED, and IK-H were responsible for recruitment, data collection, and management, assisted by the SIGGAR investigators mentioned below. WA, ED, KW, and IK-H analysed the data, and CvW, GY, RJL, and JW analysed subsets of the data. WA, ED, and SH drafted the report and all authors contributed to review and revision. All authors have seen and approved the final version. Both WA and SH will act as guarantors.

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Conflicts of interest

SH and DB have been remunerated for research and development advice by Medicsight, a software company developing computer-assisted detection for CT colonography. The other authors declare that they have no conflicts of interest.

Acknowledgments

We thank the radiologists and endoscopists who completed the case report forms, the research nurses who were responsible for data collection, and the trial participants and referring clinicians for their support of the study. We also thank Willie Hamilton (Professor of Primary Care Diagnostics, University of Exeter), Brian Saunders (Consultant Gastroenterologist, The North West London Hospitals NHS Trust), and Roland Valori (Consultant Gastroenterologist, Gloucestershire Hospitals NHS Foundation Trust) for many helpful discussions and advice. This research was undertaken jointly by Imperial College London and University College London. It was funded mainly by the NIHR Health Technology Assessment (HTA) Programme (project number 02/02/01), and will be published in full in *Health Technology Assessment*. Researchers at University College received a proportion of funding from the NIHR Biomedical Research Centres funding scheme, and additional funding for researchers at Imperial College was provided by a Cancer Research UK Population Research Committee Programme Grant (number C8171/A10391). The economic analysis was funded by the NIHR HTA Programme, the EPSRC Multidisciplinary Assessment of Technology Centre for Healthcare (MATCH), and the NIHR Collaborations for Leadership in Applied Health Research and Care for Birmingham and Black Country. The views and opinions expressed herein are those of the authors and do not necessarily reflect those of Cancer Research UK, MATCH, EPSRC, the HTA Programme, NIHR, NHS, or the Department of Health. Medicsight, Viatronix, Bracco UK, and Barco provided equipment.

References

1 Shah HA, Paszat LF, Saskin R, Stukel TA, Rabeneck L. Factors associated with incomplete colonoscopy: a population-based study. *Gastroenterology* 2007; **132:** 2297–303.

2 Anderson J, Messina C, Cohn W, et al. Factors predictive of difficult colonoscopy. *Gastrointest Endosc* 2001; **54:** 558–62.

3 Warren JL, Klabunde CN, Mariotto AB, et al. Adverse events after outpatient colonoscopy in the Medicare population. *Ann Intern Med* 2009; **150:** 849–57.

4 Levin TR, Zhao W, Conell C, et al. Complications of colonoscopy in an integrated health care delivery system. *Ann Intern Med* 2006; **145:** 880–86.

5 Pendsé DA, Taylor SA. Complications of CT colonography: a review. *Eur J Radiol* 2012; published online May 15. DOI:10.1016/j.ejrad.2012.04.011.

6 Gluecker TM, Johnson CD, Harmsen WS, et al. Colorectal cancer screening with CT colonography, colonoscopy, and double-contrast barium enema examination: prospective assessment of patient perceptions and preferences. *Radiology* 2003; **227:** 378–84.

7 Svensson MH, Svensson E, Lasson A, Hellström M. Patient acceptance of CT colonography and conventional colonoscopy: prospective comparative study in patients with or suspected of having colorectal disease. *Radiology* 2002; **222:** 337–45.

8 van Gelder RE, Birnie E, Florie J, et al. CT colonography and colonoscopy: assessment of patient preference in a 5-week follow-up study. *Radiology* 2004; **233:** 328–37.

9 Pickhardt PJ, Hassan C, Halligan S, Marmo R. Colorectal cancer: CT colonography and colonoscopy for detection—systematic review and meta-analysis. *Radiology* 2011; **259:** 393–405.

10 Halligan S, Altman D, Taylor S, et al. CT colonography in the detection of colorectal polyps and cancer: a systematic review, meta-analysis and proposed minimum data set for study level reporting. *Radiology* 2005; **237:** 893–904.

11 Mulhall BP, Veerappan GR, Jackson JL. Meta-analysis: computed tomographic colonography. *Ann Intern Med* 2005; **142:** 635–50.

12 American College of Radiology. ACR practice guideline for the performance of computed tomography (CT) colonography in adults, 2009. http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/CT_Colonography.pdf (accessed Dec 11, 2012).

13 Burling D. CT colonography standards. *Clin Radiol* 2010; **65:** 474–80.

14 Bowles C, Leicester R, Romaya C, Swarbrick E, Williams C, Epstein O. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? *Gut* 2004; **53:** 277–83.

15 Halligan S, Wooldrage K, Dadswell E, et al, for the SIGGAR investigators. Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): a multicentre randomised trial. *Lancet* 2013; published online Feb 14. http://dx.doi.org/10.1016/S0140-6736(12)62124-2.

16 von Wagner C, Smith S, Halligan S, et al, for the SIGGAR Investigators. Patient acceptability of CT colonography compared with double contrast barium enema: results from a multicentre randomised controlled trial of symptomatic patients. *Eur Radiol* 2011; **21:** 2046–55.

17 von Wagner C, Ghanouni A, Halligan S, et al. Patient acceptability and psychological consequences of CT colonography compared with colonoscopy: results from a multicenter randomized controlled trial of symptomatic patients. *Radiology* 2012; **263:** 723–31.

18 Halligan S, Dadswell E, Wooldrage K, et al. Computed tomographic colonography versus colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicentre randomised trials with economic evaluation (SIGGAR). *Health Technol Assess* (in press).

