

Meta-Analysis: Computed Tomographic Colonography

Brian P. Mulhall, MD, MPH; Ganesh R. Veerappan, MD; and Jeffrey L. Jackson, MD, MPH

Background: Computed tomographic (CT) colonography, also called virtual colonoscopy, is an evolving technology under evaluation as a new method of screening for colorectal cancer. However, its performance as a test has varied widely across studies, and the reasons for these discrepancies are poorly defined.

Purpose: To systematically review the test performance of CT colonography compared to colonoscopy or surgery and to assess variables that may affect test performance.

Data Sources: The PubMed, MEDLINE, and EMBASE databases and the Cochrane Controlled Trials Register were searched for English-language articles published between January 1975 and February 2005.

Study Selection: Prospective studies of adults undergoing CT colonography after full bowel preparation, with colonoscopy or surgery as the gold standard, were selected. Studies had to have used state-of-the-art technology, including at least a single-detector CT scanner with supine and prone positioning, insufflation of the colon with air or carbon dioxide, collimation smaller than 5 mm, and both 2-dimensional and 3-dimensional views during scan interpretation. The evaluators of the colonogram had to be unaware of the findings from use of the gold standard test.

Data Abstraction: Data on sensitivity and specificity overall and for detection of polyps less than 6 mm, 6 to 9 mm, and greater than 9 mm in size were abstracted. Sensitivities and specificities weighted by sample size were calculated, and heterogeneity was explored by using stratified analyses and meta-regression.

Data Synthesis: 33 studies provided data on 6393 patients. The sensitivity of CT colonography was heterogeneous but improved as polyp size increased (48% [95% CI, 25% to 70%] for detection of polyps <6 mm, 70% [CI, 55% to 84%] for polyps 6 to 9 mm, and 85% [CI, 79% to 91%] for polyps >9 mm). Characteristics of the CT colonography scanner, including width of collimation, type of detector, and mode of imaging, explained some of this heterogeneity. In contrast, specificity was homogenous (92% [CI, 89% to 96%] for detection of polyps <6 mm, 93% [CI, 91% to 95%] for polyps 6 to 9 mm, and 97% [CI, 96% to 97%] for polyps >9 mm).

Limitations: The studies differed widely, and the extractable variables explained only a small amount of the heterogeneity. In addition, only a few studies examined the newest CT colonography technology.

Conclusions: Computed tomographic colonography is highly specific, but the range of reported sensitivities is wide. Patient or scanner characteristics do not fully account for this variability, but collimation, type of scanner, and mode of imaging explain some of the discrepancy. This heterogeneity raises concerns about consistency of performance and about technical variability. These issues must be resolved before CT colonography can be advocated for generalized screening for colorectal cancer.

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For author affiliations, see end of text.

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Colorectal cancer is the second most frequent cause of cancer-related death in the United States. Nearly 150 000 new cases and 60 000 deaths occur each year from this disease (1). Because colorectal cancer develops insidiously over time as genetic mutations accumulate in clinically silent adenomatous polyps, it is most commonly diagnosed at an advanced stage (2–4). If the condition is diagnosed at an early stage, the prognosis is favorable, with 5-year survival rates exceeding 90% (5, 6). Colorectal cancer, unlike many other types of cancer, can be prevented by removal of precancerous lesions. The long preclinical phase, early detectability, and improved prognosis of colorectal cancer have established the need for an accurate screening method.

Various screening tests in current use reduce the incidence and rate of death from colorectal cancer (7, 8). Despite the proven efficacy of these tests, however, patient adherence to screening guidelines is low: Only 30% to 45% of persons eligible for screening undergo such tests. Low adherence rates are believed to be due to poor public awareness and poor public acceptance of current screening techniques (9–13).

An increasingly popular screening test for colorectal

cancer is computed tomographic (CT) colonography, also known as *CT colography* or *virtual colonoscopy*. Computed tomographic colonography was first described in 1994 as a radiographic technique in which thin-section images of pneumocolon could be reconstructed by sophisticated software into high-resolution 2- and 3-dimensional images (14). Over time, improvements in hardware and software have allowed faster scanning, reduced exposure to radiation, and better imaging. Newer modes of imaging (called *fly-through*) can produce results that resemble endoscopic

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images and permit sophisticated characterization of detected lesions (15–17). Early studies primarily used the spiral CT scanner, which has limitations in spatial resolution that can make small polyps more difficult to detect (17). The multidetector CT scanner has permitted rapid acquisition of finer images, obtained during a single breath-hold, that can greatly improve image quality and spatial resolution (17, 18). Many aspects of this technology are under study, including software that assists in detection of lesions, refinements in image reconstruction, and stool tagging (19–21). The latter development relies on ingestion of contrast material over several days or hours, after which software digitally subtracts residual solid and fluid fecal material from the acquired images, creating a “virtually clean” mucosal surface (22, 23). This technique may improve sensitivity and may someday obviate the need for bowel cleansing before examination.

Although it is touted as a less invasive screening method than flexible sigmoidoscopy or colonoscopy, CT colonography typically requires full bowel cleansing and insufflation of air through the rectum (24). Studies have suggested that CT colonography may be similar, and in some cases preferable, to colonoscopy in terms of comfort and acceptability, but no convincing difference between these 2 approaches has been demonstrated (25–31). If virtual colonoscopy is found to have equivalent test characteristics, improve patient adherence, and be safer or less expensive than colonoscopy, it may be more cost-effective and become the screening method of choice (32, 33).

Studies of the test characteristics of CT colonography have had mixed results. Pickhardt and colleagues used CT colonography in 1233 patients and found a sensitivity of 93.9% for adenomatous polyps larger than 8 mm (25). Other studies have had less favorable results, with sensitivities as low as 55% for polyps larger than 10 mm, raising concerns about the overall test performance of CT colonography when used in a broader range of settings (34). Various reasons for these discrepant results have been offered, but the source of this heterogeneity has not been fully explored (16, 35, 36). Such assessment is needed because patients and providers look to this technology in the hope of improving screening rates (29).

We systematically reviewed the literature to assess the test performance of CT colonography compared with colonoscopy or surgery, to define characteristics of these studies, and to attempt to explain the sources of conflicting results.

METHODS

Study Identification and Selection

We searched the PubMed, EMBASE, and MEDLINE databases and the Cochrane Controlled Trials Register for all relevant articles published in the English language between 1975 and February 2005 by using the Medical Subject Headings or text words *virtual colonoscopy*, *CT colonog-*

raphy, *CT colography*, or *CT pneumocolon*. The title and abstract of potentially relevant studies and review articles were screened for appropriateness before retrieval of the full articles. Two reviewers independently searched the literature. Inclusion criteria were a prospective, blinded design (in which results of CT colonography were interpreted independently of findings on colonoscopy or during surgery); enrollment of adult patients who were to undergo CT colonography after a full bowel preparation, followed by complete colonoscopy or surgery; and use of at least a single-detector CT scanner, with colon insufflation by air or carbon dioxide, scan intervals no greater than 5 mm, and use of both 2-dimensional and 3-dimensional views during scan interpretation.

Study Quality

Two observers independently extracted data on test characteristics; study setting; patients; and components of methodologic quality that may be associated with bias in test accuracy studies, including disease severity, disease prevalence, prospective design, relevant clinical sample (as opposed to a diagnostic case–control study), enrollment of a series of consecutive patients, assurance that all patients underwent reference testing, performance and interpretation of the index test without knowledge of the results of the reference test, and performance and interpretation of the reference test without knowledge of the results of the index test (33). A piloted standardized data extraction sheet was used, and disagreements were resolved by consensus.

Data Abstraction

We abstracted characteristics of the study (design, country, year, reference standard, and type of contrast used), patients (demographic and risk for colorectal cancer), scanners (manufacturer, type of viewer, type of contrast, software, and hardware), and study quality. Sensitivity and specificity were calculated per patient, per polyp, and for polyps of 3 size categories: smaller than 6 mm, 6 to 9 mm, and larger than 9 mm. When data on test performance were reported for 2 or more separate CT colonography readers, we calculated an average value. When possible, we excluded data on double readings. If a study reported data related specifically to adenomas instead of polyps, in general, we abstracted only the data for adenomas. For studies that performed retrospective analysis (for example, fly-through imaging in the study by Cotton and associates [34]), we abstracted only data on CT colonography findings before colonoscopy. If data could not be extracted or calculated from the manuscript with confidence, none were entered. Two reviewers independently abstracted data, and disagreements were resolved by consensus.

Statistical Analysis

Pooled sensitivities and specificities on a per-patient basis were combined and weighted according to sample size. Confidence intervals for each study were calculated by using exact binomial methods in a random-effects model. We focused our analysis on per-patient data because this is

