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Computed Tomographic (CT) Colonography for Colorectal Cancer Screening

An Evidence-Based Analysis

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Contact Information

The Medical Advisory Secretariat
Ministry of Health and Long-Term Care
20 Dundas Street West, 10th floor
Toronto, Ontario
CANADA
M5G 2N6
Email: MASinfo.moh@ontario.ca
Telephone: 416-314-1092

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The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

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List of Abbreviations

AUC	Area under the curve
BEIR	Biological effect of ionizing radiation
CI	Confidence interval(s)
CRC	Colorectal cancer
CT	Computed tomographic
CTC	Computed tomographic colonography
FIT	Fecal immunological test
FOBT	Fecal occult blood test
FS	Flexible sigmoidoscopy
IAEA	International Atomic Energy Agency
ICRP	International Commission on Radiological Protection
kVp	Peak kilovoltage
LET	Linear energy transfer
mA	milliampere
mSv	milli sievert
OC	Optical colonoscopy
OR	Odds ratio
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
SEER	The Surveillance, Epidemiology, and End Results
SROC	Summary receiver operating characteristic

Glossary

Ampere	Unit for measuring electric current
Average risk for CRC	People 50 years of age and older who do not have any other risk factors for colorectal cancer
Cecum	The proximal section of the colon
Neoplasia	Abnormal growth of cells that may be benign or malignant
Segmental unblinding	A technique used in CT colonography studies in which there is discrepancy between the results of CT colonography and colonoscopy. In the technique, findings of CT colonography are revealed to the endoscopist after initial examination of each colonic segment. If a lesion was found at CT colonography but not at the initial colonoscopy, the endoscopist reexamines that segment to see whether the finding in CT colonography is a true positive or a false positive.
Sigmoid colon	The distal section of the colon
Sv	Sievert [1 sievert = 1 joule/kg]; derived unit mSv (millisievert)

Background

The colorectal cancer (CRC) screening project was undertaken by the Medical Advisory Secretariat (MAS) in collaboration with the Cancer Care Ontario (CCO).

In November 2007, the Ontario Health Technology Advisory Committee (OHTAC) MAS to conduct an evidence-based analysis of the available data with respect to colorectal cancer diagnosis and prevention. The general purpose of the project was to investigate the effectiveness, cost effectiveness, and safety of the various methods and techniques used for colorectal cancer screening in average risk people, 50 years of age and older.

The options currently offered for colorectal cancer screening were reviewed and five technologies were selected for review:

- Computed tomographic (CT) colonography
- Magnetic resonance (MR) colonography
- Wireless capsule endoscopy (PillCam Colon)
- Fecal occult blood test (FOBT)
- Flexible sigmoidoscopy

In this review, colonoscopy was considered as the "gold standard" technique by which the effectiveness of all other modalities could be evaluated. An economic analysis was also conducted to determine cost-effectiveness of different screening modalities.

Evidence-based analyses have been prepared for each of these technologies, as well as summary document that includes an economic analysis, all of which are presented at the MAS Web site: http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html

Objective

The objective of this report was to systematically review the published literature on computed tomographic (CT) colonography as a diagnostic tool for identification of cancers and adenomatous polyps in the colon and rectum in average risk people, 50 years of age and older, in the context of colorectal cancer (CRC) screening.

Colorectal Cancer

The colon is a frequent site of carcinoma with CRC being the third most common form of cancer and the second leading cause of cancer-related death in the Western world. When detected, the prognosis of CRC depends to a great extent upon the depth of tumour penetration into the bowel wall, regional lymph node involvement, and the presence of distant metastases. In practice, the Duke's classification system is used to determine the extent of disease and the likelihood for 5-year survival in CRC patients depends closely on the Duke stage at the time of treatment (see Table 1).

