Evidence Tables

Citation: Burling D, Halligan S, Slater A, Noakes M and Taylor S (2006) Potentially Serious Adverse Events at CT Colonography in Symptomatic Patients: National Survey of the United Kingdom *Radiology* 239;2:464-471

Design: Retrospective Clinical Audit

Country: UK

Setting:

Aim: To determine the incidence of potentially serious adverse events associated with computed tomographic colonography performed in patients with symptoms of rectal cancer

Inclusion criteria
Any radiology department offering CT Colonography

Exclusion criteria

Sample Size
N/A

Randomisation Method
N/A

Population
N=216 UK National Health Service hospitals offering radiology service for adults

Study Duration
Survey carried out in February 2005

Interventions
CT Colonography

Outcomes
Adverse Events

Results
Responses were received from 138/216 (64%) of departments, of which 50 (36%) provided CT colonography as part of everyday clinical practice.

All patients within the survey underwent CT colonography for symptoms that might have been attributable to colorectal cancer including change in bowel habits, rectal bleeding and weight loss.
No patients were undergoing screening.

Ethical requirements stipulated that no details of patients' age or sex be revealed during the study.

The lead gastrointestinal radiologist in each of the 50 centres where CT colonography was performed was contacted and was asked a series of six questions, read from a study sheet. The questions were as follows:

Approximately how many CT colonographic studies does your department perform on average?	More than one per day, one per day, one per week or one per month
Approximately how many CT colonographic studies has your department performed in total?	Total given
How frequently does your department use inflated rectal balloon catheters for CT colonography?	Never, occasionally (approx. %) of always
Does your department use an automated colonic insufflation device?	Yes/No
To the best of your knowledge, has bowel perforation related to CT colonography occurred?	Yes/No (please give number)
To the best of your knowledge, has there been any other serious adverse event associated with CT colonography? For example, have there been reactions to intravenous contrast or spasmolytic agents?	Yes/No (please give number)

17,067 CT Colonographic examinations had been performed across 50 centres; mean number per centre = 359, range 10-3000.
At 36 centres (72%), a total of 100 examinations or more had been performed.

At the time of the study, more than one examination per day was performed at 5 centres (10%); at 21 centres (42%) one examination per day was performed, at 7 centres (14%) one examination per month was performed and at 3 (6%) CT colonography was no longer performed.

No deaths were reported and 13 patients (0.08%; 1 in 1313 patients) had experienced potentially serious adverse events believed to be related to CT colonography, 9 of which were luminal perforations giving a perforation rate of 0.05% (1 in 1896 patients).
8/9 perforations were discovered during or after the CT procedure; 4 patients were entirely asymptomatic with extraluminal gas discovered incidentally by the reporting radiologist between 6 hours and 4 days after the procedure.

The symptomatic perforation rate was 0.03% (1 in 3413 patients).

8/9 patients with perforation were treated conservatively either as inpatients or outpatients and to the knowledge of the respondents, all patients were alive and well at the time of the survey.

At 29 centres (58%) an inflated balloon catheter was never used, at 7 centres (14%) one was used occasionally (on average, for 14% of the examinations when anal incontinence was encountered; range 1-50%) and at 14 centres (28%) one was always used.
Overall, 9378 CT Colonographic examinations were performed using an inflated balloon in the rectum and among these there were 6 perforations. Further, 7689 CT colonographic examinations were performed without an inflated balloon and among these there were 2 perforations.
At 6 centres (12%) an automated insufflation device was used with 2 perforations associated.
There was no significant difference in the proportion of perforations associated with and without rectal balloon inflation (p=0.3)

At 3/50 centres (6%), contributing 4350 patients to the total, investigators had published peer reviewed indexed articles relating to CT colonography and 2 perforations occurred at one of these centres. No significant difference was observed in the proportion of perforations originating from research and non-research centres (p=0.82).

Citation: Chaparro M, Gisbert J, del Campo L, Cantero J, and Mate J (2009) Accuracy of Computed Tomographic Colonography for the Detection of Polyps and Colorectal Tumours: A systematic review and meta-analysis *Digestion* 80:1-17

Design: Systematic Review and Meta-analysis

Country: Various

Setting:

Aim: To perform a meta-analysis of the diagnostic accuracy of CT-Colonography compared with colonoscopy for the detection of polyps and colorectal tumours.

Inclusion criteria
Prospective blinded studies in which the results of CTC were interpreted independently of colonoscopy findings or during surgery.
Enrolment of adult patients who were to undergo CTC after a full bowel preparation, followed by complete colonoscopy or surgery and use of at least a single detector scanner with colon insufflation by air or carbon dioxide.
If there are multiple studies originating from the same institution, the dates for patient inclusion were evaluated to ensure that there were no patient overlaps.

Exclusion criteria
Studies with elevated computer aided detection systems
Technical Studies
Cost utility studies
Studies not reporting on CTC
Studies examining patient comfort
No appropriate gold standard
Not a diagnostic study
Reviews
Case Reports
Studies of preparation
Studies of Adverse Events
Clinical Practice Guidelines
Extracolonic Findings
Phantom Studies
Not in Humans

Sample Size
N/A

Randomisation Method
N/A

Population
The total population included in the review was 10,546 from 47 studies.

Study Duration
N/A

Interventions
CT Colonography versus an appropriate Gold Standard

Outcomes
Sensitivity
Specificity
(taken directly from the individual study as reported or calculated through analysis of true positives, true negatives, false positives and false negatives on a per patient and per polyp basis).

Positive and negative likelihood ratios and their 95% confidence intervals were calculated for each study. In calculating the likelihood ratios, if any of the cells of a 2x2 table contained a 0 value, 0.5 was added to all the cells.

Heterogeneity of all indexes was calculated through examination of forest plots, the X^2 test for homogeneity and through the calculation of the I^2 statistic where a value of >50% was considered substantial heterogeneity.

Results
1,798 articles were identified during initial searches of which 1,751 were excluded for reasons outline above.

From 47 studies, the total patient population was 10,546 with an average of 224 participants per study.

- 16 studies used single detector scanners, 27 used multidetector scanners and 4 studies used both.
- In 44 studies, colonoscopy was the gold standard while in 3 studies surgery was the gold standard.
- 24 studies used 2-D imaging with 3-D imaging on selected slices, 20 studies used both 2-D and 3-D imaging and 2 studies used flythrough imaging with 2-D reconstruction.
- Sodium phosphate was used for bowel preparation in 10 studies and polyethylene glycol was used in 21 studies
- Faecal tagging was used in 6 studies and in 12 studies intravenous contrast was used
- Average collimation was 3.7mm and average reconstruction interval was 2mm
- 41 studies were carried out in high risk populations with the remaining 6 carried out in an average risk population

Quality of included studies
The quality of studies included in the review was assessed using the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) tool which is based on a 14- item questionnaire. The QUADAS tool does not incorporate a global quality score for a number of reasons including the fact that a quality score ignores the importance of individual items and the direction of potential biases associated with these items may vary according to the context in which they are applied.

Sensitivity of CT Colonography
Across the studies, per polyp sensitivity ranged from 28-100% for polyps >6mm. Overall pooled sensitivity was 66% (95% CI 64-68%).
Sensitivity increased with polyp size with a pooled sensitivity of 59% (95% CI 56%-61%, range 16%-90%) for polyps 6-9mm and a pooled sensitivity of 76% (95% CI 73-79%, range 50-100%) for polyps >9mm.
There was significant heterogeneity between studies in all three comparison groups with the I^2 value >50% for all three groups.

The per patient sensitivity for CT colonography ranged from 24%-100% across the individual studies and the overall pooled sensitivity was 69% (95% CI, 66%-72%).
Sensitivity again increased with increasing polyp size with a pooled sensitivity of 60% (95% CI 56%-65%) for patients with polyps 6-9mm (range 20%-91%) and 83% (95% CI, 70%-85%) for patients with polyps >9mm (range 46%-100%).
Again there was significant between studies heterogeneity for each of the analyses groups.