Table 1. Characteristics of the 33 Included Studies*

Study, Year (Reference)	Patients, n	Mode of Imaging	Collimation, mm	Reconstruction	Type of Scanner	Contrast Material Used?	Gold Standard	Software†
Rockey et al., 2005 (68)	614	Primarily 2-D, with 3-D confirmation	2.5	1	Multidetector	No	Segmentally unblinded colonoscopy	Vitrea 3.2
Chung et al., 2005 (69)	51	2-D and 3-D	0.75	1	Multidetector	Intravenous contrast	Colonoscopy and surgery	Rapidia
Cotton et al., 2004 (34)	600	Primarily 2-D, with 3-D confirmation‡	NR	1.5/1.0	Mixed	No	Segmentally unblinded colonoscopy	Picker/Siemens
Van Gelder et al., 2004 (40)	249	Primarily 3-D, with 2-D confirmation	4 × 2.5	1.6	Multidetector	No	Colonoscopy, optimized colonoscopy§	Proprietary
Macari et al., 2004 (42)	186	2-D and 3-D	4 × 1	1.25	Multidetector	No	Colonoscopy	Vitrea 2
Macari et al., 2004 (41)	68	Primarily 2-D, with 3-D confirmation	4 × 1	1.25	Multidetector	No	Colonoscopy	Vitrea 2
Hoppe et al., 2004 (43)	92	Primarily 2-D, with 3-D confirmation	2	1	Multidetector	Intravenous contrast	Segmentally unblinded colonoscopy	Voxtool 3.0.51f
Pickhardt et al., 2003 (25)	1233	Flythrough and 2-D	1.25–2.5	1	Multidetector	Oral contrast	Segmentally unblinded colonoscopy	Viatronix V3D 1.2
Iannaccone et al., 2003 (44)	158	Primarily 2-D, with 3-D confirmation	3	1	Multidetector	Intravenous contrast	Colonoscopy	Vitrea 2.6
Johnson et al., 2003 (45)	703	Primarily 2-D, with 3-D confirmation	5	3	Single detector	No	Colonoscopy	Freeflight (developed internally)
Pineau et al., 2003 (46)	205	2-D and 3-D	5	1	Single detector	Oral contrast	Segmentally unblinded colonoscopy	Proprietary
Taylor et al., 2003 (47)	54	Primarily 2-D, with 3-D confirmation	1.25–2.5	Half nominal	Multidetector	Intravenous contrast	Segmentally unblinded colonoscopy	Advantage
Ginnerup Pedersen et al., 2003 (48)	148	Primarily 2-D, with 3-D confirmation	3	1.6	Multidetector	No	Segmentally unblinded colonoscopy	MxView
Yee et al., 2003 (49)	182	Flythrough and 2-D	3		Single detector	No	Colonoscopy	Navigator
Munikrishnan et al., 2003 (50)	80	Primarily 2-D, with 3-D confirmation	1	1	Multidetector	Intravenous contrast	Colonoscopy	Not stated
Laghi et al., 2002 (51)	165	2-D and 3-D	3 or 1	2 or 1	Mixed	Intravenous contrast	Colonoscopy	Vitrea 2.0/2.2
Gluecker et al., 2002 (52)	50	2-D and 3-D	5	2	Multidetector	No	Colonoscopy	Advantage/Navigator
Lefere et al., 2002 (22)	100	2-D and 3-D	3	5	Single detector	Oral contrast	Segmentally unblinded colonoscopy	Endview Easy Vision
Macari et al., 2002 (53)	105	Primarily 2-D, with 3-D confirmation	1	1.25	Multidetector	No	Colonoscopy	Vitrea 2.0
McFarland et al., 2002 (54)	70	Primarily 2-D, with 3-D confirmation	5	2	Single detector	No	Colonoscopy	Vitrea 1.2
Yee et al., 2001 (55)	300	2-D and 3-D	3	1.5	Single detector	No	Colonoscopy	Navigator
Hara et al., 2001 (56)	237	2-D and 3-D	5	3	Mixed	No	Colonoscopy	Proprietary
Spinzi et al., 2001 (57)¶	96	Primarily 3-D, with 2-D confirmation	5	2.5	Single detector	No	Colonoscopy	Navigator
Fletcher et al., 2000 (58)	180	Primarily 2-D, with 3-D confirmation	5	3	Single detector	Oral contrast	Colonoscopy	Proprietary
Morrin et al., 2000 (59)	81	Primarily 2-D, with 3-D confirmation	3	1.5	Mixed	Intravenous contrast	Colonoscopy and surgery	Advantage
Mendelson et al., 2000 (60)	53	2-D and 3-D	5	2	Single detector	No	Colonoscopy	Navigator
Macari et al., 2000 (61)	42	2-D and 3-D	5	2.5	Single detector	No	Colonoscopy	Advantage/Navigator
Morrin et al., 2000 (59)	34	Primarily 2-D, with 3-D confirmation	3	1.5	Single detector	Intravenous contrast	Optimized colonoscopy§ and surgery	Advantage
Fenlon et al., 1999 (63)	100	2-D and 3-D	5	2	Single detector	No	Colonoscopy	Episcope 3.4/Voyager
Rex et al., 1999 (64)	46	2-D and 3-D	5	2	Single detector	No	Optimized colonoscopy§	Proprietary

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the most important perspective for a screening test, whereas per-polyp data emphasize the ability of CT colonography to find colonic lesions. That is, the latter analysis assesses the performance of the technology rather than its

utility as a screening tool. Heterogeneity was assessed by using the I² statistic (37). The I² statistic provides an estimate of the amount of variance due to heterogeneity rather than chance and is based on the traditional measure of

Table 1—Continued

Study, Year (Reference)	Patients, n	Mode of Imaging	Collimation, mm	Reconstruction	Type of Scanner	Contrast Material Used?	Gold Standard	Software†
Dachman et al., 1998 (65)	44	Primarily 2-D, with 3-D confirmation	5	2.5	Single detector	No	Colonoscopy	Navigator
Royster et al., 1997 (66)	20	2-D and 3-D	5	2	Single detector	No	Colonoscopy double-contrast barium enema, and surgery	Episcope 3.4/Voyager
Hara et al., 1997 (67)	70	2-D and 3-D	5	3	Single detector	No	Optimized colonoscopy§	Proprietary

* 2-D = 2-dimensional; 3-D = 3-dimensional.

† The manufacturers of the software (listed in alphabetical order) are as follows: Advantage Windows, General Electric Medical System, Milwaukee, Wisconsin; Endoview Easy Vision, Philips, Best, the Netherlands; Episcope, Picker International, Cleveland, Ohio; MxView, Marooni Medical Systems Inc., Cleveland, Ohio; Navigator, General Electric Medical Systems, Milwaukee, Wisconsin; Picker, Picker International Inc., Cleveland, Ohio; Rapidia, 3D-Med Corp., Long Beach, California; Siemens, Siemens Medical Solutions, Iselin, New Jersey; Viatronix V3D Colon, Viatronix, Stony Brook, New York; Vitrea, Vital Imaging, Minneapolis, Minnesota; Voyager, Picker International, Cleveland, Ohio; Voxtool, General Electric Medical Systems, Milwaukee, Wisconsin.

‡ Fly-through technique conducted later and reported separately.

§ Tape viewed again after colonoscopy for confirmation.

|| Given to some patients only.

¶ The first 49 underwent computed tomographic colonography after colonoscopy, when polypectomy was not performed.

variance, the Cochrane Q statistic. Potential threshold effects were assessed by using the Spearman statistic and by creating receiver-operating characteristic curves according to the method of Moses and coworkers (38). Heterogeneity was assessed by performing stratified analyses when the potential confounding variable was dichotomous or categorical, by plotting the weighted effect size against the potential confounding variable when that variable was continuous, and by applying meta-regression methods in either case (39). Subgroup analyses were done by year of publication, imaging technique (2-dimensional imaging with 3-dimensional confirmation only when a lesion was noted, 3-dimensional imaging with 2-dimensional confirmation, 2-dimensional imaging with concomitant 3-dimensional imaging, or fly-through technology), collimation width and reconstruction interval (in millimeters), type of scanner (single-detector, multidetector, or mixed), and use of a contrast agent (yes or no). When collimation or reconstruction thickness was given in half-millimeter increments, we rounded the values up to the next whole number. The meta-regression analysis used the restricted maximum likelihood method and was performed by using indicator variables to assess differences among the strata. All analyses were performed with Stata software, version 8.2 (Stata Corp., College Station, Texas).

DATA SYNTHESIS

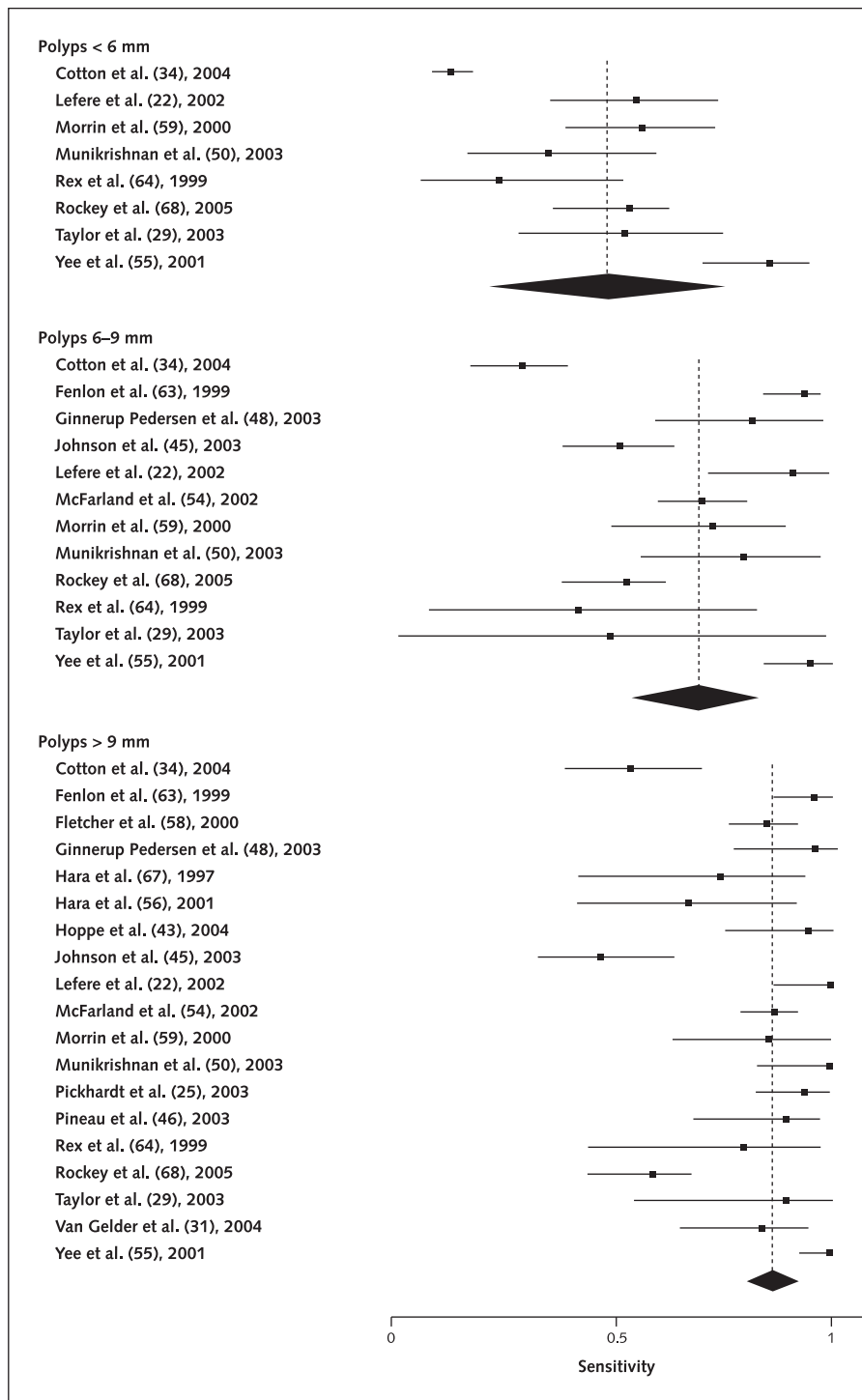
Our final pool of eligible studies (Appendix Figure, available at www.annals.org) included 33 prospective studies involving 6393 patients that compared CT colonography to the reference standard of colonoscopy or surgery (22, 25, 34, 40–69). Studies originated from 7 different countries, but most were done in the United States (64%). The average number of participants in a study was 248 (range, 20 to 1233). The mean age of participants was 61.9 years; 63.6% of participants were male, and 74% were at

high risk for colorectal cancer. Sixteen studies used single-detector scanners, 13 used multidetector scanners, and 4 used both single-detector and multidetector scanners. Fifteen studies used 2-dimensional imaging, with 3-dimensional imaging on selected slices at the discretion of the radiologist; 14 studies used dedicated 2-dimensional and 3-dimensional imaging; and 2 studies used fly-through imaging with 2-dimensional reconstruction. The average collimation was 4 mm (range, 1 to 5 mm), and the average reconstruction interval was 1.86 mm (range, 1 to 5 mm). Tables 1 and 2 show detailed information from individual studies.