Table 1: Modified Duke Classification of Colorectal Cancer

Stage	Pathologic Description	Approximate 5-Year Survival Rate, %
A	Cancer limited to mucosa and submucosa	>90
B1	Cancer extends into muscularis	85
B2	Cancer extends into or through serosa	70–85
C	Cancer involves regional lymph nodes	30–60
D	Distant metastases are present (e.g., liver, lung)	5

Source: Isselbacher et al., Harrison's Principles of Internal Medicine. (1)

Cancer of the colon generally spreads to regional lymph nodes or the liver via portal venous circulation. The liver is the most frequent site of metastatic dissemination; in general, CRC rarely metastasizes to the lung, supraclavicular lymph nodes, bone, or brain without prior spread to the liver. A major exception to this occurs among patients in whom the primary tumour is located in the distal rectum. In these patients, tumours can readily spread to the lungs or supraclavicular lymph nodes without hepatic involvement. (1)

Colonic Distribution

Many reports have indicated a shift in colonic distribution of colorectal cancers over the last 25 years. (2) The increase in prevalence of right colonic tumors has been reported particularly in elderly patients. (3) Lieberman et al. (4) studied 3,196 individuals (including both average-risk and high-risk patients) who were recruited for screening and observed a trend toward an increased prevalence of advanced proximal neoplasia with age ($P < .001$). The observed prevalence was 2% for patients who were 50 to 59 years old, 4.9% for those 60 to 69 years old, and 5.9% for those 70 to 75 years old.

Obrand and Gordon (5) retrospectively reviewed the charts of 2,169 patients admitted to one hospital between 1979 and 1994 with a diagnosis of colorectal carcinoma. They reported that the right-sided colonic cancers steadily increased from 20.6% to 29.9% over the 16 years ($P = .001$), whereas rectal cancers decreased from 22% for the first 4 years to 11.3% in the last interval ($P = .002$). In contrast, the frequency of transverse, left, and sigmoid colon lesions remained relatively unchanged. The authors suggested that any effective screening examination for carcinoma should include a complete examination of the colon.

Incidence and Prevalence of CRC in Ontario

The incidence of CRC in Ontario is among the highest in the world (Figure 1) with an estimated 8,000 new cases diagnosed in the province through 2008 (Canadian Cancer Society, Canadian Cancer Statistics, 2008). Over the same year, the disease is also estimated to have caused more than 3,250 deaths in the province, establishing it as a major public health concern (Figure 2). Examining the disease by age group, CRC is uncommon before age 50, after which it increases from 55 cases per 100,000 people in the 50 to 54 age group, to 423 cases per 100,000 in persons aged 85 and older. Similarly, disease mortality increases from 16 to 351 per 100,000 persons over the same age brackets (Figure 3).

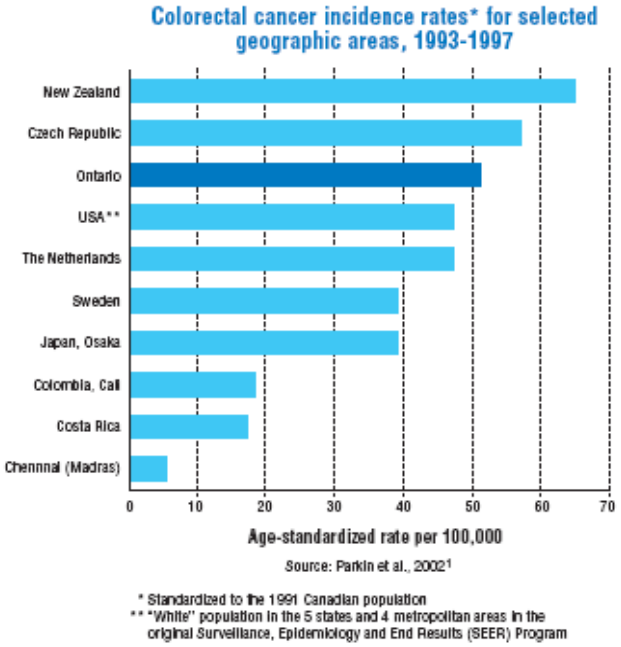


Figure 1: Colorectal Cancer Incidence Rates for Selected Geographic Areas, 1993–1997

Used with permission from Cancer Care Ontario and the Canadian Cancer Society. Insight on Cancer. News and information on colorectal cancer. Toronto: Canadian Cancer Society (Ontario Division), 2004