Subgroup	Mean Sensitivity (95% CI)	Comparison	Mean Sensitivity (95% CI)
Phospho-soda for bowel preparation	83.3% (95% CI, 79%-87%), I^2=73%	No Phospho-soda	62% (95% CI, 58%-66%), I^2=93%
With fecal tagging	88% (95% CI 84%-91%), I^2<50%	Without fecal tagging	59% (95% CI 56%-63%), I^2=91%
Collimation thinner than 5mm	72% (95% CI 68%-76%), I^2=89%	Collimation ≥5mm	65% (95% CI, 68%-76%), I^2=95%
Reconstruction thinner than 3mm	64% (95% CI, 60%-68%), I^2=90%)	Reconstruction ≥3mm	58% (95% CI, 49%-67%), I^2=87%
2-D imaging with 3-D confirmation	64% (95% CI, 60-67%), I^2=90%	3-D imaging	83% (95% CI, 78%-87%), I^2=84%
Radiation dose <100mA	63% (95% CI, 60%-67%), I^2=95%	Radiation dose >100mA	79% (95% CI, 75%-83%), I^2=83%
Patients at high risk of CRC or polyps	65% (95% CI, 61%-68%), I^2=94%	Patients at average risk	82% (95% CI, 77&-87%), I^2=83%
No differences were found in other variables analysed, including study quality			

Results of the sensitivity analyses by subgroup

Specificity of CT Colonography
The overall specificity of CT colonography was 83% (95% CI, 81%-84%, I^2=89%).
Specificity improved with increasing polyp size; specificity was 90% (95% CI, 89%-91%, I^2=21%) for patients with polyps 6-9mm in size and increased to 92% (95% CI, 92%-93%, I^2=62%) for polyps >9mm.

Likelihood Ratios
Overall positive likelihood ratio was 2.9 (1.8-4) and the overall negative likelihood ratio was 0.38 (0.27-0.53).

For polyps between 6-9mm, the positive likelihood ratio was 3.8 (2.5-5.7) and the negative likelihood ratio was 0.4 (0.27-0.59).
For polyps >9mm, the positive likelihood ratio was 12.3 (7.7-19.4) and the negative likelihood ratio was 0.19 (0.12-0.3).

General comments
Not all the studies included in this review are relevant to the current topic as it included studies which are looking at diagnostic accuracy in asymptomatic patients which is not a relevant population group as it relates more to screening.

As the systematic review included the QUADAS assessment and the 2x2 tables both by per-patient and per-polyp analysis where appropriate for all the included studies, the data for the relevant studies was extracted.

Meta-analyses were performed in which the sensitivities and specificities and likelihood ratios of studies in the corresponding pooled indexes were combined using a random effects model.

Subgroup	Categories
Polyp size	6-9mm or >9mm
Colonic Preparation	
Use of Faecal Tagging	Yes or No
Collimation width and reconstruction interval	
Type of scanner	Single detector, multi detector or mixed
Imaging technique	2-D imaging with 3-D confirmation when a lesion was observed or always 3-D imaging
Radiation dose	
Risk of colorectal cancer	

Subgroup analysis comparisons

Citation: Halligan S, Altman D, Taylor S, Mallett S, Deeks J, Bartram C, and Atkin W (2005) CT Colonography in the Detection of Colorectal Polyps and Cancer: Systematic Review, Meta-analysis and Proposed Minimum Data Set for Study Level Reporting

Design: Systematic Review and Meta-analysis

Country:

Setting:

Aim: To assess methodological quality of available data in published reports of CT colonography

Inclusion criteria
Studies which focused on the detection of polyps and if the key methods for CT colonography were based on the consensus document presented at the fourth international symposium on virtual colonoscopy (i.e. full bowel preparation should be administered, prone and supine images should be acquired and helical scanners should be used).
Inclusion of studies was restricted to full reports
Software used for interpretation of CT colonography findings was to be commercially available and allow 2-D interpretation with luminal 3-D rendering for problem solving. Although a primary 3-D interpretation was equally acceptable.

Exclusion criteria
Studies using computer aided diagnostic systems
Any studies with fewer than 30 patients (in an attempt to diminish the effect of incorporating any learning curve for CT colonography).
Studies in which the prevalence of abnormality could be guessed to be excessively high by CT observers because *a priori* patient selection criteria were used.
Studies in which patients underwent CT as a result of incomplete colonoscopy due to obstructing tumour unless they formed less than 50% of the patient population group or an identifiable subset that could be excluded during data extraction.
Studies without details of polyps and verification with a reference test.
Studies with artificially inserted polyps, digital or otherwise
Studies in which intravenous iodinated contrast material was routinely administered to patients

Sample Size
N/A

Randomisation Method
N/A

Population

Study Duration
Searches carried out from January 1994 (the point at which CT Colonography was first described) to December 2003.

Interventions
CT Colonography with finding to be verified with a within subject reference test. Conventional endoscopy was the standard reference test used, though studies using surgical findings were considered acceptable as an alternative.

Outcomes
Per patient detection of colorectal polyps
Per polyp detection of colorectal polyps
Per patient sensitivity and specificity for different lesion sizes
Per polyp sensitivity

Results
1398 citations were identified with 65 considered for inclusion after search criteria were applied.
41/65 were excluded for reasons such as;

- Dual positioning not used
- Fewer than 30 patients
- Intravenous contrast material routinely used
- Overlap with other studies
- No results detailing neoplasia
- Inadequate reference standard

- Bi blind, disease prevalence too high
- Reduced or no bowel preparation
- Custom software, digital polyp library

A total of 24 studies were included in the review for a total of 4181 patients with a prevalence of abnormality ranging from 15% to 72%. Studies were assessed for quality and potential bias according to the Standards for Reporting of Diagnostic Accuracy and Quality Assessment of Studies of Diagnostic Accuracy
A total of 5 studies did not report on small polyps (<6mm)
23/24 studies included symptomatic or a subset of asymptomatic patients with a prior history of colorectal neoplasia, were under surveillance, or had recently had positive findings for a previous screening test.

Studies used between 1 and 4 observers per patient with findings for individual observers were presented in 58% (n=14) of studies and only after consensus in 42% (n=10).
5 studies investigated possible learning effects.
6 studies performed the reference test on the same day in all but 6 patients (from 2 studies).
6 studies used segmental unblinding to modify reference colonoscopy.

CT technique could be replicated from the details provided in all articles while details of reference colonoscopy were insufficiently described in 11 studies.
CT technical failures were reported in 17 studies and 4 more studies explicitly stated that there were no technical failures; the remaining 3 studies provided no details.

11 studies reported on incomplete colonoscopy, 6 stated that colonoscopy was complete in all patients and 7 studies did not provide details.

18 studies measured polyps during colonoscopy and described the method used, 2 studies described measurement but not the method used and 4 studies did not mention colonoscopic measurement.
The recording of lesion location was not described in 6 studies.

Fully populated 2x2 contingency tables for per patient data for any polyp size category could be extracted from 12 studies and data for a further 5 studies were obtained after contacting the authors.
1x2 contingency table for per polyp data for any polyp size category was extracted from all studies, though in one study it was reported for adenomas only.

Per Patient Analysis
Three polyp size categories were defined small (<6mm), medium (6-9mm) and large (≥1cm) and forest plots of sensitivity, specificity and ROC curves of sensitivity versus 1 minus specificity were produced for each category. Summary ROC curves were calculated for the small and medium polyp categories, however considerable heterogeneity between studies meant a summary ROC curve could not be calculated for the category of large polyps.

For large polyps, meta analysis was based on data from 2610 patients from 7 studies and the majority of studies had high sensitivity and all studies had excellent specificity. At least one large polyp was identified in 206 patients.
For medium polyps, meta-analysis was based on data from 1834 patients from 7 studies; 477 of whom were identified as having at least 1 medium polyp.
For small polyps, studies were heterogenous in sensitivity (range: 45%-97%), specificity (range: 26%-97%) and overall performance and so meta-analysis was not performed. From 12 studies with a total of 1361 patients, 650 patients were identified as having at least one small polyp. According to the authors, the variation in the mix of polyp sizes across the studies, in particular, the proportion of patients with only small polyps

Category	Average Sensitivity	95% CI	Range	Average Specificity	95% CI	Range
Large Polyps (≥1cm)	93%	73%-98%	64%-100%	97%	95%-99%	95%-100%
Medium Polyps (6-9mm)	86%	75%-93%	79%-100%	86%	76%-93%	55%-100%

Average Sensitivities and Specificities of the operating point for large and medium polyps (operating point is the point on the summary ROC curve representing the sensitivity and specificity results at the average threshold, together with 95% CI's).