Computed tomographic colonography was compared to various reference standards, including standard colonoscopy, segmental unblinded colonoscopy (after each colon segment is examined, the results of CT colonography are revealed to the endoscopist and discrepant segments are reexamined), optimized colonoscopy (in which videotapes of the endoscopy are reviewed in comparison with discrepant CT colonography findings), and surgical findings or results of double-contrast barium enema (when subsequent colonoscopy was not or could not be performed). Several studies used a combination of these reference standards.

Table 2 shows biases that may be present in the studies, as defined by Whiting and colleagues (70). One important source of bias was differences in disease severity or prevalence among studies. Because the baseline risk of the study participants may have been apparent to the investigators, clinical review bias was probably present in many of the studies. In addition, because the reference standards varied not only among studies but among segments from a single patient, bias could result from differential verification of findings or might be considered incorporation bias in some cases. Although most studies did not define observer variability, those that did had a range of κ values. The studies that used consensus readings may not be rep-

Figure 1. Reported per-patient sensitivities in the included studies, by polyp size.



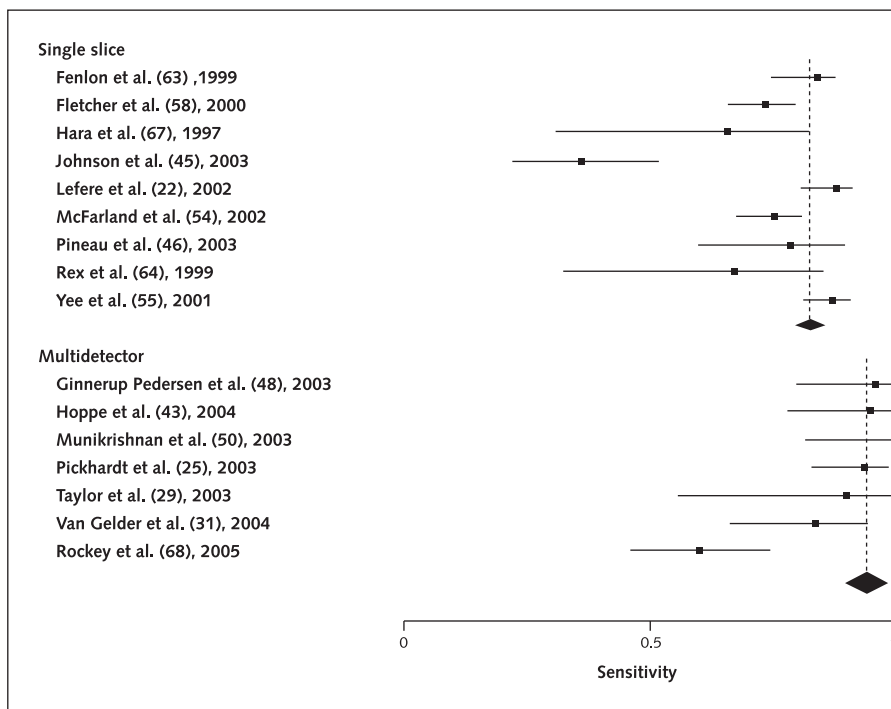
Summary statistics: For polyps <6 mm, 0.48 (95% CI, 0.25 to 0.70); for polyps 6–9 mm, 0.70 (CI, 0.55 to 0.84); for polyps >9 mm, 0.85 (CI, 0.79 to 0.91).

representative of typical CT image-reading practice and may have increased bias. In several studies, many persons interpreted the images (from CT colonography or colonoscopy), but most studies involved few readers or a single reader. The nature of these studies precluded quantitative comparisons of quality.

Sensitivity of CT Colongraphy

Per-patient sensitivity for CT colonography varied from 21% to 96% (Figure 1). The overall pooled sensitivity for CT colonography was 70% (95% CI, 53% to 87%). Sensitivity increased progressively as polyp size increased: It was 48% (CI, 25% to 70%) (range, 14% to

Figure 2. Reported per-patient sensitivities in the included studies, by type of scanner.



86%) for detection of polyps smaller than 6 mm, 70% (CI, 55% to 84%) (range, 30% to 95%) for polyps 6 to 9 mm, and 85% (CI, 79% to 91%) (range, 48% to 100%) for

polyps larger than 9 mm. Each of these analyses was statistically heterogeneous ($P < 0.001$ for each), and most of the variance was attributable to between-study heterogene-

Figure 3. Reported per-patient sensitivities in the included studies by mode of imaging.

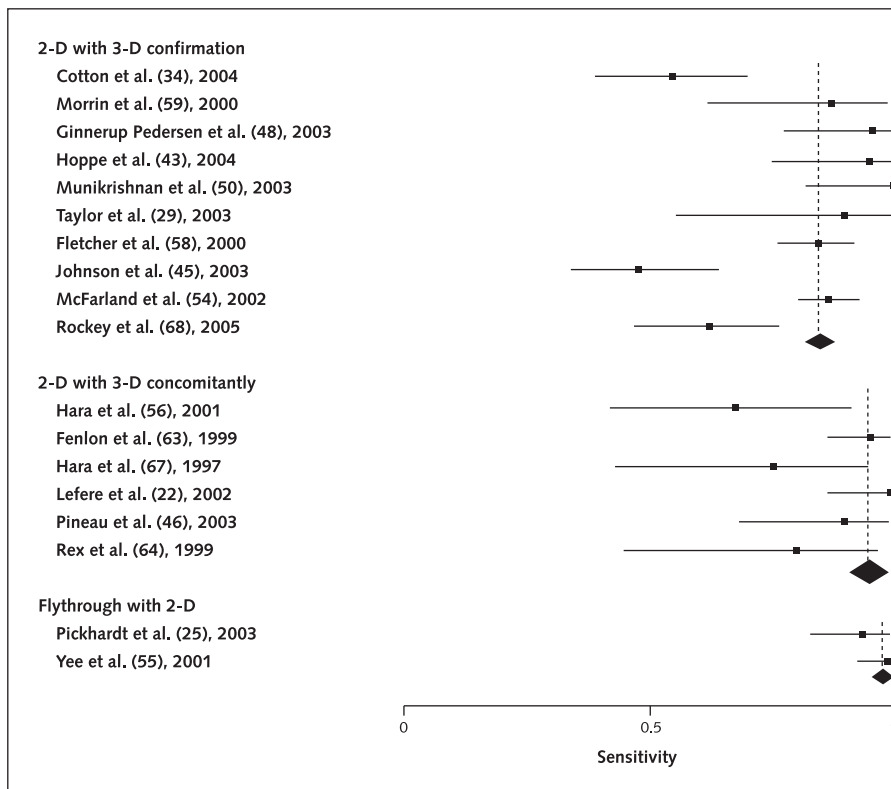
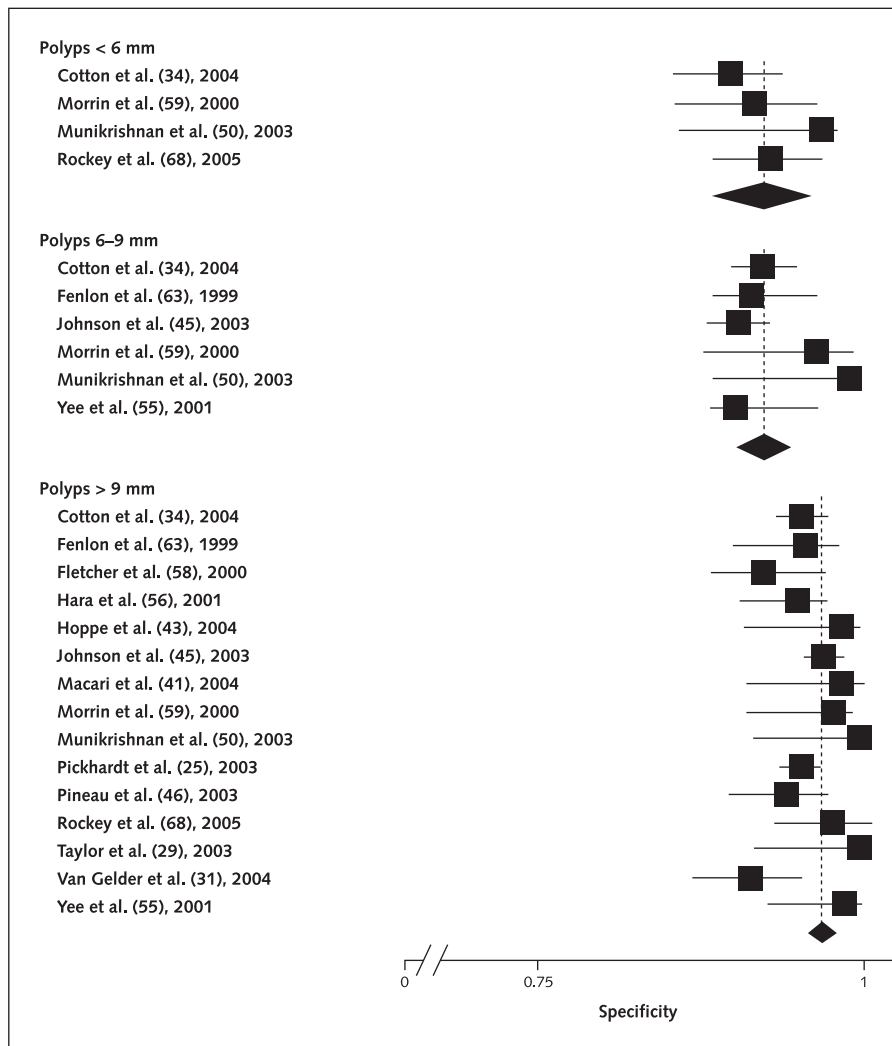


Figure 4. Reported per-patient specificities in the included studies, by polyp size.



ity. The I^2 statistic was 96.7% for polyps smaller than 6 mm, 93.1% for polyps 6 to 9 mm, and 85.2% for polyps larger than 9 mm. Appendix Tables 1 and 2 (available at www.annals.org) show data from individual studies.