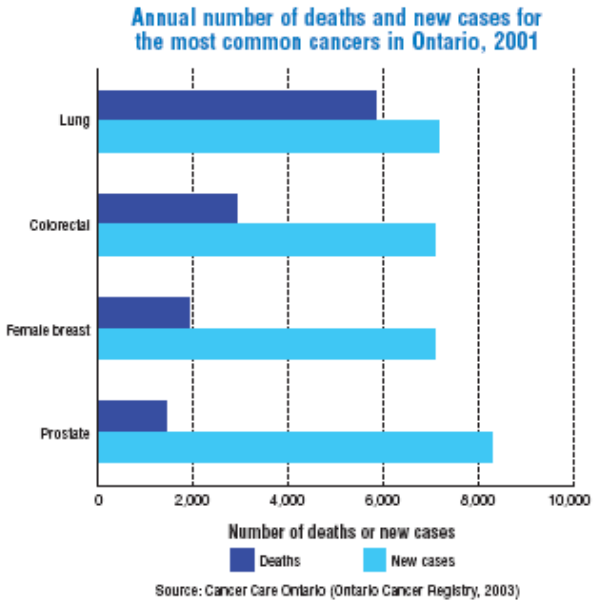


Figure 2: Annual Number of Deaths and New Cases for the Most Common Cancers in Ontario, 2001

Used with permission from Cancer Care Ontario and the Canadian Cancer Society. Insight on Cancer. News and information on colorectal cancer. Toronto: Canadian Cancer Society (Ontario Division), 2004

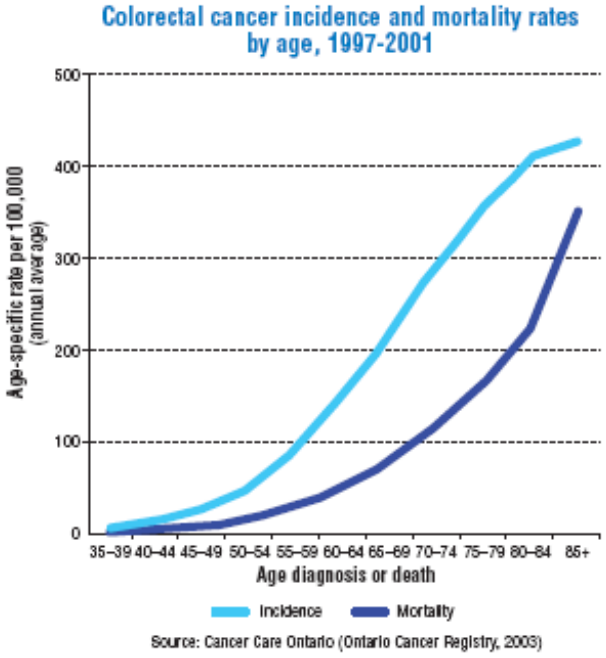


Figure 3: Colorectal Cancer Incidence and Mortality Rates in Ontario by Age, 1997–2001

Used with permission from Cancer Care Ontario and the Canadian Cancer Society. Insight on Cancer. News and information on colorectal cancer. Toronto: Canadian Cancer Society (Ontario Division), 2004

Colorectal Polyps

Colorectal polyps are one of the most common conditions affecting the colon and rectum. A colorectal polyp is a protrusion of the mucosal surface that occurs in the lumen of the colon or rectum. The majority of polyps are noncancerous and cause no symptoms. Of various polyp types encountered in the colon, only neoplastic polyps are regarded as having malignant potential. Neoplastic polyps include tubular adenomas, villous adenomas, and villotubular adenomas (mixed adenomas). The most common form of nonneoplastic polyps is hyperplastic polyp. Hyperplastic polyps are benign and, in most circumstances, are not considered to be premalignant.

Characteristics

Colorectal polyps can be classified into three size categories:

- Small: ≤5 mm
- Medium: 6–9 mm
- Large: ≥10 mm

Polyps ≥10 mm in diameter are generally regarded as being clinically significant and those ≤5 mm in diameter as clinically insignificant as the majority of small polyps are of non-adenomatous type. The optimal threshold for screening may thus lie within the range of medium to large polyps.