Incorporation bias, which potentially occurs when information from the test being reviewed is included in the reference standard by using a modified reference standard, could have resulted in the over estimation of sensitivity and specificity. Exploratory analysis, comparing studies with and without a modified reference standard and

comparing individual observer agreement with consensus agreement, was attempted however there were too few studies to allow meaningful analysis.

Per Polyp Analysis
The performance of CT deteriorates for smaller polyps with an average sensitivity of 77% (95% CI 70%-83%) for large polyps down to 70% (95% CI 63%-76%) for medium polyps. Data for small polyps was not pooled due to the large amount of heterogeneity.

Cancer Detection
144/150 tumours were detected on CT but no meta-analysis could be performed as the numbers of established cancers per individual studies was too small.
Treating the data as if it were from a single study resulted in sensitivity (detection rate) of 96% (91%-99%).

General comments
Although there were some patients included in this study which were not relevant to the PICO, they were from a single study (Pickhardt et al) however this also represented the largest study in the meta-analysis with 1233 patients and was one of the studies which was included in the per patient meta-analysis and therefore the results of the meta-analysis cannot be considered to be directly relevant to the PICO.

References of Included Studies

Pickhardt P, Choi J, Hwang I et al (2003) Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults *New England Journal of Medicine* 349;2191-2200

Iannaccone R, Laghi A, Catalono C et al (2003) Detection of colorectal lesions: lower dose multi-detector row helical CT colonography compared with conventional colonoscopy *Radiology* 229;775-781

Taylor, S, Halligan S, Vance M et al (2003). Use of multidetector-row CT colonography for detection of colorectal neoplasia in patients referred via the Department of Health "2-week-wait" initiative. *Clinical Radiology* 58;11:855-861.

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Ginnerup Pederson B, Christiansen T, Bjerregaard N et al (2003) Colonoscopy and multidetector array computed tomographic colonography: detection rates and feasibility *Endoscopy* 35:736-742

Johnson C, Harmsen W, Wilson L et al (2003) Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. *Gastroenterology* 125:311-319

Pineau B, Paskett E, Chen et al (2003) Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. *Gastroenterology* 125;304-310

Thomeer M, Carbone I, Bosmans H et al (2003) Stool tagging applied in thin slice multi detector computed tomography colonography. *Journal of Computer Assisted Tomography* 27:132-139

McFarland E, Pilgram T, Brink J et al (2002) CT colonography: multi observer diagnostic performance *Radiology* 225;380-390

Macari M, Bini EJ, Xue X et al (2002) Colorectal neoplasms: prospective comparison of thin section low dose multi detector row CT colonography and conventional colonoscopy for detection *Radiology* 224;383-392

Gluecker, T, Dorta, G, Keller, W, Jornod, P, Meuli, R, and Schnyder, P (2002). Performance of multidetector computed tomography colonography compared with conventional colonoscopy. *Gut* 51;2:207-211.

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Laghi A, Iannaccone R, Carbone I et al (2002) Detection of colorectal lesions with virtual tomographic colonography *American Journal of Surgery* 183:124-131

Wessling J, Fischbach R, Domagk D et al (2001) Colorectal Polyps: detection with multi-slice CT colonography *Rofo* 173;1069-1071

Yee, J, Akerkar G Hung R et al (2001) Colorectal neoplasia: Performance characteristics of CT colonography for detection in 300 patients. *Radiology* 219;3:685-692

Regge D, Galatola G, Martincich L et al (2000) Use of virtual endoscopy in the identification of colorectal neoplasms: prospective study with symptomatic patients [in Italian] *Radiol Med (Torino)* 99;449-455

Spinzi, G, Belloni, G, Martegani, A, Sangiovanni, A, Del, Favero C, and Minoli, G. (2001) Computed tomographic colonography and conventional colonoscopy for colon diseases: a prospective, blinded study. American Journal of *Gastroenterology* 96;2:394-400.

Mendelson R, Foster N, Edwards J, Wood C, et al (2000) Virtual colonoscopy compared with conventional colonoscopy: a developing technology *Med J Aust* 173;472-475

Morrin M, Farrell R, Kruskal R et al (2000) Raptopoulous v. utility of intravenously administered contrast material at CT colonography *Radiology* 216:704-711

Fletcher J, Johnson C, Welch T et al (2000) Optimisation of CT colonography technique: prospective trial in 180 patients *Radiology* 216;704-711

Macari M, Milano A, Lavelle M (2000) Comparison of time efficient CT colonography with two and three dimensional colonic evaluation for detecting colorectal polyps *Am J Roentgenol* 174;1543-1549

Fenlon H, Nunes D, Schroy P et al (1999) A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps *New England Journal of Medicine* 341;1496-1503

Rex D, Vining S Kopecky K et al (1999) An initial experience with screening for colon polyps using spiral CT with and without CT colonography (virtual colonoscopy) *Gastro-intest Endosc*

Citation: Hoppe H, Netzer P, Spreng A, Quattropani C et al (2004) Prospective comparison of contrast enhanced CT colonography for detection of colorectal neoplasms in a single institutional study using second look colonoscopy with discrepant results *American Journal of Gastroenterology* 99;1924-1935

Design: Prospective Diagnostic Study

Country: Switzerland

Setting:

Aim: to prospectively compare CT colonography with conventional colonoscopy for detection of colorectal neoplasms.

Inclusion criteria
Adult patients referred to the gastroenterology clinic for conventional colonoscopy to evaluate symptoms including:
Haematochezia
Positive haemoccult test result
Iron deficiency anaemia
Personal or family history of neoplasia

Exclusion criteria
No definitive criteria detailed though 8 patients were excluded for reasons including:
Residual stool and fluid rendered colonoscopic and CT evaluation impossible
Anal sphincter insufficiency
Unable to establish a reference standard due to impassable stenosis on flexible colonoscopy

Sample Size
No details

Randomisation Method
N/A

Population
N=100 patients enrolled (62 men, 38 women)

N=92

Study Duration
N/A

Interventions
CT Colonography which was immediately followed by conventional colonoscopy (reference standard)

Outcomes
Sensitivity and Specificity by size (using colonic lesion size as determined at colonoscopy as the reference standard)

Sensitivity, specificity, positive and negative predictive values (using conventional colonoscopic findings after unblinding as the reference standard)

Results
The reference standard for location and size was conventional colonoscopy. When CT colonography detected a lesion missed on initial conventional colonoscopy, results of a second look colonoscopy following unblinding were used as the reference standard.

If there was discord between CT colonography and conventional colonoscopy regarding individual lesion status, 2 negative findings on conventional colonoscopy were considere to be a true negative for convention colonoscopy and false positive finding for CT colonography.
If initial findings were negative, but second look colonoscopy confirmed the positive CT colonography , the result was considered a true positive for CT colonography.
For positive conventional colonoscopy and negative CT colonography, the positive colonoscopy finding was considered to be the true positive with a false negative reported for CT colonography.

Complete conventional colonoscopy to the caecum was achieved in 94 patients and failed to demonstrate the entire colon in 6% (6/100) patients.

8 patients were excluded from analysis (see exclusion criteria).

Conventional colonoscopy found 122 lesions which included 8 colorectal carcinomas and colonoscopy results were normal in 43 patients.

		Lesion size at colonoscopy		
Colon Segment	**N**	**≤5mm**	**6-9mm**	**≥10mm**
Caecum	7	2	0	5
Ascending Colon	14	6	2	6
Transverse Colon	27	14	8	5
Descending Colon	14	8	4	2
Sigmoid	30	13	8	9
Rectum	30	20	6	4
Total	122	63	28	31

Distribution of conventional colonoscopic findings according to lesion size and colonic segment

Second look colonoscopy after unblinding was performed in 19 segments. There were 2 negative looks on conventional colonoscopy in 17 segments considered to be a true-negative for conventional colonoscopy and false positive for CT colonography.
In 2 segments initial colonoscopy was negative but second look colonoscopy confirmed the positive CT colonography findings (true positive for CT colonography).
The by-polyp sensitivity of conventional colonoscopy was 94% (32/34) for the detection of polyps of 6mm and larger.