We found several potential sources for this heterogeneity. First, studies that used thinner slices for collimation appeared to have better sensitivity, and meta-regression of data from 19 studies suggested that every 1-mm increase in collimation width decreases sensitivity by 4.9% (CI, 0.8% to 7.1%). Second, the 7 studies that used multidetector scanners and that reported overall sensitivity had homogeneously high sensitivity (95% [CI, 92% to 99%]; $I^2 = 40\%$; $P > 0.2$) (Figure 2). This sensitivity was higher than that in the 9 studies reporting overall sensitivity in which a scanner with a single-detector was used (82% [CI, 76% to 92%]), although the latter results were heterogeneous ($I^2 = 87.1\%$; $P < 0.001$). The 10 studies that used 2-dimensional imaging, with confirmation by 3-dimensional imaging only when considered necessary, yielded a sensitivity of 81.9% (CI, 71% to 91%) ($I^2 = 87.5\%$; $P =$

0.02), whereas the 6 studies that used standard 2-dimensional imaging and concomitant 3-dimensional imaging had a pooled sensitivity of 91% (CI, 83% to 99%) ($I^2 = 53.1\%$; $P = 0.06$) and the 2 studies that used fly-through technology had a pooled sensitivity of 99% (CI, 95% to 100%) ($I^2 = 47.6\%$; $P = 0.17$) (Figure 3).

Analysis of year of publication, type of scanner hardware or software, thickness of the reconstruction interval, use of contrast (bowel, intravenous, or none), and patient characteristics (age, sex, and high or average risk) yielded no other source of heterogeneity. We found no evidence of a threshold effect between sensitivity and specificity when the Spearman statistic was calculated or receiver-operating characteristic curves were constructed.

Specificity of CT Colonography

In contrast to the broad range of sensitivities reported, per-patient specificity was more consistent across polyp sizes (Figure 4). Overall, CT colonography was 86% specific (CI, 84% to 88%) ($I^2 = 92.6\%$; $P = 0.001$) on the

Table 2. Potential Biases in the 33 Included Studies*

Study, Year (Reference)	Patient Characteristics						Source of Bias		
	Patients, n	Mean Age, y	Men, %	White Ethnicity, %	Disease Severity	Disease Prevalence	Distorted Selection	Test Exe- cution†	Test Tech- nology
Rockey et al., 2005 (68)	614	57	70	70	Family history of colorectal cancer, 32%; high-risk screening, 68%	High risk (symptoms or family history), 100%	Yes	No	Yes
Chung et al., 2005 (69)	51	63	63	–	High risk, 100%	High risk, 100%	Yes	No	Yes
Cotton et al., 2004 (34)	600	61	45	87	History of polyps, 13.5%; symptoms, 87%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Van Gelder et al., 2004 (40)	249	56	59	–	History of polyps or colorectal cancer, 64%; symptoms, 8%; family history of colorectal cancer or polyps, 36%	High risk (symptoms, family history, or surveillance), 100%	Yes	No	Yes
Macari et al., 2004 (42)	186	62	100	–	History of polyps, 10%; average-risk screening, 31%; high-risk screening, 35%; symptoms, 23%	High risk, 69%; average risk, 31%	Yes	No	Yes
Macari et al., 2004 (41)	68	55	100	–	Average-risk screening, 100%	Average risk, 100%	No	No	Yes
Hoppe et al., 2004 (43)	92	66	62	–	High-risk, 100%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Pickhardt et al., 2003 (25)	1233	58	59	–	Family history of colorectal cancer, 3%; average-risk screening, 97%	Average risk, 97%	No	No	Yes
Iannaccone et al., 2003 (4)	158	63	57	–	History of polyps or colorectal cancer, 34%; average-risk screening, 19%; high-risk screening, 38%; symptoms, 8%	High risk, 81%; average risk, 19%	Yes	No	Yes
Johnson et al., 2003 (45)	703	64	63	97	History of polyps, 73%; family history of colorectal cancer, 25%; high-risk screening, 2%	High risk (symptoms, family history, or surveillance), 100%	Yes	No	Yes
Pineau et al., 2003 (46)	205	59	45	92	Family history of colorectal cancer, 20%; high-risk screening, 36%; symptoms, 45%	Most at high risk (symptoms, family history, or surveillance)	Yes	No	Yes
Taylor et al., 2003 (47)	54	69 (median)	41	–	High-risk screening, 7%; symptoms, 76%	High risk (symptoms), 83%	Yes	No	Yes
Ginnerup Pedersen et al., 2003 (48)	148	–	48	–	History of polyps or colorectal cancer, 51%; symptoms, 45%; known colorectal cancer, 5%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Yee et al., 2003 (49)	182	63	97	–	Average-risk screening, 40%; high-risk screening, 60%	High risk, 60%	Possible	No	Yes

Continued on pages 643, 644, 645, and 646

Table 2—Continued

Source of Bias (continued)									
Treatment Paradox?	Inappropriate Reference Standard	Differential Verification	Partial Verification Bias	Review Bias	Clinical Review Bias‡	Incorporation Bias	Observer Variability	Handling of Indeterminate Results	Arbitrary Choice of Threshold Value
No (same day)	Segmentally un-blinded colonoscopy	Possible (2nd look in some segments)	No	No	Possible	Possible (in 2nd-look cases)	Unknown number of radiologists, CTC readers, and gastroenterologists	No	No threshold defined
Yes (up to a mean of 2-week interval)	Colonoscopy or surgery	Yes (compared with colonoscopy or surgical findings)	No	No	Possible	No	2 CTC readers; unknown number of gastroenterologists or surgeons	No	No threshold defined
No (<2 h)	Segmentally un-blinded colonoscopy	Possible (2nd look in some segments)	No	Yes	Possible	Possible (in 2nd-look cases)	Yes	No	No threshold defined
No (<1 h)	Colonoscopy (videotaped for later correlation; 2nd look in 3.6%)	Possible (during videotape review or 2nd look)	No	Yes	Possible	Possible (during videotape review or 2nd look)	2 CTC readers ($\kappa = 0.7$); unknown number of gastroenterologists or surgeons	No	Polyps <6 mm not reported
No (<3 h)	Colonoscopy (2nd look in 1.6%)	Possible (2nd look in 1.6%)	No	Yes	Possible	Possible (in 2nd-look cases)	1 CTC reader; unknown number of gastroenterologists	No	No threshold defined
No (<1 mo)	Colonoscopy	No	No	No	Possible	No	1 CTC reader, 2 gastroenterologists	No	No threshold defined
No (same day)	Colonoscopy (2nd look in 1.6%)	Possible (2nd look in some segments)	No	No	Possible	Possible (in 2nd-look cases)	3 CTC readers; unknown number of gastroenterologists	Yes (some CTCs excluded from analysis)	No threshold defined
No (same day)	Segmentally un-blinded colonoscopy	Yes	No	Yes	Possible	Yes	2 radiologists ($\kappa = 0.75-0.8$) and 17 endoscopists (3 surgeons and 14 gastroenterologists)	No	Polyps <6 mm not reported
No (same day)	Colonoscopy	No	No	No	Possible	No	Consensus of 2 radiologists; 1 endoscopist	No	No threshold defined
No (same day)	Colonoscopy	Possible (during videotape review)	No	No	Possible	Possible (during videotape review)	2 radiologists ($\kappa = 0.34-0.62$)	No	Polyps <5 mm ignored
No (<3 h)	Segmentally un-blinded colonoscopy	Possible (2nd look in some segments)	No	Yes	Possible	Possible (in 2nd-look cases)	Yes	No	No threshold defined
No (same day)	Segmentally un-blinded colonoscopy	Possible (2nd look in some segments)	No	Yes	Possible	Possible (in segmentally un-blinded colonoscopy)	Unknown number of CTC readers; 4 gastroenterologists	No	No threshold defined
No (same day in 97.3%)	Segmentally un-blinded colonoscopy (2.7% double-contrast barium enema)	Possible (2nd look in some segments)	No	Yes	Possible	Possible (in segmentally un-blinded colonoscopy)	1 CTC reader, 20 colorectal surgeons	No	Polyps <6 mm not reported
No (same day)	Colonoscopy	No	No	No	Possible	No	Consensus of 2 CTC readers; unknown number of gastroenterologists	No	No threshold defined

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Table 2—Continued

Study, Year (Reference)	Patient Characteristics						Source of Bias		
	Patients, n	Mean Age, y	Men, %	White Ethnicity, %	Disease Severity	Disease Prevalence	Distorted Selection	Test Execution†	Test Technology
Munikrishnan et al., 2003 (50)	80	68	56	—	Symptoms, 100%	High risk (symptoms), 100%	Yes	No	Yes
Laghi et al., 2002 (51)	165	62	48	—	History of polyps or colorectal cancer, 25%; symptoms, 74%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Gluecker et al., 2002 (52)	50	Range, 50–75	—	—	Symptoms or high-risk screening, 100%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Lefere et al., 2002 (22)	100	60	Mixed sex	—	Symptoms or high-risk screening, 100%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Macari et al., 2002 (53)	105	58	97	—	High risk, 100%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
McFarland et al., 2002 (54)	70	62	63	—	High risk, 100%	Polyps on flexible sigmoidoscopy, 100%	Yes	No	Yes
Yee et al., 2001 (55)	300	63	97	—	Symptoms or high-risk screening, 100%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Hara et al., 2001 (56)	237	63	64	—	Symptoms or high-risk screening, 100%	High risk (symptoms, family history, or surveillance), 100%	Yes	No	Yes
Spinzi et al., 2001 (57)	96	NR	NR	NR	History of polyps, 15%; high-risk screening, 12%; symptoms, 69%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Fletcher et al., 2000 (58)	180	NR	NR	NR	Symptoms, surveillance, or high-risk screening, 100%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Morrin et al., 2000 (59)	81	NR	NR	NR	History of colorectal cancer, 7%; high-risk screening, 70%; symptoms, 22%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Mendelson et al., 2000 (60)	53	65	47	—	Symptoms, 81; family history of colorectal cancer, 19%	High risk (symptoms or family history), 100%	Yes	No	Yes
Macari et al., 2000 (61)	42	56	58	—	Average-risk screening, 71%; family history of colorectal cancer, 29%	Average risk, 71% family history of colorectal cancer, 29%	Yes	No	Yes
Morrin et al., 2000 (59)	34	64	59	—	Known colorectal masses, 100%	High risk, 100% (all had masses)	Yes	No	Yes
Fenlon et al., 1999 (63)	100	62	60	—	Symptoms, surveillance, or high-risk screening, 100%	100% high risk; symptoms or surveillance	Yes	No	Yes