A polyp may be classified into any of several morphologies: pedunculated, sessile, or flat/depressed. The detection of large flat lesions is especially important, as these are more likely to become cancerous than a large polypoid lesion. (6) Though flat and depressed polyps appear to be common in Japan, some now believe that these types of polyps are more common in North Americans than previously thought. (7) Flat lesions do, however, remain difficult to detect. Scientists in Japan have thus developed advanced methods to detect small flat lesions during optical colonoscopy.

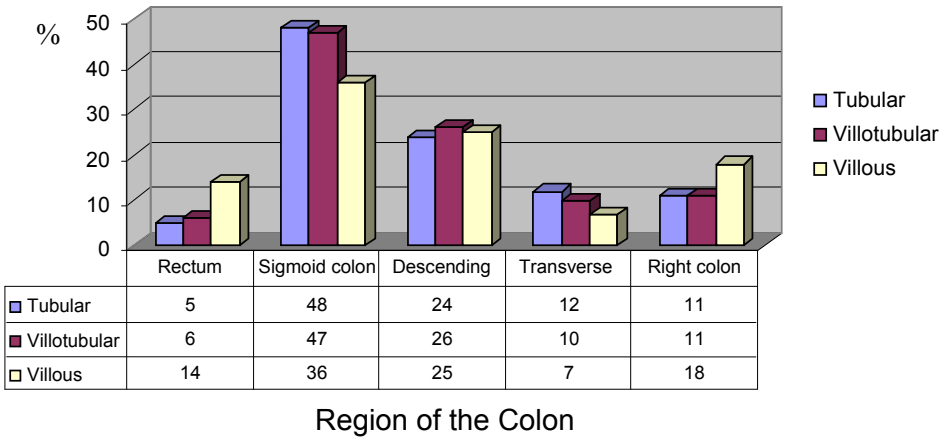
The least common form of neoplastic polyps are adenomas with villous pathology, which, more often than others, are sessile in configuration. They have long been recognized as having the highest tendency toward malignant change. (8)

Prevalence

According to the study by Pickhardt et al. (9), a large adenomatous polyp is seen in 3.9% of asymptomatic people 50 years of age and older and an adenomatous polyp 6 mm or larger is seen in 13.6% of this group.

Colonic Distribution

Shinya et al. (8) analyzed a series of 5,786 adenomas from over 7,000 polyps that were removed endoscopically. Each form of adenoma (tubular, villous, villotubular) occurred more frequently in the sigmoid colon, followed by descending colon. This finding is in line with the results of several studies which reported the association of sigmoidoscopy and reduced mortality from CRC (see Figure 4).



	Rectum	Sigmoid colon	Descending	Transverse	Right colon
Tubular	5	48	24	12	11
Villotubular	6	47	26	10	11
Villous	14	36	25	7	18

Region of the Colon

Figure 4: Distribution of Types of Adenomas

Source: Shinya and Wolff, 1979. (8)

Transformation to Cancer

The majority of CRCs are believed to arise from asymptomatic adenomatous polyps, which have been shown to take about 10 years to transform into invasive CRC. This leaves a substantial window of opportunity to find and remove these precancerous polyps before they become malignant.

In a rigorous test of the hypothesis that polypectomy via colonoscopy can reduce the incidence of CRC, The National Polyp Study has demonstrated that polypectomy could reduce CRC incidence by as much as 76%. (10) The study cohort consisted of 1,418 patients (mean age of 61 ± 10 years) who had undergone complete colonoscopy, during which one or more adenomas of the colon or rectum were removed. At the time of enrolment, 494 patients (35%) had adenomas ≥10 mm in diameter and 137 (10%) had adenomas with high-grade dysplasia. Patients underwent periodic colonoscopy with an average follow-up of 5.9 years. The incidence of CRC in the patient cohort was compared with that of three reference groups:

- The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, which represents people at average risk in the United States.
- Data from Mayo Clinic in the United States (1965-1970) consisting of patients in whom a colorectal polyp ≥10 mm or larger, beyond the reach of a rigid sigmoidoscope, was detected by barium enema. Polypectomy was not performed in these patients because they declined such intervention.
- Data from St. Mark's Hospital in the United Kingdom (1957-1980) consisting of patients in whom a rectosigmoid adenomatous polyp was removed.