CT colonography had a sensitivity of 88% (7/8) for the detection of colorectal carcinoma; all carcinomas detected by CT colonography were larger than 10mm, one small carcinoma (7mm) in the ascending colon was not detected.

Using direct polyp matching, the sensitivity of CT colonography fpr polyp detection was 61% (36/59) for all lesions with a 6mm cut-off.
Sensitivity of CT colonography was 71% (22/31) for polyps sized ≥10mm, 50% (14/28) for polyps 6-9mm and 25% (16/63) for polyps 5mm or smaller.
The sensitivity for the detection of histologically confirmed adenomas was 64% (23/36) for the 6mm cut-off and 71% (12/17) for the 10mm cut-off.

CT colonography demonstrated 65 false positive polyps using by-polyp matching, 7 of which were ≥10mm, 25 of which were 6-9mm and 33 were 5mm or smaller.
39 of the false positives were reported in colonic segments that were poorly distended or poorly prepared.

70 polyps found at conventional colonoscopy, 9 of which were ≥10mm, 14 of which were 6-9mm and 47 of which were <5mm, were not found on CT colonography.
40 of the missed lesions were in poorly distended or poorly prepared segments.

36/67 adenomas identified by conventional colonoscopy were not observed on CT colonography; 5/36 were ≥10mm and 4 of these adenomas were in patients who had another polyp correctly identified at CT colonography.

	By Polyp					
	N	**TP**	**FN**	**FP**	**PPV (95% CI)**	**Sensitivity (95% CI)**
10mm and larger	31	22	9	7	76% (0.56-0.9)	71% (0.52-0.96)
6mm and larger	59	36	23	32	53% (0.4-0.65)	61% (0.47-0.73)
6-9mm	28	14	14	25	35% (0.21-0.53)	50% (0.31-0.7)
5mm and smaller	63	16	47	33	30% (0.17-0.45)	25% (0.13-0.35)
All sizes	122	52	70	65	44% (0.35-0.54)	43% (0.34-0.51)

CT colonography results for the detection of lesions using by polyp comparison analysis

34 patients had polyps of ≥6mm and16 patients had only 1 polyp while 18 patients had more than one. Using by patient comparisons, the sensitivity and specificity of CT colonography was 76% (26/34) and 88% (51/58) for the detection of patients with at least 1 polyp ≥6mm.
The positive predictive value was 79% (26/33) and the negative predictive value was 86% (51/59).
20 patients had clinically important polyps ≥10mm in size.
Patient sensitivity for polyps ≥10mm was 95% (19/20) and specificity was 98% (65/66).
The negative predictive value of CT colonography was 98% (65/66) for a 10mm cut off.
The positive predictive value of CT colonography for clinically important polyps ≥10mm was 95% (19/20).

The overall sensitivity (comparison analysis) for detecting adenomas using by-patient comparison analysis was 73% (22/30). CT colonography resulted in false positive results in 7 patients for whom conventional colonoscopy results were normal.

	By Patient									
	n	**TP**	**FN**	**FP**	**TN**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**p**
≥6mm	34	26	8	7	51	76% (0.59-0.89)	88% (0.77-0.95)	79% (0.61-0.91)	86% (0.75-0.94)	<0.0001
≥10mm	20	19	1	1	65	95% (0.75-0.99)	98% (0.92-1.00)	95% (0.75-0.99)	98% (0.92-1.00)	<0.0001

Sensitivity and Specificity of CT Colonography for lesion detection using by patient comparison analysis

Citation: Laghi A, Iannaccone R, Carbone I, Catalano C et al (2002) Computed Tomographic Colonography (Virtual Colonoscopy): Blinded Prospective Comparison with Conventional Colonoscopy for the Detection of Colorectal Neoplasia *Endoscopy* 34;441-446

Design: Prospective blinded diagnostic study

Country: Italy

Setting: gastrointestinal unit

Aim: to evaluate the performance of CTC in a blinded comparison with conventional colonoscopy with suspected colorectal neoplasia

Inclusion criteria
Symptomatic patients referred for conventional colonoscopy

Exclusion criteria
Patients with suspected inflammatory bowel disease
Patients that were pregnant

Sample Size
No details

Randomisation Method
N/A

Population
N=66

Study Duration
No details

Interventions
CT Colonography
Conventional Colonoscopy (reference standard)

Outcomes
Per polyp analysis (location and size)
Per patient analysis (sensitivity and specificity for polyps of any size)

Results
Conventional colonoscopy
In 32 patients there were 15 colorectal carcinomas and 52 polyps detected and 34/66 patients had normal findings.
Conventional colonoscopy failed to visualise the entire colon in 5 patients due to the presence of occlusive neoplastic lesions.
No complications were reported in any patient.
26.9% of polyps were ≥10mm, 25% were 6-9mm and 48.1% were ≤5mm.
26 polyps were removed endoscopically and 26 were removed at surgery in a patient affected by familial polyposis with a coexisting colon carcinoma.

Location	Colorectal Carcinoma	Polyps
Rectum	5	
Sigmoid Colon	7	20
Ascending Colon	1	8
Transverse Colon	2	13
Descending Colon		7
Cecum		4

Location of colorectal carcinoma and polyps on conventional colonoscopy

CT Colonography
There were no reported complications on CT colonography.

Due to previous surgery in 7 patients only 372 colonic segments were considered; the segments were judged as collapsed in 4.8% of cases, poorly distended in 5.3% and optimally distended in 89.7% of cases.

CT colonpgrahy detected all 15 cases of colorectal carcinoma and location and size were correctly documented in all cases.
In the 5 patients with incomplete colonoscopy, CT colonography was able to visualise the whole colon and found

no additional lesions and these findings were confirmed at surgery.

CT colonography identified 30/52 polyps for an overall per polyp sensitivity of 57.6% (95% CI 44%-72%).
CT colonography correctly identified 13/14 polyps ≥10mm for a sensitivity of 92.8 % (95% CI 77%-100%); 11/13 polyps 6-9mm in diameter for a sensitivity of 84.6% (95% CI, 62%-100%) and 6/25 polyps ≤5mm for a sensitivity of 24% (95% CI, 6%-42%).

CT colonography missed 22/52 polyps , 4 due to residual stool, 2 due to collapsed bowel and the remaining 16 could not be identified even retrospectively.

There were 6 lesions seen on CT colonography that were not observed on conventional colooscopy and on re-evaluation of the CT colonography data, these findings were associated with misinterpretaion eith of hypertrophic haustral folds or residual stool.

The per patient senstivity and specificity of CT colonography was 93.7% (95% CI 85%-100%) and 94.1% (CI 86%-100%) respectively.

	CT Colonography
True Positives	30
True Negatives	32
False Positives	2
False Negatives	2

CT colonography performance

General comments
Conventional Colonoscopy was performed with 4 hours of CT colonography.

Per Polyp Analysis
True Positive: lesion detected at CT colonography matched exactly the location and size at conventional colonoscopy.
False Positive: lesion detected at CT colonography not confirmed at conventional colonography.

Per Patients Analysis
True Positive: at least one polyp per patient identified on CT colonography was confirmed on conventional colonoscopy.

Citation: Mulhall B, Veerappan G & Jackson J (2005) Meta-analysis: Computed Tomographic Colonography *Ann Intern Med* 142;635-650

Design: Systematic Review and Meta-analysis

Country:

Setting:

Aim: to assess the test performance of CT colonography compared with colonoscopy or surgery and to assess variables that may impact test performance.