Table 2—Continued

Source of Bias (continued)									
Treatment Paradox?	Inappropriate Reference Standard	Differential Verification	Partial Verification Bias	Review Bias	Clinical Review Bias‡	Incorporation Bias	Observer Variability	Handling of Indeterminate Results	Arbitrary Choice of Threshold Value
No (same day)	Colonoscopy	No	No	Not stated	Possible	No	Consensus of 2 CTC readers; unknown number of gastroenterologists	No	No threshold defined
No (<4 h)	Colonoscopy	No	No	No	Possible	No	Consensus of 2 radiologists	No	No threshold defined
No (<1 h)	Colonoscopy	No	No	No	No	No	1 radiologist and 1 gastroenterologist	No	No threshold defined
No (<3 h)	Colonoscopy with 2nd look for confirmation	Possible (2nd look in some?)	No	Yes	Probable	Possible (in 2nd-look cases)	Consensus of 2 CTC readers; 1 gastroenterologist	No	No threshold defined
No (same day)	Colonoscopy (photographed for later correlation)	No	No	No	Possible	No	1 CTC reader, ≥1 gastroenterologist	No	No threshold defined
No (same day)	Colonoscopy	No	No	No	Yes	No	4 CTC readers, 2 gastroenterologists	No	No threshold defined
No (<3 h)	Colonoscopy	No	No	No	No	No	Consensus of 2 radiologists; 3 gastroenterologists	No	No threshold defined
No (immediately after)	Colonoscopy	Possible (during videotape review)	No	Possible	Possible	Possible (during videotape review)	3 radiologists	No	Polyps <5 mm ignored
Possible (not mentioned)	Colonoscopy	No	Yes (some CTCs were done after colonoscopy)	Possible	Possible	No	1 radiologist	No	No threshold defined
No (same day)	Colonoscopy	No	No	No	No	No	3 radiologists	No	Polyps <5 mm not reported
No (<2 h)	Colonoscopy or surgery	Yes (compared with colonoscopy or surgical findings)	No	No	Possible	No	Consensus of 2 CTC readers; unknown number of gastroenterologists or surgeons	No	No threshold defined
No (same day)	Colonoscopy	No	No	No	Possible	No	1 CTC reader; unknown number of gastroenterologists	No	No threshold defined
No (<1 h)	Colonoscopy	No	No	No	Possible	No	2 CTC readers (similar findings?); unknown number of gastroenterologists	No	No threshold defined
No (same day)	Colonoscopy or surgery	Yes (compared to colonoscopy or surgical findings)	No	No	Possible	No	2 CTC readers (consensus?); unknown number of gastroenterologists or surgeons	No	Evaluated masses only
No (same day)	Colonoscopy	No	No	No	Possible	No	Consensus of 2 CTC readers; unknown number of gastroenterologists	No	No threshold defined

Continued on following page

Table 2—Continued

Study, Year (Reference)	Patient Characteristics						Source of Bias		
	Patients, <i>n</i>	Mean Age, <i>y</i>	Men, %	White Ethnicity, %	Disease Severity	Disease Prevalence	Distorted Selection	Test Exe- cution†	Test Tech- nology
Rex et al., 1999 (64)	46	68	96	—	100% average-risk screen- ing	Average risk, 100%	No	No	Yes
Dachman et al., 1998 (65)	44	58	61	—	History of polyps or colo- rectal cancer, 50%; high-risk screening, 36%; symptoms, 3%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Royster et al., 1997 (66)	20	53	60	—	High-risk screening, 35%; symptoms, 65%	High risk (symptoms or surveillance), 100%	Yes	No	Yes
Hara et al., 1997 (67)	70	66	—	—	History of polyps or colo- rectal cancer, 50%; high-risk screening, 50%	High risk (symptoms or surveillance), 100%	Yes	No	Yes

* CTC = computed tomographic colonography; NR = not reported.

† In several studies, customized software was used, which would limit the ability for results to be repeated elsewhere.

‡ In most studies, the endoscopist probably knew the patients' clinical history; in some studies, the radiologist probably had this information.

basis of data from 14 studies. Specificity improved as polyp size increased, and the results were homogenous within each strata. Only 4 studies reported specificity for detection of polyps smaller than 6 mm, and the pooled specificity from these studies was 91% (CI, 89% to 95%) ($I^2 = 47.1\%$; $P = 0.15$). For polyps 6 to 9 mm in size (6 studies), specificity was 93% (CI, 91% to 95%) ($I^2 = 50\%$; $P = 0.07$) and increased to 97% (CI, 96% to 97%) ($I^2 = 41.8\%$; $P > 0.2$) for polyps larger than 9 mm (15 studies). Appendix Tables 1 and 2 (available at www.annals.org) show data from individual studies.

DISCUSSION

We found that CT colonography is highly specific, particularly for polyps greater than 9 mm in size. However, the reported sensitivities for CT colonography vary widely, even for larger polyps. Before any screening method can be recommended for general use, it must be demonstrated to be highly and consistently sensitive in a variety of settings. The inability of our meta-analysis to clearly explain why the reported sensitivities vary so widely suggests that CT colonography needs further refinement before it can be recommended for general use in screening for colorectal cancer.

Our analysis revealed some factors that account for the wide range of sensitivities. First, scanners that used thinner collimation had higher sensitivity. Every 1-mm increase in collimation width decreased the subsequent sensitivities by almost 5%. That is, if scanners with 1-mm slices had 98%

sensitivity, increasing the collimation width to 2 mm would decrease sensitivity to 93%. Second, scanners that used multiple detectors rather than single detectors were more sensitive. Finally, the mode of imaging also appeared to be important: The more recently developed fly-through technology had a sensitivity of 99%. However, this latter finding must be interpreted with caution because it is based on data from only 2 studies and considerable heterogeneity was found for the other types of imaging used. These results suggest that CT colonography is promising as a screening test for colorectal cancer. Before it is put into general use, however, it must be shown to be reliably sensitive and questions about the optimal technological characteristics of the technique must be settled. Our results are not definitive, but rather suggestive of avenues of pursuit in refinement of this method.

Our conclusions differ from those of another recent systematic review that favored use of CT colonography (71). That review included data from 14 trials and 1324 patients, compared with the 33 trials and 6393 patients in our analysis. The investigators reported a summary sensitivity of 87% for detection of polyps 6 to 9 mm and 88% for detection of polyps larger than 10 mm, and a specificity of 95% for detection of polyps larger than 10 mm. Their conclusion that “the specificity and sensitivity of CT colonography are high for polyps larger than 10 mm” does not take into account the sources of heterogeneity in the sensitivities reported among the studies that they included. Until new technology, particularly for screening tests, can

Table 2—Continued

Source of Bias (continued)									
Treatment Paradox?	Inappropriate Reference Standard	Differential Verification	Partial Verification Bias	Review Bias	Clinical Review Bias‡	Incorporation Bias	Observer Variability	Handling of Indeterminate Results	Arbitrary Choice of Threshold Value
No (same day)	Colonoscopy (videotaped for later correlation; 2nd look in ~11%)	Possible (during videotape review)	No	No	Possible	Possible (during videotape review)	2 CTC readers (consensus?); unknown number of gastroenterologists	No	No threshold defined
No (same day)	Colonoscopy	No	No	No	Possible	No	Consensus of 2 CTC readers; 5 gastroenterologists	No	No threshold defined
No (<3 h)	Colonoscopy (surgery in 85%)	Yes (compared with colonoscopy, double-contrast barium enema, and surgical findings)	Yes	Uncertain	Probable	No	Consensus of 2 CTC readers; unknown number of gastroenterologists	Yes (some CTCs excluded from analysis)	No threshold defined
No (same day)	Colonoscopy (videotaped for later correlation; 2nd look in >8.5%)	Possible (during videotape review)	No	Yes	Possible	Possible (during videotape review)	3 CTC readers (variability among readers); unknown number of gastroenterologists	No	No threshold defined

be demonstrated to be consistently reliable, we believe it cannot be recommended for general use.

Other sources for the wide range in reported sensitivities may exist. Previous reports have implied that the differences in test performance among studies of CT colonography is related to the CT colonography technology used, the type of contrast medium, the mode of imaging, and the expertise of the radiologists reading the images. The available data are sufficient only to suggest that multidetector scanners, mode of imaging, and low collimation width affect test performance. Many other possible sources of false-negative results exist, including limitations in technology and technique, insufficient resolution, poor bowel distention, poor preparation, breath-hold artifacts, misinterpretation of stool or folds, sessile or flat polyps, paired lesions, software limitations, and errors in reading (perceptive errors) (45, 46, 55, 58, 63, 72–75). Whether a study used CT colonography to detect all polyps (including hyperplastic polyps) or adenomas only may also affect test performance, because CT colonography may have a higher sensitivity for detection of adenomas (76). Delineation of these possible sources of heterogeneity requires a more sensitive technique than meta-analysis. We abstracted information on these study characteristics, but our ability to discriminate whether any of these is the source of heterogeneity is limited. In addition, we could not evaluate such factors as the expertise of the radiologists reading the CT colonography scans. Our findings cannot be taken to mean that none of these other variables are the source of heterogeneity,

only that the current data do not allow us to clearly demonstrate that one of these characteristics is the explanation.

Our analysis has limitations. First, 18 of the studies used colonoscopy as the gold standard, yet colonoscopy may miss more than 10% of small polyps, up to 10% of large polyps, and up to 5% of colorectal cancers (64–68). Eleven studies used segmental unblinded colonoscopy or optimized colonoscopy so that CT colonography and augmented colonoscopy could be used in tandem, to maximize overall detection of lesions. However, even these methods do not ensure that each segment of the colon is examined multiple times, so that no lesion is missed by either method. Studies that used segmental unblinded colonoscopy (in which results from CT colonography are revealed after the endoscopist has examined each colonic segment) or optimized colonoscopy (in which video images from colonoscopy are reviewed for discrepant results) demonstrated that CT colonography found polyps (and several tumors or masses) that were missed on blinded colonoscopy (25, 34, 40, 46). In addition, only 3 studies were designed to evaluate a true screening population: persons who are at average risk for colorectal cancer (Table 2) (25, 41, 64). In 1 of these studies, the rate of false-negative findings of polyps larger than 9 mm was similar to the rate of false-negative results with colonoscopy reported in studies of tandem colonoscopy, although other studies have not shown such favorable results (77).