19 Halligan S, Lilford RJ, Wardle J, et al. Design of a multicentre randomized trial to evaluate CT colonography versus colonoscopy or barium enema for diagnosis of colonic cancer in older symptomatic patients: the SIGGAR study. *Trials* 2007; **8:** 32.

20 Joint Advisory Group on Gastrointestinal Endoscopy. Guidelines for the training, appraisal and assessment of trainees in gastrointestinal endoscopy and for the assessment of units for registration and re-registration, March 2006. http://www.bsg.org.uk/pdf_word_docs/jag_recommendations_2004.pdf (accessed Dec 11, 2012).

21 Barish MA, Soto JA, Ferrucci JT. Consensus on current clinical practice of virtual colonoscopy. *AJR Am J Roentgenol* 2005; **184:** 786–92.

22 Medicines and Healthcare products Regulatory Agency. Device bulletin: reporting adverse incidents and disseminating medical device alerts. http://www.mhra.gov.uk/home/groups/dts-bs/documents/publication/con111568.pdf (accessed Dec 11, 2012).

23 Office for National Statistics. Cancer statistics registrations, England (series MB1), no. 40, 2009. http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-222747 (accessed Jan 12, 2012).

24 Lee KJ, Thompson SG. Clustering by health professional in individually randomised trials. *BMJ* 2005; **330:** 142–44.

25 Moll FL, Powell JT, Fraedrich G, et al. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. *Eur J Vasc Endovasc Surg* 2011; **41** (suppl 1)**:** S1–58.

26 Office for National Statistics. Information paper: summary quality report for cancer statistics registrations, England, 2011. http://www.ons.gov.uk/ons/guide-method/method-quality/quality/quality-information/social-statistics/summary-quality-report-for-cancer-registration-statistics.pdf (accessed Dec 11, 2012).

27 Office for National Statistics. Births and deaths in England and Wales, 2011 (final). http://www.ons.gov.uk/ons/guide-method/method-quality/quality/quality-information/social-statistics/sqr-annual-mortality.pdf (accessed Dec 11, 2012).

28 Brenner H, Altenhofen L, Hoffmeister M. Sex, age, and birth cohort effects in colorectal neoplasms. *Ann Intern Med* 2010; **152:** 697–703.

29 Hur C, Gazelle GS, Hsu EH, Halpern EF, Podolsky DK. The effect of prior colonic imaging on endoscopic productivity: potential impact of computed tomographic colonography. *Clin Gastroenterol Hepatol* 2005; **3:** 1124–27.

30 Plumb AA, Halligan S, Taylor SA, Burling D, Patnick J. CT colonography in the English Bowel Cancer Screening Programme: national survey of current practice. *Clin Radiol* 2012; published online Dec 11. DOI:10.1016/j.crad.2012.10.018.

31 Nagata K, Okawa T, Honma A, Endo S, Kudo SE, Yoshida H. Full-laxative versus minimum-laxative fecal-tagging CT colonography using 64-detector row CT: prospective blinded comparison of diagnostic performance, tagging quality, and patient acceptance. *Acad Radiol* 2009; **16:** 780–89.

32 Gavin DR, Valori RM, Anderson JT, Donnelly MT, Williams JG, Swarbrick ET. The national colonoscopy audit: a nationwide assessment of the quality and safety of colonoscopy in the UK. *Gut* 2013; **62:** 242–49.

33 Verma A, Mcgrath N, Bennett P, et al. Scope to improve: a multi-centre audit of 16 064 colonoscopies looking at caecal intubation rates, over a two-year period. *Frontline Gastroenterol* 2012; **3:** 124–29.

34 Rex D, Rahmani E, Haseman J, Lemmel G, Kaster S, Buckley J. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. *Gastroenterology* 1997; **112:** 17–23.

35 Rabeneck L, Paszat LF. Circumstances in which colonoscopy misses cancer. *Frontline Gastroenterol* 2010; **1:** 52–58.

36 Bressler B, Paszat LF, Chen Z, Rothwell DM, Vinden C, Rabeneck L. Rates of new or missed colorectal cancers after colonoscopy and their risk factors: a population-based analysis. *Gastroenterology* 2007; **132:** 96–102.

37 Doshi T, Rusinak D, Halvorsen RA, Rockey DC, Suzuki K, Dachman AH. CT colonography: false-negative interpretations. *Radiology* 2007; **244:** 165–73.

38 Fletcher JG, Chen MH, Herman BA, et al. Can radiologist training and testing ensure high performance in CT colonography? Lessons from the National CT Colonography Trial. *AJR Am J Roentgenol* 2010; **195:** 117–25.

39 Joint Advisory Group on GI Endoscopy. BSG quality and safety indicators for endoscopy. http://www.thejag.org.uk/downloads%5CUnit%20Resources%5CBSG%20Quality%20and%20Safety%20Indicators.pdf (accessed Dec 11, 2012).

40 Johnson CD, Chen MH, Toledano AY, et al. Accuracy of CT colonography for detection of large adenomas and cancers. *N Engl J Med* 2008; **359:** 1207–17.

41 Kim DH, Pickhardt PJ, Hanson ME, Hinshaw JL. CT colonography: performance and program outcome measures in an older screening population. *Radiology* 2010; **254:** 493–500.

42 Tolan DJM, Armstrong EM, Chapman AH. Replacing barium enema with CT colonography in patients older than 70 years: the importance of detecting extracolonic abnormalities. *AJR Am J Roentgenol* 2007; **189:** 1104–11.

43 Xiong T, McEvoy K, Morton DG, Halligan S, Lilford RJ. Resources and costs associated with incidental extracolonic findings from CT colonogaphy: a study in a symptomatic population. *Br J Radiol* 2006; **79:** 948–61.