Inclusion criteria
Prospective, blinded design where CT colonography results were interpreted independently of colonoscopy or surgery findings.
Studies which included adult patients that were to undergo CT colonography after full bowel preparation, followed by complete colonoscopy or surgery
Studies which utilised at least a single-detector CT scanner with colon insufflations by air or carbon dioxide
Scan intervals no greater than 5mm
Use of 2D and 3D views

Exclusion criteria
Reasons for excluding studies included:
Not a diagnostic study
Studies of patient comfort
Not on CT colonography
Cost Utility study
Clinical Practice Guideline
Extracolonic findings
Not in humans
Not of CRC screening
Technical studies
Studies of preps
Phantom studies
Case reports/series
No appropriate gold standard
Subset data
Did not meet inclusion criteria

Sample Size
N/A

Randomisation Method
N/A

Population
N=33 studies with a total population of 6393 patients

Study Duration

Interventions

Outcomes
Pooled Sensitivities and specificities on a per patient basis

Subgroup analysis was conducted by year of publication, imaging technique, collimation width and reconstruction interval, type of scanner and use of a contrast agent.

Results
The average number of participants per study was 248 (range 20-1233) and the mean age of participants was 61.9 years.
74% of patients included across the studies were at high risk for colorectal cancer.

CT colonography was compared to a number of reference standards including standard colonoscopy, segmental

unblinded colonoscopy, optimised colonoscopy and surgical findings or results of double contrast barium enema. Several studies used a combination of reference standards.

Potential sources of bias in the included studies were numerous and varied; one important source of bias was the differences in disease severity or prevalence among studies. Another specific source of bias could result from the differential verification of findings. A full table outlining the potential sources of bias can be found in the original publication.

Sensitivity of CT Colonography
Per patient sensitivity ranged from 21% to 96% with an overall pooled sensitivity of 70% (95% CI, 53% to 87%).
Sensitivity progressively increased as polyp size increased with sensitivity of 48% (95% CI, 25%-70%, range, 14%-86%) for the detection of polyps <6mm, 70% (95% CI, 55%-84%, range, 30%-95%) for polyps 6-9mm and 85% (95% CI 79%-91%, range, 48%-100%) for polyps >9mm.
Significant statistical heterogeneity was observed for each of these analyses ($p<0.001$ for each group) with most of the variance attributed to between-study heterogeneity. Several potential sources of heterogeneity were identified by the authors including:
Studies using thinner slices for collimation appeared to have better sensitivity and meta-regression (19 studies) appeared to suggest that for every 1mm increase in collomation width there was a decrease in sensitivity of 4.9% (95% CI 0.8%-7.1%)
In the 7 studies that used multidetector scanners reported homogenously high sensitivities (95% (95% CI, 92%-99%), $I^2=40\%$, $p>0.2$) compared to the 9 studies using single detector scanners which reported pooled sensitivity of 82% (95% CI, 76%-92%) with statistically significant heterogeneity reported ($I^2=87.1\%$, $p<0.001$).
From the 10 studies which used 2D imaging with 3D confirmation, the pooled sensitivity was 81.9% (95% CI, 71%-91%, $I^2=87.5\%$, $p=0.02$) compared with 6 studies using 2D and 3D imaging which reported a pooled sensitivity of 91% (95% CI, 83%-99%, $I^2=53.1\%$, $p=0.06$). The 2 studies using fly through technology reported a pooled sensitivity of 99% (95% CI, 95%-100%, $I^2=47.6\%$, $p=0.17$).
For the other subgroups investigated (year of publication, type of scanner, thickness of reconstruction interval, use of contrast and patient characteristics) no source of possible heterogeneity was found.

No evidence of a threshold effect between sensitivity and specificity on calculation of the Spearman statistic or construction of ROC curves.

Specificity of CT Colonography
Per patient specificity was relatively consistent across polyp sizes; from 14 studies, overall specificity was 86% (95% CI, 84%-88%, $I^2=92.6\%$, $p=0.001$).
Specificity also improved as polyp size increase and there was no heterogeneity in the groups.
4 studies reported specificity for the detection of polyps <6mm with a pooled specificity of 91% (95% CI, 89%-95%, $I^2=47.1\%$, $p=0.15$).
For polyps 6-9mm in size (from six studies), pooled specificity was 93% (95% CI, 91%-95%, $I^2=50\%$, $p=0.07$) and for polyps >9mm (15 studies) the pooled specificity was 97% (95% CI, 96%-97%, $I^2=41.8\%$, $p>0.2$).

General comments
Per patient analysis was considered to be more important than per polyp analysis because it was felt that this was the most important perspective for screening

Citation: Pescatore P, Glucker T, Delarive J et al (2000) Diagnostic accuracy and interobserver agreement of CT colonography (virtual colonoscopy) *Gut* 47:126-130

Design: Prospective Diagnostic Study

Country: Switzerland

Setting:

Aim: to assess the diagnostic accuracy and interobserver agreement of CT colonography for correct patient identification compared with conventional colonoscopy

Inclusion criteria
No specific inclusion criteria were detailed. The population included patients referred for conventional colonoscopy. Indications for colonoscopy included abdominal pain, iron deficiency anaemia of unknown origin, surveillance due to personal history of colon polyps, haematochezia or positive faecal occult blood test, tumour search or personal history of colorectal cancer.

Exclusion criteria
Inflammaory bowel disease
Refusal to give consent

Sample Size
No details

Randomisation Method
N/A

Population
N=50

Study Duration
March 1997-March 1998

Interventions
CT colonography (index test)
Conventional colonoscopy (reference test)

Outcomes
Sensitivity and specificity of CT colonography for correct classification of patients with or without polyps with CT colonography results considered to correlate with conventional colonoscopy findings when polyp size was identical ±3mm, when polyp morphology was similar and when CT colonography located the polyp in the same segment of the colon as conventional colonoscopy.

Results
Conventional colonoscopy found 65 polyps in 24 patients; 46/65 were ≤5mm, 8/65 were 6-9mm and 11/65 were ≥10mm in diameter.

According to histology there were 35 adenomas and 11 hyperplasic polyps ≤5mm, 8 adenomas 6-9mm and 7 adenomas and 4 carcinomas ≥10mm.
Two colonoscopies were incomplete due to stenosing masses.

Interpretation of CT colonography was carried out by two independent investigator teams consisting of a radiologist and a gastroenterologist.

	Team 1	Team 2
Sensitivity (95% CI)	75% (±18%)	71% (±18%)
Specificity (95% CI)	62% (±19%)	69% (±19%)
Positive Predictive Value	72%	72%
Negative Predictive Value	64%	68%

Diagnostic values of CT colonography for the identification of any patient with polyps of any size

	Team 1	Team 2
Sensitivity (95% CI)	37% (±33%)	62% (±33%)
Specificity (95% CI)	74% (±13%)	74% (±13%)
Positive Predictive Value	21%	31%
Negative Predictive Value	86%	91%

Diagnostic values of CT colonography for the identification of any patient with polyps ≥10mm

	Team 1	Team 2
Sensitivity (95% CI)	71% (±19%)	71% (±19%)
Specificity (95% CI)	59% (±18%)	69% (±17%)
Positive Predictive Value	55%	62%
Negative Predictive Value	74%	77%

Diagnostic values of CT colonography for the identification of any patient with polyps <10mm

False negative findings for patients with polyps ≥10mm occurred in 6 cases in team 1 and in 3 cases in team 2.
To try to explain the low sensitivities, all false negative results from polyps ≥10mm were analysed in 6 patients with 11 lesions. 7 lesions, including 3/4 carcinomas were missed by team 1 while team 2 missed 4 lesions, including 1/4 carcinomas.
Reasons for missing lesions in team 1 were primarily perceptive errors (n=4), explained by inadequate analysis of the 2D CT images in 3 cases and the polyp was masked by fluid in 1 case. The 3 remaining polyps missed by team 1 could not be found on a review of the data set and repeated multiplanar reconstructions.

For patients 1-24 sensitivity of CT colonography for the detection of polyps was 100% for team 1 and 92% for team 2 and specificity was 42% for team 1 and 58% for team 2.
For patients 25-50 sensitivity of CT colonography for the identification of polyps was 50% and specificity was 79% for both teams.
There were statistically significant differences in sensitivity between the two study periods for both teams; team 1 p=0.01 and team 2 p=0.04.
Differences in specificity between the two study periods did not differ significantly (team 1, p=0.1 and team 2, p=0.4).