Second, the power to elucidate sources of heterogeneity,

ity is limited by the information reported in each article and by the relatively small number of included articles. Finally, meta-regression using summary covariates for each article has limited accuracy. Finer evaluation of the source of heterogeneity would require procurement of patient-level data.

Computed tomographic colonography is very specific, particularly for detection of polyps larger than 9 mm. In studies that used a multidetector scanner, low collimation, and an optimal mode of imaging, the sensitivity of CT colonography to detect polyps larger than 9 mm was the highest and most consistent. However, results were inconsistent when other technical approaches were used and smaller polyps were present. Acceptable techniques for colorectal cancer screening should have consistently high sensitivity over specificity so that preneoplastic polyps are effectively ruled out in patients with a negative result. Although some studies have reported high sensitivities for CT colonography, the range among all studies is broad (as low as 21% overall, and as low as 48% for polyps greater than 9 mm).

Until the source of this heterogeneity is more clearly explained and CT colonography is demonstrated to be consistently and reliably sensitive, it cannot be recommended for general use. However, the technology shows much promise in this regard. Refinement of CT scanners, improved patient preparations, and evolving software for CT colonography will probably improve diagnostic accuracy. For the time being, CT colonography should be used in research protocols or when other accepted screening methods are not appropriate.

From Walter Reed Army Medical Center and Uniformed Services University, Washington, DC.

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Requests for Single Reprints: Brian P. Mulhall, MD, MPH, Gastroenterology Service, Walter Reed Army Medical Center, 6900 Georgia Avenue NW, Building 2, 7F18, Washington, DC 20307; e-mail, brian.mulhall@na.amedd.army.mil.

Current author addresses are available at www.annals.org.

References

- Jemal A, Tiwari RC, Murray T, Ghafoor A, Samuels A, Ward E, et al. Cancer statistics, 2004. *CA Cancer J Clin*. 2004;54:8-29. [PMID: 14974761]
- Leslie A, Carey FA, Pratt NR, Steele RJ. The colorectal adenoma-carcinoma sequence. *Br J Surg*. 2002;89:845-60. [PMID: 12081733]
- Bond JH. Clinical evidence for the adenoma-carcinoma sequence, and the management of patients with colorectal adenomas. *Semin Gastrointest Dis*. 2000; 11:176-84. [PMID: 11057945]
- Terdiman JP. Genomic events in the adenoma to carcinoma sequence. *Semin Gastrointest Dis*. 2000;11:194-206. [PMID: 11057947]

- Roncucci L, Fante R, Losi L, Di Gregorio C, Micheli A, Benatti P, et al. Survival for colon and rectal cancer in a population-based cancer registry. *Eur J Cancer*. 1996;32A:295-302. [PMID: 8664045]
- Ponz de Leon M, Benatti P, Di Gregorio C, Fante R, Rossi G, Losi L, et al. Staging and survival of colorectal cancer: are we making progress? The 14-year experience of a Specialized cancer Registry. *Dig Liver Dis*. 2000;32:312-7. [PMID: 11515629]
- Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale—update based on new evidence. *Gastroenterology*. 2003;124:544-60. [PMID: 12557158]
- Pignone M, Rich M, Teutsch SM, Berg AO, Lohr KN. Screening for colorectal cancer in adults at average risk: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2002;137:132-41. [PMID: 12118972]
- Ioannou GN, Chapko MK, Dominitz JA. Predictors of colorectal cancer screening participation in the United States. *Am J Gastroenterol*. 2003;98:2082-91. [PMID: 14499792]
- Seeff LC, Shapiro JA, Nadel MR. Are we doing enough to screen for colorectal cancer? Findings from the 1999 Behavioral Risk Factor Surveillance System. *J Fam Pract*. 2002;51:761-6. [PMID: 12366896]
- DiPalma AM, Barnes SE, DiPalma JA. Patient participation in colon cancer screening programs. *South Med J*. 1998;91:342-4. [PMID: 9563424]
- Colorectal cancer test use among persons aged > or = 50 years—United States, 2001. *MMWR Morb Mortal Wkly Rep*. 2003;52:193-6. [PMID: 12653456]
- Brenes GA, Paskett ED. Predictors of stage of adoption for colorectal cancer screening. *Prev Med*. 2000;31:410-6. [PMID: 11006067]
- Vining DJ, Gelfand DW, Bechtold RE, Scharling ES, Grishaw EK, Shifrin GY. Technical feasibility of colon imaging with helical CT and virtual reality [Abstract]. *Am J Roentgenol*. 1994;162(Suppl):S104.
- Geenen RW, Hussain SM, Cademartiri F, Poley JW, Siersema PD, Krestin GP. CT and MR colonography: scanning techniques, postprocessing, and emphasis on polyp detection. *Radiographics*. 2004;24:e18. [PMID: 14527992]
- Dachman AH, Yoshida H. Virtual colonoscopy: past, present, and future. *Radiol Clin North Am*. 2003;41:377-93. [PMID: 12659344]
- Laghi A, Lannaccone R, Panebianco V, Carbone L, Passariello R. Multislice CT colonography: technical developments. *Semin Ultrasound CT MR*. 2001;22: 425-31. [PMID: 11665921]
- Rogalla P, Meiri N, Ruckert JC, Hamm B. Colonography using multislice CT. *Eur J Radiol*. 2000;36:81-5. [PMID: 11116171]
- Yoshida H, Dachman AH. CAD techniques, challenges, and controversies in computed tomographic colonography. *Abdom Imaging*. 2005;30:26-41. [PMID: 15647868]
- Nicholson FB, Taylor S, Halligan S, Kamm MA. Recent developments in CT colonography. *Clin Radiol*. 2005;60:1-7. [PMID: 15642287]
- Summers RM, Franaszek M, Miller MT, Pickhardt PJ, Choi JR, Schindler WR. Computer-aided detection of polyps on oral contrast-enhanced CT colonography. *AJR Am J Roentgenol*. 2005;184:105-8. [PMID: 15615958]
- Lefere PA, Gryspeerdt SS, Dewyspelaere J, Baekelandt M, Van Holsbeeck BG. Dietary fecal tagging as a cleansing method before CT colonography: initial results polyp detection and patient acceptance. *Radiology*. 2002;224:393-403. [PMID: 12147834]
- Bielen D, Thomeer M, Vanbeckevoort D, Kiss G, Maes F, Marchal G, et al. Dry preparation for virtual CT colonography with fecal tagging using water-soluble contrast medium: initial results. *Eur Radiol*. 2003;13:453-8. [PMID: 12594546]
- Johnson CD, Dachman AH. CT colonography: the next colon screening examination? *Radiology*. 2000;216:331-41. [PMID: 10924550]
- Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med*. 2003;349:2191-200. [PMID: 14657426]
- Akerkar GA, Yee J, Hung R, McQuaid K. Patient experience and preferences toward colon cancer screening: a comparison of virtual colonoscopy and conventional colonoscopy. *Gastrointest Endosc*. 2001;54:310-5. [PMID: 11522970]
- Angtuaco TL, Banaad-Omiotek GD, Howden CW. Differing attitudes toward virtual and conventional colonoscopy for colorectal cancer screening: sur-