	Sensitivity	
	Team 1	**Team 2**
Rectum	0%	0%
Left Colon	32%	32%
Transverse Colon	63%	50%
Right Colon	33%	25%

Sensitivity of CT Colonography for individual polyp detection for anatomical location

Kappa values for patients with polyps of any size were 0.56 (0.12) and 0.72 (0.10) for patients with polyps ≥10mm in diameter.

Citation: Reuterskiold MH, Lasson A, Svensson E et al (2006) Diagnostic performance of computed tomography colonography in symptomatic patients and in patients with increased risk for colorectal disease *Acta Radiologica* 9;888-898

Design: Prospective, observer blind diagnostic study

Country: Sweden

Setting: Specialist endoscopy department of a university hospital

Aim: to evaluate diagnostic performance of CT colonography in symptomatic patients and patients at increased risk of colorectal carcinoma on a per lesion and a per patient basis.

Inclusion criteria
Patients referred for colonoscopy

Exclusion criteria
Women younger than 50 years
Patients with acute colitis or colostomy

Sample Size
No details

Randomisation Method
N/A

Population
N=111 (66 men and 45 women)

Study Duration
16 months (no dates given)

Interventions
CT Colonography
Conventional Colonoscopy (reference standard)

Outcomes
Diagnostic performance of CT Colonography on a per lesion and per patient basis
Impact of lesion size and histological type of results
Impact of observer's diagnostic certainty on results
Ability to identify patients in need of further work up

Results
Indications for referral for colonoscopy included anaemia and or rectal bleeding and or positive faecal occult blood test (n=48), suspected malignancy without symptoms (n=5), previous findings on barium enema (n=11). Diarrhoea (n=16), history of abdominal pain and/or diverticulitis (n=16), surveillance after polypectomy (n=9) or surveillance due to colitis (n=6).

CT colonography was performed immediately before colonoscopy and detailed analysis of the results were carried out by one observer.

Examination was complete to the caecum in 101 (91%) of patients; in the remaining patients examination was discontinued in the rectum (n=2), in the sigmoid colon (n=3), in the transverse colon (n=1), in the right flexure (n=1) and in the ascending colon (n=3).
Reasons for discontinuation included stenosis (n=3), insufficient bowel preparation (n=2), technical difficulties in combination with pain (n=2) or insufficient bowel preparation (n=1).

108 polyps and carcinomas were identified by colonoscopy and/or CT colonography: 23 of which were ≥10mm, 24 of which were 5-9mm and 61 of which were <5mm.
60/108 lesions were identified by both CT colonography and colonoscopy and 32 /48 of the unmatched lesions were <5m.
Matching certainty increased with lesion size; for 30/31 matched lesions≥5mm the matching was 'rather certain' or 'completely certain'.

72/108 lesions were identified at CT colonography.
Sensitivity increased with lesion size ($p<0.001$) and was 83% for lesions ≥5mm and 91% for lesions ≥10mm.
Sensitivity in the 5-9mm group was higher concerning adenoma than concerning any lesion (92% (11/12) versus

75% (18/24)).
Sensitivity was 91% (29/32) for the detection of adenoma/carcinoma ≥5mm.

45/11 patients had one or more confirmed lesions with the most advanced lesion identified by CT colonography in 33/45 patients.
Sensitivity increased with lesion size (p=0.01) and was 82% for detection of patients with a lesion ≥5mm.
Sensitivity for the detection of patients with adenoma/carcinoma was 80% (91% for lesions ≤5mm).

There were 10 carcinomas in 10 patients, all ≥20mm and all were correctly identified at both examinations.
There were 43 adenomatous polyps, 30 of which were identified on CT colonography in 20 patients with 14 patients correctly identified on CT colonography.
CT colonography therefore identified 40/53 (75%) clinically important lesions.
27/98 polyps had no histological diagnosis, the majority of which were <5mm (63%) and found in patients with other lesions (23/27).

36 lesions were identified at colonoscopy alone, 2 of which were ≥10mm.
12 lesions were identified at CT colonography and not at colonoscopy, though they were retrospectively confirmed.

There were 5 false positive results at colonoscopy (all <5mm) and 14 findings (all ≥5mm) at CT colonography could be defined as false positives.
Among the remaining 154 unconfirmed findings, 6 were 10-15mm and 101 were <5mm. (These numbers do not fit with anything else in the paper and it is possible that they are an error, however it is not possible to confirm this based on the data provided.)

58/72 (81%) of all confirmed CT colonography findings were classified as being completely certain or rather certain.
12/14 uncertain or very uncertain findings were <5mm.
A weak but statistically significant relationship was found between the size of confirmed CT colonography findings and the level of certainty (r_s=0.33, p=0.005) indicating that qualities other than size were important for diagnostic certainty as the relationship between size and certainty explains 11% of the variability in these variables.

103/168 (61%) of the unconfirmed or false-positive findings were uncertain or very uncertain.
7/13 findings ≥10mm were classified as rather certain, 4 of which turned out to be false positive and 3 remained unconfirmed.

One or more CT colonography findings were made in 77 patients and if all were referred for follow-up, 41/45 patients with confirmed lesions would be identified. However 36/66 patients without any confirmed lesion had CT findings.
Of 24 patients with any 'completely certain' or 'rather certain' CT finding ≥10mm, 17 had a confirmed lesion ≥10mm, 3 had a smaller lesion and 4 had only false positive or unconfirmed lesions. 2 patients with confirmed lesions ≥10mm would have been missed.
The specificity of CT colonography would be 45% (30/66, 95% CI 34%-57%) if patients with findings of any size and any diagnostic certainty were selected for follow-up and 92% (85/92, 95% CI 85%-96%) if only patients with completely certain or rather certain CT findings ≥10mm were selected.

	Per Lesion			**Per Patient**		
	Lesion Size			**Lesion Size**		
	<5mm	**5-9mm**	**≥10mm**	**<5mm**	**5-9mm**	**≥10mm**
Any Lesion						
Total, n	61	24	23	17	9	19
CC true positive, n	57	19	20	16	8	17
CTC true positive, n	33	18	21	10	5	18
CTC sensitivity	54%	75%	91%	59%	56%	95%
Adenoma or carcinoma						
Total, n	21	12	20	8	5	17
CC true positive, n	20	11	18	8	5	15
CTC true positive, n	11	11	18	4	4	16
CTC sensitivity	52%	92%	90%	50%	80%	94%

Detection Rate according to lesion size, by colonoscopy (CC) and CT colonography (CTC)

	Lesion Size		
Histologic Type	**<5mm (n=61)**	**5-9mm (n=24)**	**≥10mm (n=23)**
Adenocarcinoma, n			9
CC/CTC true positive, n/n			9/9

Squamous cell carcinoma, n			1
CC/CTC true positive n/n			1/1
Adenoma	21	12	10
CC/CTC true positive n/n	20/11	11/11	8/8
Hyperplastic Polyp, n	21	2	1
CC/CTC true positive, n/n	21/9	1/1	1/1
Other polyp, n*	2	1	1
CC/CTC true positive, n/n	2/1	1/0	1/1
No histologic diagnosis, n	17	9	1
CC/CTC true positive, n/n	14/12	6/6	0/1

*including 1 juvenile polyp, 2 inflammatory polyps and 1 lipoma

All confirmed lesions according to size and histologic type and detection rate by colonoscopy and CT colonography

	Lesion Size		
Histologic Type	**<5mm (n=61)**	**5-9mm (n=24)**	**≥10mm (n=23)**
Adenocarcinoma, n			9
CC/CTC true positive, n/n			9/9
Squamous cell carcinoma, n			1
CC/CTC true positive n/n			1/1
Adenoma	8	5	7
CC/CTC true positive n/n	8/4	5/4	5/6
Hyperplastic Polyp, n	6	1	1
CC/CTC true positive, n/n	6/4	1/0	1/1
Other polyp, n*	1	1	1
CC/CTC true positive, n/n	1/1	1/0	1/1
No histologic diagnosis, n	2	2	0
CC/CTC true positive, n/n	1/1	1/1	0/0

All patients with confirmed lesions according to size and histologic type and detection rate by colonoscopy and CT colonography

General comments

Matching of findings was performed jointly by a CT colonography observer and an endoscopist level of matching certainty (completely certain, rather certain, uncertain, very uncertain) were recorded.