- veys among primary care physicians and potential patients. *Am J Gastroenterol.* 2001;96:887-93. [PMID: 11280570]
28. Scott RG, Edwards JT, Fritschi L, Foster NM, Mendelson RM, Forbes GM. Community-based screening by colonoscopy or computed tomographic colonography in asymptomatic average-risk subjects. *Am J Gastroenterol.* 2004;99:1145-51. [PMID: 15180739]
 29. Taylor SA, Halligan S, Saunders BP, Bassett P, Vance M, Bartram CI. Acceptance by patients of multidetector CT colonography compared with barium enema examinations, flexible sigmoidoscopy, and colonoscopy. *AJR Am J Roentgenol.* 2003;181:913-21. [PMID: 14500202]
 30. Gluecker TM, Johnson CD, Harmsen WS, Offord KP, Harris AM, Wilson LA, 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. [PMID: 12732696]
 31. van Gelder RE, Birnie E, Florie J, Schutter MP, Bartelsman JF, Snel P, et al. CT colonography and colonoscopy: assessment of patient preference in a 5-week follow-up study. *Radiology.* 2004;233:328-37. [PMID: 15358854]
 32. Ladabaum U, Song K, Fendrick AM. Colorectal neoplasia screening with virtual colonoscopy: when, at what cost, and with what national impact? *Clin Gastroenterol Hepatol.* 2004;2:554-63. [PMID: 15224279]
 33. Sonnenberg A, Delco F, Bauerfeind P. Is virtual colonoscopy a cost-effective option to screen for colorectal cancer? *Am J Gastroenterol.* 1999;94:2268-74. [PMID: 10445561]
 34. Cotton PB, Durkalski VL, Pineau BC, Palesch YY, Mauldin PD, Hoffman B, et al. Computed tomographic colonography (virtual colonoscopy): a multi-center comparison with standard colonoscopy for detection of colorectal neoplasia. *JAMA.* 2004;291:1713-9. [PMID: 15082698]
 35. Fletcher JG, Johnson CD. Computed tomographic colonography: current and future status for colorectal cancer screening. *Semin Roentgenol.* 2000;35:385-93. [PMID: 11060924]
 36. Pickhardt PJ. Virtual colonoscopy [Letter]. *JAMA.* 2004;292:431. [PMID: 15280335]
 37. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327:557-60. [PMID: 12958120]
 38. Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. *Stat Med.* 1993;12:1293-316. [PMID: 8210827]
 39. Thompson SG, Sharp SJ. Explaining heterogeneity in meta-analysis: a comparison of methods. *Stat Med.* 1999;18:2693-708. [PMID: 10521860]
 40. Van Gelder RE, Nio CY, Florie J, Bartelsman JF, Snel P, De Jager SW, et al. Computed tomographic colonography compared with colonoscopy in patients at increased risk for colorectal cancer. *Gastroenterology.* 2004;127:41-8. [PMID: 15236170]
 41. Macari M, Bini EJ, Jacobs SL, Naik S, Lui YW, Milano A, et al. Colorectal polyps and cancers in asymptomatic average-risk patients: evaluation with CT colonography. *Radiology.* 2004;230:629-36. [PMID: 14739311]
 42. Macari M, Bini EJ, Jacobs SL, Lui YW, Laks S, Milano A, et al. Significance of missed polyps at CT colonography. *AJR Am J Roentgenol.* 2004;183:127-34. [PMID: 15208126]
 43. Hoppe H, Netzer P, Spreng A, Quattropiani C, Mattich J, Dinkel HP. Prospective comparison of contrast enhanced CT colonography and conventional colonoscopy for detection of colorectal neoplasms in a single institutional study using second-look colonoscopy with discrepant results. *Am J Gastroenterol.* 2004;99:1924-35. [PMID: 15447751]
 44. Iannaccone R, Laghi A, Catalano C, Mangiapane F, Piacentini F, Passariello R. Feasibility of ultra-low-dose multislice CT colonography for the detection of colorectal lesions: preliminary experience. *Eur Radiol.* 2003;13:1297-302. [PMID: 12764645]
 45. Johnson CD, Harmsen WS, Wilson LA, Maccarty RL, Welch TJ, Ilstrup DM, et al. Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. *Gastroenterology.* 2003;125:311-9. [PMID: 12891530]
 46. Pineau BC, Paskett ED, Chen GJ, Espeland MA, Phillips K, Han JP, et al. Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. *Gastroenterology.* 2003;125:304-10. [PMID: 12891529]
 47. Taylor SA, Halligan S, Saunders BP, Morley S, Riesewyk C, Atkin W, et al. Use of multidetector-row CT colonography for detection of colorectal neoplasia in patients referred via the Department of Health "2-Week-wait" initiative. *Clin Radiol.* 2003;58:855-61. [PMID: 14581009]
 48. Ginnerup Pedersen B, Christiansen TE, Bjerregaard NC, Ljungmann K, Laurberg S. Colonoscopy and multidetector-array computed-tomographic colonography: detection rates and feasibility. *Endoscopy.* 2003;35:736-42. [PMID: 12929020]
 49. Yee J, Kumar NN, Hung RK, Akerkar GA, Kumar PR, Wall SD. Comparison of supine and prone scanning separately and in combination at CT colonography. *Radiology.* 2003;226:653-61. [PMID: 12601201]
 50. Munikrishnan V, Gillams AR, Lees WR, Vaizey CJ, Boulos PB. Prospective study comparing multislice CT colonography with colonoscopy in the detection of colorectal cancer and polyps. *Dis Colon Rectum.* 2003;46:1384-90. [PMID: 14530680]
 51. Laghi A, Iannaccone R, Carbone I, Catalano C, Di Giulio E, Schillaci A, et al. Detection of colorectal lesions with virtual computed tomographic colonography. *Am J Surg.* 2002;183:124-31. [PMID: 11918874]
 52. Gluecker T, Dorta G, Keller W, Jornod P, Meuli R, Schnyder P. Performance of multidetector computed tomography colonography compared with conventional colonoscopy. *Gut.* 2002;51:207-11. [PMID: 12117881]
 53. Macari M, Bini EJ, Xue X, Milano A, Katz SS, Resnick D, et al. Colorectal neoplasms: prospective comparison of thin-section low-dose multi-detector row CT colonography and conventional colonoscopy for detection. *Radiology.* 2002;224:383-92. [PMID: 12147833]
 54. McFarland EG, Pilgram TK, Brink JA, McDermott RA, Santillan CV, Brady PW, et al. CT colonography: multiobserver diagnostic performance. *Radiology.* 2002;225:380-90. [PMID: 12409570]
 55. Yee J, Akerkar GA, Hung RK, Steinauer-Gebauer AM, Wall SD, McQuaid KR. Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients. *Radiology.* 2001;219:685-92. [PMID: 11376255]
 56. Hara AK, Johnson CD, MacCarty RL, Welch TJ, McCollough CH, Harmsen WS. CT colonography: single- versus multi-detector row imaging. *Radiology.* 2001;219:461-5. [PMID: 11323473]
 57. Spinzi G, Belloni G, Martegani A, Sangiovanni A, Del Favero C, Minoli G. Computed tomographic colonography and conventional colonoscopy for colon diseases: a prospective, blinded study. *Am J Gastroenterol.* 2001;96:394-400. [PMID: 11232681]
 58. Fletcher JG, Johnson CD, Welch TJ, MacCarty RL, Ahlquist DA, Reed JE, et al. Optimization of CT colonography technique: prospective trial in 180 patients. *Radiology.* 2000;216:704-11. [PMID: 10966698]
 59. Morrin MM, Farrell RJ, Kruskal JB, Reynolds K, McGee JB, Raptopoulos V. Utility of intravenously administered contrast material at CT colonography. *Radiology.* 2000;217:765-71. [PMID: 11110941]
 60. Mendelson RM, Foster NM, Edwards JT, Wood CJ, Rosenberg MS, Forbes GM. Virtual colonoscopy compared with conventional colonoscopy: a developing technology. *Med J Aust.* 2000;173:472-5. [PMID: 11149303]
 61. Macari M, Milano A, Lavelle M, Berman P, Megibow AJ. Comparison of time-efficient CT colonography with two- and three-dimensional colonic evaluation for detecting colorectal polyps. *AJR Am J Roentgenol.* 2000;174:1543-9. [PMID: 10845478]
 62. Morrin MM, Farrell RJ, Raptopoulos V, McGee JB, Bleday R, Kruskal JB. Role of virtual computed tomographic colonography in patients with colorectal cancers and obstructing colorectal lesions. *Dis Colon Rectum.* 2000;43:303-11. [PMID: 10733110]
 63. Fenlon HM, Nunes DP, Schroy PC 3rd, Barish MA, Clarke PD, Ferrucci JT. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. *N Engl J Med.* 1999;341:1496-503. [PMID: 10559450]
 64. Rex DK, Vining D, Kopecky KK. An initial experience with screening for colon polyps using spiral CT with and without CT colography (virtual colonoscopy). *Gastrointest Endosc.* 1999;50:309-13. [PMID: 10462648]
 65. Dachman AH, Kuniyoshi JK, Boyle CM, Samara Y, Hoffmann KR, Rubin DT, et al. CT colonography with three-dimensional problem solving for detection of colonic polyps. *AJR Am J Roentgenol.* 1998;171:989-95. [PMID: 9762982]
 66. Royster AP, Fenlon HM, Clarke PD, Nunes DP, Ferrucci JT. CT colonoscopy of colorectal neoplasms: two-dimensional and three-dimensional virtual-reality techniques with colonoscopic correlation. *AJR Am J Roentgenol.* 1997;169:1237-42. [PMID: 9353434]
 67. Hara AK, Johnson CD, Reed JE, Ahlquist DA, Nelson H, MacCarty RL, et al. Detection of colorectal polyps with CT colography: initial assessment of sensitivity and specificity. *Radiology.* 1997;205:59-65. [PMID: 9314963]
 68. Rockey DC, Paulson E, Niedzwiecki D, Davis W, Bosworth HB, Sanders L, et al. Analysis of air contrast barium enema, computed tomographic colonog-

- raphy, and colonoscopy: prospective comparison. *Lancet*. 2005;365:305-11. [PMID: 15664225]
69. Chung DJ, Huh KC, Choi WJ, Kim JK. CT colonography using 16-MDCT in the evaluation of colorectal cancer. *AJR Am J Roentgenol*. 2005;184:98-103. [PMID: 15615957]
70. Whiting P, Rutjes AW, Reitsma JB, Glas AS, Bossuyt PM, Kleijnen J. Sources of variation and bias in studies of diagnostic accuracy: a systematic review. *Ann Intern Med*. 2004;140:189-202. [PMID: 14757617]
71. Sosna J, Morrin MM, Kruskal JB, Lavin PT, Rosen MP, Raptopoulos V. CT colonography of colorectal polyps: a metaanalysis. *AJR Am J Roentgenol*. 2003;181:1593-8. [PMID: 14627580]
72. Taylor SA, Halligan S, Burling D, Morley S, Bassett P, Atkin W, et al. CT colonography: effect of experience and training on reader performance. *Eur Radiol*. 2004;14:1025-33. [PMID: 14872280]
73. Rex DK, Vining D, Kopecky KK. An initial experience with screening for colon polyps using spiral CT with and without CT colography (virtual colonoscopy). *Gastrointest Endosc*. 1999;50:309-13. [PMID: 10462648]
74. Pavone P, Luccichenti G, Cademartiri F. Improving the results of virtual colonoscopy: what the future will bring. *Semin Ultrasound CT MR*. 2001;22:400-2. [PMID: 11665916]
75. Miao YM, Amin Z, Healy J, Burn P, Murugan N, Westaby D, et al. A prospective single centre study comparing computed tomography pneumocolon against colonoscopy in the detection of colorectal neoplasms. *Gut*. 2000;47:832-7. [PMID: 11076883]
76. Pickhardt PJ, Choi JR, Hwang I, Schindler WR. Nonadenomatous polyps at CT colonography: prevalence, size distribution, and detection rates. *Radiology*. 2004;232:784-90. [PMID: 15247435]
77. Rex DK, Cutler CS, Lemmel GT, Rahmani EY, Clark DW, Helper DJ, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology*. 1997;112:24-8. [PMID: 8978338]

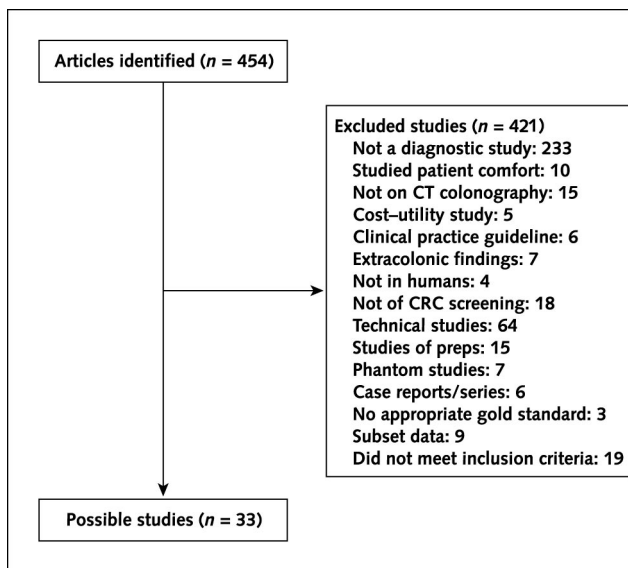
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Current Author Addresses: Dr. Mulhall: Gastroenterology Service, Walter Reed Army Medical Center, 6900 Georgia Avenue NW, Building 2, 7F18, Washington, DC 20307.