All polyps and masses described at conventional colonoscopy were considered to be true positive findings unless histologically confirmed as normal colon mucosa.

CT colonography and conventional colonoscopy findings were considered to be matched when observed lesions were of a similar size and location, or if other characteristics indicated identity.

If the finding was ≥5mm and was graded as completely certain or rather certain on CT colonography and could not be matched to any colonoscopy finding, a review of the colonoscopy video recordings and/or other clinical documentation was performed. CT colonography findings were considered to be false positive if a true lesion could be excluded; true positive if a true lesion could be confirmed and unconfirmed if the analyses was inconclusive or not performed.

Diagnostic performance of CT colonography was analysed in relation to all confirmed lesions identified by either colonoscopy, CT colonography or both.
For per patient analysis the ability of CT colonography to identify the histologically advanced lesion in patients with confirmed lesions was investigated.

Citation: Rex D, Mark D, Clarke B et al (1995) Flexible sigmoidoscopy plus air contrast barium enema versus colonoscopy for evaluation of symptomatic patients without evidence of bleeding *Gastrointestinal Endoscopy* 42;2:132-138

Design: Randomised Trial

Country: USA

Setting: Single Medical Centre

Aim: to investigate the effectiveness and cost-effectiveness of initial diagnostic strategies in patients without evidence of intestinal bleeding

Inclusion criteria
Aged ≥40 years
Patients referred with suspected

Exclusion criteria
Prior colorectal neoplasms or vascular malformations
Patients who had undergone colonoscopy or barium enema within 18 months previous to randomisation
Patients who had hematochezia or significant coagulopathy
Patients unable to give informed consent
Haemoglobin <14 g/100ml in men and <12g/100ml in women

Sample Size
No details provided

Randomisation Method
Randomisation was done using a randomly varying block design with block sizes of two and four. It was stated that randomised patients did not represent consecutive patients for a number of reasons including:
Location of physicians involved in randomisation
Referral of private patients or managed care patients specifically for flexible sigmoidoscopy or colonoscopy
Insufficient space on the endoscopy schedule to perform potential colonoscopy generated by randomisation

Population
N=180 patients randomized (91 to flexible sigmoidoscopy + ACBE and 89 to initial colonoscopy)

Study Duration
No details

Interventions
Initial colonoscopy versus flexible sigmoidoscopy + air contrast barium enema (ACBE)

Outcomes
Not clearly reported appear to be findings in each group and prevalence of neoplasia

Results
149 patients kept their appointments and completed initial tests.
There were no significant differences in baseline information collected from patients.
Reasons for referral included constipation (18%), diarrhoea (6.5%), abdominal pain (17%), weight loss (9.5%) and a combination of these symptoms (49%).

Finding	Flexible Sigmoidoscopy + ACBE (n=75)	Colonoscopy (n=75)
	N (%)	N (%)
Cancer	1 (1)	0 (0)
Diverticulosis	46 (62)	31 (41)
Adenomas	13 (18)	23 (31)
Only adenomas (≤4mm)	4 (5)	8 (11)
Largest adenoma (5-9mm)	7 (9)	10 (13)
Any adenoma ≥1cm	2 (3)	5 (7)
Arteriovenous malformation	0 (0)	1 (1)

Findings for the two patient groups

In the flexible sigmoidoscopy + ACBE group, 1 patient had Dukes A cancer for which endoscopic resection appeared to be definitive and the patient did not undergo surgery.
No patient in the colonoscopy group was diagnosed with cancer.

Significantly fewer patients in the colonoscopy group were diagnosed with diverticulosis compared with the flexible sigmoidoscopy + ACBE group (OR=0.41, 95% CI 0.21-0.87).
More patients undergoing colonoscopy were found to have at least one adenoma (OR=2.07, 95% CI 0.90-4.92).

Patients undergoing flexible sigmoidoscopy were more likely to require an alternative procedure such as colonoscopy than were patients undergoing colonoscopy to require ACBE (OR 4.46, 95% CI 1.47-16.4).

18/75 patients in the flexible sigmoidoscopy group required colonoscopy and in all cases a polypectomy was indicated. 16/18 patients actually underwent colonoscopy and 14 patients had one or more polyps.

5 patients in the colonoscopy group required ACBE due to incomplete colonoscopy; 4 patients underwent ACBE but no additional lesions were detected.

There were no perforations, postpolypectomy bleeds or requirements for hospitalisation in either group.

Citation: Rex D, Weddle R, Lehman G et al (1990) Flexible Sigmoidoscopy plus Air Contrast Barium Enema versus Colonoscopy for suspected lower gastrointestinal bleeding *Gastroenterology* 98;855-861

Design: Randomised Trial

Country: USA

Setting: Single Medical Centre

Aim: to compare colonoscopy with flexible sigmoidoscopy plus air contrast barium enema for the evaluation of suspected lower GI bleeding.

Inclusion criteria
Patients aged ≥40 years who were referred with a clinical suspicion of nonemergent lower GI bleeding

Exclusion criteria
Prior colorectal neoplasia or vascular malformations
Prior colonoscopy or barium enema within the previous 18 months
Patients with significant coagulopathy
Patients who could not give informed consent

Sample Size
The study sample size provided a power of 0.8 at an alpha of 0.05 to detect a 10% difference in cancer prevalence between the two groups.

Randomisation Method
Randomisation was done using a randomly varying block design with block sizes of two and four.
It was stated that randomised patients did not represent consecutive patients for a number of reasons including:
Location of physicians involved in randomisation
Referral of private patients or managed care patients specifically for flexible sigmoidoscopy or colonoscopy
Insufficient space on the endoscopy schedule to perform potential colonoscopy generated by randomisation
The sample of non-consecutive patients was compared with a sample of 100 consecutive patients and was found to be demographically similar.

Population
N=380 (191 to flexible sigmoidoscopy + ACBE and 189 to colonoscopy)

Study Duration
Recruitment: March 1985-November 1987

Interventions
Flexible sigmoidoscopy + ACBE versus colonoscopy

Outcomes
Not clearly reported in the text

Results
332/390 patients kept their appointments and completed initial test: 168 in the flexible sigmoidoscopy group and 164 in the colonoscopy group.

There was no significant difference between the groups in relation to demographic or historical data.

Reasons for referral included haemoccult positive stools, hematochezia and melena with negative upper GI evaluation.

Flexible sigmoidoscopy was successful (insertion to at least 30cm) in 161 patients with a mean depth of insertion of 50cm.
Findings on flexible sigmoidoscopy included haemorrhoids (58%), diverticulosis (19%), any polyps (23%), cancer (4%) and proctitis (2%).

Air contrast barium enema was sufficient to rule out major pathology in 157 patients and reasons for unsuccessful ACBE included; inability to distend or fill the right colon adequately in 5 patients, repeatedly inadequate preparation to rule out mass lesions (n=4) and inability to retain the enema adequately in 2 patients.
ACBE findings were normal in 48/168 patients and abnormalities identified included haemorrhoids (n=1), diverticulosis (n=82), any polyp (n=43), stricture (n=3) and cancer (n=4%).

Colonoscopy was successful in 151 patients (insertion to the cecum) and reasons for unsuccessful colonoscopy

included; obstructing cancers in 6 patients and technical factors in 7 patients.
Colonoscopy findings were normal in 18/162 patients.

In the flexible sigmoidoscopy plus ACBE group, 64 patients had a total of 101 polyps ranging in size from ≤4mm (n=45) to ≥9mm (n=27) and included 4 patients with 7 polyps who also had colorectal cancer. Patients with polyps ≥5mm were referred for colonoscopy where the polyps in 4/38 patients could not be found; these patients were considered to have false positive ACBE results.
28 patients, including the 4 with cancer, were referred for polypectomy and all had at least 1 adenoma.
33 patients in the flexible sigmoidoscopy plus ACBE group had either cancer or adenoma documented by initial testing or subsequent colonoscopy.
Colonoscopy detected a further 25 polyps not visualised by initial flexible sigmoidoscopy + ACBE; 18 were ≤4mm, 5 were 5-8mm and 2 were ≥9mm.