Dr. Veerappan: Department of Medicine, Walter Reed Army Medical Center, 6900 Georgia Avenue NW, Building 2, 7F18, Washington, DC 20307.

Dr. Jackson: Medicine-EDP, 4301 Jones Bridge Road, Bethesda, MD 20814.

Appendix Figure. Map of the literature search and selection process.



The QUORUM (Quality of Reporting of Meta-Analyses) guidelines for reporting of meta-analyses were used. CRC = colorectal cancer; CT = computed tomographic.

Appendix Table 1. Test Performance of Computed Tomographic Colonography, by Per-Patient Analysis

Author, Year (Reference)	Patients, n	Sensitivity, %		Overall Specificity, %	Detection of Polyps > 6 mm					
		Overall	Patients with Cancer		True-Positive Result, n	False-Positive Result, n	False-Negative Result, n	True-Negative Result, n	Sensitivity, %	Specificity, %
Rockey et al., 2005 (68)	614	–	78.0	–	85	50	70	409	55.0	89.0
Chung et al., 2005 (69)	51	–	–	–	–	–	–	–	–	–
Cotton et al., 2004 (34)	600	20.5	75.0	90.5	41	47	63	449	39.4	90.5
Macari et al., 2004 (42)	186	–	–	83.1	–	–	–	–	–	–
Van Gelder et al., 2004 (40)	249	62.1	–	30.6	35	62	10	142	77.8	69.6
Macari et al., 2004 (41)	68	–	–	89.7	–	–	–	–	–	–
Hoppe et al., 2004 (43)	92	73.3	87.5	–	26	7	8	51	76.5	87.9
Pickhardt et al., 2003 (25)	1233	–	–	–	149	217	19	848	88.7	79.6
Iannaccone et al., 2003 (44)	158	96.0	100.0	96.5	–	–	–	–	–	–
Johnson et al., 2003 (45)	703	–	–	–	–	–	–	–	–	–
Pineau et al., 2003 (46)	205	61.8	–	70.7	38	27	7	133	84.4	83.1
Taylor et al., 2003 (47)	54	64.5	83.3	–	–	–	–	–	–	–
Ginnerup Pedersen et al., 2003 (48)	144	–	–	–	30	–	3	–	90.9	–
Yee et al., 2003 (49)	182	90.4	–	82.4	–	–	–	–	–	–
Munikrishnan et al., 2003 (50)	61	74.3	96.6	96.2	–	–	–	–	–	–
Laghi et al., 2002 (51)	165	93.0	100.0	–	–	–	–	–	–	–
Gluecker et al., 2002 (52)	50	–	–	90.5	–	–	–	–	–	–
Lefere et al., 2002 (22)	100	86.0	–	–	–	–	–	–	–	–
Macari et al., 2002 (53)	105	57.6	100.0	87.0	–	–	–	–	–	–
McFarland et al., 2002 (54)	70	–	–	–	–	–	–	–	–	–
Yee et al., 2001 (55)	300	93.9	100.0	56.5	–	–	–	–	–	–
Hara et al., 2001 (56)	237	–	–	–	–	–	–	–	–	–
Spinzi et al., 2001 (57)	96	–	87.5	–	–	–	–	–	–	–
Fletcher et al., 2000 (58)	180	–	–	–	114	14	16	36	87.7	72.0
Morrin et al., 2000 (59)	81	–	–	–	–	–	–	–	–	–
Mendelson et al., 2000 (60)	53	–	–	–	15	2	4	32	78.9	94.1
Macari et al., 2000 (61)	42	–	–	–	–	–	–	–	–	–
Morrin et al., 2000 (59)	34	–	100.0	–	–	–	–	–	–	–
Fenlon et al., 1999 (63)	100	82.4	100.0	83.7	–	–	–	–	–	–
Rex et al., 1999 (64)	46	45.5	–	–	11	–	6	–	64.7	–
Dachman et al., 1998 (65)	44	43.8	–	89.3	–	–	–	–	–	–
Royster et al., 1997 (66)	20	–	95.0	–	–	–	–	–	–	–
Hara et al., 1997 (67)	70	–	–	–	16.5	17	8.5	28	66.0	62.2

Appendix Table 1—Continued

Detection of Polyps 6–9 mm						Detection of Polyps > 9 mm					
True-Positive Result, <i>n</i>	False-Positive Result, <i>n</i>	False-Negative Result, <i>n</i>	True-Negative Result, <i>n</i>	Sensitivity, %	Specificity, %	True-Positive Result, <i>n</i>	False-Positive Result, <i>n</i>	False-Negative Result, <i>n</i>	True-Negative Result, <i>n</i>	Sensitivity, %	Specificity, %
59	–	57	–	51.0	–	37	22	26	529	59.0	96.0
–	–	–	–	–	–	–	–	–	–	–	–
23	36	53	488	30.3	93.1	23	23	19	535	54.8	95.9
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	26	17.5	5	200.5	83.9	92.0
–	–	–	–	–	–	–	1.0	–	64.0	–	98.5
–	–	–	–	–	–	19	1	1	65	95.0	98.5
–	–	–	–	–	–	45	47	3	1138	93.8	96.0
–	–	–	–	–	–	–	–	–	–	–	–
36	56	33	578	52.2	91.2	22.5	16.5	24.5	639	47.9	97.5
–	–	–	–	–	–	18	10	2	175	90.0	94.6
1	–	1	–	50.0	–	9	0	1	44	90.0	100.0
14	–	3	–	82.4	–	22	–	1	–	95.7	–
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–
21	6	2	71	91.3	92.2	25	0	0	75	100.0	100.0
–	–	–	–	–	–	–	–	–	–	–	–
57	–	–	–	71.3	–	98	–	14	–	87.5	–
40	–	2	–	95.2	–	47	–	0	–	100.0	–
–	–	–	–	–	–	9.5	10	4.5	212.5	67.9	95.5
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	82	6	14	78	85.4	92.9
16	2	6	57	72.7	96.6	14	0	2	65	87.5	100.0
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–
47	4	3	46	94.0	92.0	48	2	2	48	96.0	96.0
3	–	4	–	42.9	–	8	4	2	32	80.0	88.9
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	9	5.5	3	52.5	75.0	90.5

Appendix Table 2. Test Performance of Computed Tomographic Colonography, by Per-Polyp Analysis

Study, Year (Reference)	Patients, <i>n</i>	Sensitivity, %			Detection of Polyps 6–9 mm*			Detection of Polyps > 9 mm*			
		Overall	Detection of Polyps < 6 mm	Detection of Polyps 6–9 mm	Detection of Polyps > 9 mm	True- Positive Result, <i>n</i>	False- Positive Result, <i>n</i>	False- Negative Result, <i>n</i>	True- Positive Result, <i>n</i>	False- Positive Result, <i>n</i>	False- Negative Result, <i>n</i>
Rockey et al., 2005 (68)	614	–	–	60.0	64.0	58	–	39	35	–	20
Chung et al., 2005 (69)	51	90.0	84.0	94.0	100.0	15	–	1	6	–	0
Cotton et al., 2004 (34)	600	12.7	7.6	22.7	51.9	27	–	92	28	–	26
Macari et al., 2004 (42)	186	27.7	14.7	46.2	90.9	12	8	14	20	3	2
Van Gelder et al., 2004 (40)	249	51.8	40.6	76.7	77.8	11.5	–	3.5	21	–	6
Macari et al., 2004 (41)	68	21.4	11.5	52.9	100.0	9	–	8	3	–	0
Hoppe et al., 2004 (43)	92	42.6	25.4	57.9	70.6	11	–	8	12	–	5
Pickhardt et al., 2003 (25)	1233	–	–	83.6	92.2	133	–	26	47	–	4
Iannacconne et al., 2003 (44)	158	70.3	51.4	83.3	100.0	20	–	4	13	–	0
Johnson et al., 2003 (45)	703	–	–	47.1	46.3	24	–	27	19	–	22
Pineau et al., 2003 (46)	205	46.8	29.4	75.0	77.8	36	38	12	21	13	6
Taylor et al., 2003 (47)	54	48.4	37.5	75.0	100.0	3	–	1	3	–	0
Ginnerup Pedersen et al., 2003 (48)	144	–	–	73.7	92.3	14	–	5	24	–	2
Yee et al., 2003 (49)	182	69.9	60.3	79.8	92.7	71	–	18	38	–	3
Munikrishnan et al., 2003 (50)	61	75.8	53.3	83.3	100.0	5	1	1	12	–	0
Laghi et al., 2002 (51)	165	78.4	50.0	82.4	91.7	14	–	3	11	–	1
Gluecker et al., 2002 (52)	50	22.4	2.4	33.3	81.8	5	–	10	9	–	2
Lefere et al., 2002 (22)	100	77.5	56.5	90.3	100.0	28	9	3	25	0	0
Macari et al., 2002 (53)	105	32.6	12.1	70.4	92.9	19	3	8	13	1	1
McFarland et al., 2002 (54)	70	–	–	36.1	68.1	65	61	115	109	35	51
Yee et al., 2001 (55)	300	77.5	66.9	81.8	94.1	72	97	16	64	24	4
Hara et al., 2001 (56)	237	–	–	–	–	–	–	–	–	–	–
Spinzi et al., 2001 (57)	96	57.8	–	–	61.5	–	–	–	8	–	5
Fletcher et al., 2000 (58)	180	60.1	–	47.2	75.2	67	–	75	91	–	30
Morrin et al., 2000 (59)	81	–	32.9	64.5	90.9	20	–	11	20	–	2
Mendelson et al., 2000 (60)	53	27.5	17.5	22.2	72.7	4	1	14	8	2	3
Macari et al., 2000 (61)	42	37.5	20.0	60.0	100.0	3	2	2	1	–	0
Morrin et al., 2000 (59)	34	–	–	–	–	–	–	–	–	–	–
Fenlon et al., 1999 (63)	100	71.3	66.7	89.7	90.9	26	0	3	20	0	2
Rex et al., 1999 (64)	46	22.0	11.1	42.9	50.0	6	–	8	7	–	7
Dachman et al., 1998 (65)	44	46.7	7.7	33.3	83.3	1	0	2	5	0	1
Royster et al., 1997 (66)	20	91.4	66.7	90.0	100.0	9	0	1	2	0	2
Hara et al., 1997 (67)	70	37.4	25.9	57.1	70.0	12	31	9	10.5	6.5	4.5

* No study reported a true-negative result.