9 patients in the flexible sigmoidoscopy plus ACBE group had cancer: 3 had Dukes B tumours with serosal involvement, 1 had a Dukes C tumour and 4 had Dukes D tumours. One patient in the group has a negative ACBE and four weeks later underwent colonoscopy which showed a cecal cancer which was resected.
One patient with transverse colon cancer diagnosed on ACBE refused surgery.

In the colonoscopy group, 86 patients had a total of 194 polyps ranging in size from ≤4mm (n=108) to ≥9mm (n=29). 9 patients with a total of 16 polyps also had colorectal cancer. In total, 76/146 patients in the colonoscopy group had colonic adenoma or carcinoma.
13 patients in the colonoscopy group had cancer, 2 patients had Dukes A tumours, 8 had Dukes B, 2 had Dukes D and 1 had transverse colon cancer and refused surgery.

There was a significant difference between the arms in relation to the proportion of patients recommended alternative lower GI procedures (p≤0.0001).
53/168 (32%) patients in the flexible sigmoidoscopy group were referred for subsequent colonoscopy due to inadequate study (n=11), for polypectomy (n=38) and for biopsies on lesions outside the reach of flexible sigmoidoscopy.
13/164 (8%) patients in the colonoscopy arm were referred for ACBE because of difficulty advancing the colonoscope to the cecum.

When examining the diagnostic yields with respect to age there was an indication of diversion in polyp and cancer yield for patients aged ≥55 years. There was no significant difference between the two groups within each age group in relation to demographic data, patient history or laboratory variables. The superior detection of polyps in the colonoscopy group was accounted for by the finding of polyps <9mm in patients ≥55years.
Overall, the yield of cancers in patients <55 years was very low at 1% compared with 8% in those aged ≥55years.
Flexible sigmoidoscopy + ACBE found more patients <55 years with polyps ≥9mm than did colonoscopy (p=0.021).

There was no significant difference between the two groups in relation to procedural complications. Phlebitis occurred in 7 patients in the colonoscopy group versus 4 patients in the flexible sigmoidoscopy +ACBE group, this difference was not statistically significant, however the authors state that the study did not have sufficient power to detect a true difference in the incidence of phlebitis of this magnitude.

No deaths, transfusions, hospitalisations, or prolonged hospital stays were reported in either group.

	All patients		
	Flexible Sigmoidoscopy + ACBE (N=168)	**Colonoscopy (N=164)**	**p**
	N (%)	**N (%)**	
Internal or external haemorrhoids	99 (59)	97 (59)	NS
Diverticulosis	85 (51)	56 (34)	0.002
Any colorectal polyp	64 (38)	86 (52)	0.009
Any colorectal polyp ≥5mm	38 (23)	53 (32)	0.048
Any colorectal polyp ≥9mm	21 (13)	22 (13)	NS
Colonic Stricture	3 (2)	3 (2)	NS
Colon cancer	9 (5)	13 (8)	NS
Colitis pr Proctitis	4 (2)	10 (6)	NS
Arteriovenous malformation	0 (0)	9 (5)	0.002

Comparison of Abnormalities on Initial Lower Gastrointestinal Procedures (all patients)

	Age ≥55 years		
	Flexible Sigmoidoscopy + ACBE	**Colonoscopy (N=123)**	**p**

	(N=127)		
	N (%)	N (%)	
Internal or external haemorrhoids	76 (60)	75 (61)	NS
Diverticulosis	67 (53)	45 (37)	0.01
Any colorectal polyp	50 (39)	74 (60)	0.001
Any colorectal polyp ≥5mm	30 (24)	47 (38)	0.012
Any colorectal polyp ≥9mm	16 (13)	22 (18)	NS
Colonic Stricture	2 (2)	3 (2)	NS
Colon cancer	9 (7)	12 (10)	NS
Colitis pr Proctitis	3 (2)	7 (6)	NS
Arteriovenous malformation	0 (0)	8 (7)	0.003

Comparison of Abnormalities on Initial Lower Gastrointestinal Procedures (patients ≥55 years)

	Age <55 years		
	Flexible Sigmoidoscopy + ACBE (N=43)	Colonoscopy (N=41)	p
	N (%)	N (%)	
Internal or external haemorrhoids	23 (56)	22 (54)	NS
Diverticulosis	18 (44)	11 (26)	NS
Any colorectal polyp	14 (34)	12 (29)	NS
Any colorectal polyp ≥5mm	8 (20)	6 (15)	NS
Any colorectal polyp ≥9mm	5 (12)	0 (0)	0.021
Colonic Stricture	1 (2)	0 (0)	NS
Colon cancer	0 (0)	1 (2)	NS
Colitis pr Proctitis	1 (2)	3 (7)	NS
Arteriovenous malformation	0 (0)	1 (2)	NS

Comparison of Abnormalities on Initial Lower Gastrointestinal Procedures (patients <55 years)

Citation: Sosna J, Blachar A, Amitai M, Barmeir E, Peled N, Nahum-Goldberg S, Bar-Ziv J (2006) Colonic Perforation at CT Colonography: Assessment of Risk in a Multicentre Large Cohort *Radiology* 239;2:457-463

Design: Retropsective Case Series

Country: Israel

Setting: Multicentre

Aim: To assess the incidence, clinical features and treatment of colonic perforation at computed tomographic colonography in a large multicentre cohort.

Inclusion criteria
All patients who underwent CT colonography during a 48 month period (January 2001 – December 2004)

Exclusion criteria
No details

Sample Size
N/A

Randomisation Method
N/A

Population
N=11,870 CT colonographic studies performed in 6837 men and 5033 women

Study Duration
January 2001 – December 2004

Interventions
CT Colonography

Outcomes
Rates of colonic perforation and surgical treatment

Results
7 colonic perforations were identified at 5 centres for a perforation risk rate of 0.059% (95% CI 0.02%-0.1%), translating to an event occurrence of 1/1695 studies (95% CI 1/974 - 971/6537).

6/7 cases of perforations were in symptomatic patients at high risk of colorectal neoplasia and only 1 occurred in an asymptomatic patient with average risk who underwent screening.
4 cases of perforation were in patients undergoing CT Colonography as completion studies following incomplete conventional colonoscopy.

There were 5 cases of perforation in the sigmoid colon and 2 in the rectum.

6 cases of perforation occurred in patients in whom a rectal tube was inserted and in 5/6 cases the balloon was inflated. In the remaining patient a 16-F Foley catheter was inserted and 5ml of saline was inflated into the balloon.

4/7 patients with perforation required surgical treatment with a one-stage procedure performed in 3 patients and a two-stage procedure performed in 1.
The incidence of surgical intervention was 1/2968 patients (95% CI 1.5 of 10,000 – 14.7 of 10,000).
The remaining 3 patients had multiple comorbidities and were at high risk for surgery and so received conservative treatment without any complications.
No deaths were recorded.

3 cases of perforation occurred at 3 medical centres at which 40, 50 and 120 CT colonographic studies had been performed at the time perforation occurred.
4 cases of perforation occurred at non-academic centres, 3 in one centre at which approximately 2,700, 4,000 and 5,200 CT colonographic studies had been performed and one case at a centre at which 2,500 studies had been performed.
The physicians performing the air insufflation in 2 cases of perforation did not have any experience in the performance of CT colonography at the time of examination with neither having performed unsupervised air insufflation previously nor read images from CT colonographic studies on a regular basis.

General comments

The population under investigation included both symptomatic and asymptomatic (screening) and it appears that part of the population is patients referred for CT Colonography following failed/incomplete colonoscopy. It is not possible to separate the population according to the indications/reasons for CT Colonography in order that only data relevant to the population of interest for the PICO can be reported. The results and data reported in this study can be considered indirect evidence of the risk of perforation with CT Colonography.