The results of the study showed that during follow-up, asymptomatic CRC was detected in five patients. No symptomatic cancer was found and none of the patients died of CRC. The observed incidence of CRC in the study cohort was significantly lower than expected ($P < .001$) based on the rates found in the three reference groups. The observed incidence of CRC per 1,000 person-years was 0.6 in the study cohort, compared with the expected incidence of 2.5 in the SEER group, 5.8 in the Mayo Clinic group, and 5.2 in the St. Mark's Hospital group. Percentage reduction in CRC incidence was 76% compared with SEER data ($P < 001$), 90% compared with Mayo Clinic data, and 88% compared with St. Mark's Hospital data. The study thus provided evidence of the progression of adenoma to carcinoma, as well as evidence that the incidence of CRC can be reduced by colonoscopic polypectomy.

Average Versus High Risk for Colorectal Cancer

Persons in whom age is the only risk factor for CRC are considered to be at average risk. Factors that place individuals at higher risk include a family history of CRC or adenoma, personal history of CRC or adenoma, and inflammatory bowel disease. (11) There is mounting evidence endorsing the provision of CRC screening to average-risk individuals, beginning at age 50, to detect cancers at a favourable stage before they have advanced to a potentially lethal disease state.

The introduction of a method to identify high-risk patients would allow for their prompt diagnosis and treatment and further reduce the burden of the disease in Ontario. For those at high risk, screening beginning at an earlier age may be reasonable; however, such a consideration is beyond the scope of this review.

Colorectal Cancer Screening

The objective of CRC screening is to reduce the burden of CRC and thereby the morbidity and mortality rate of the disease. It is believed that this goal can be achieved by regularly screening the average-risk population, enabling the detection of cancer at an early and curable stage and polyps before they become cancerous.

Several methods of screening for CRC have been proposed by various organizations, each with their own advantages and drawbacks. It should be borne in mind that no infallible technique exists and there is a need for continued improvement in screening methods. However, as with other screening tests, the ideal screening technique for CRC should be feasible, accurate, safe, acceptable, and cost-effective.

Optical Colonoscopy

Colonoscopy is currently considered the gold standard for the detection of colorectal neoplasia, yet its true sensitivity is difficult to determine. One needs to remember that the success of the technique in identification of colorectal lesions is highly dependent on the skills of the endoscopist. The initial measures of sensitivity of colonoscopy for adenomas were made by tandem colonoscopy studies. (12;13) Rex et al. (12) determined miss rate of colonoscopy by same day back-to-back colonoscopy. The miss rate was shown to be 13% for adenomas 6-9 mm, and 6% for adenomas >= 10 mm. Right colon adenomas were missed more often (27%) than left colon adenomas (21%), but the difference was not statistically significant. Hixson et al. (13) studied the colonoscopic miss rate in a blinded trial. In this study colonoscopy did not miss any of the 63 lesions 10 mm or larger while 12% of the 6-9 mm lesions were missed.

More recently, the technique of segmental unblinding in CT colonography studies has been used to demonstrate the true sensitivity of colonoscopy for detection of adenomas. However, this technique is not a reliable method for determination of sensitivity of colonoscopy for polyps less than 10 mm in size. Pickhardt et al. used the technique of segmental unblinding and reported that colonoscopy had a higher sensitivity for detection of patients with adenomas 6 mm and larger (90%) than that for detection of patients with adenomas 10 mm or larger (88%).

The interior lining of the colon from anus to cecum can be visualized through colonoscopy, allowing for a high rate of detection for potentially curable CRCs and precancerous adenomatous polyps. Colonoscopy does, however, fail to reach the cecum in 5% to 10% of average-risk people due a variety of reasons such as tortuousity or malrotation of the loops, bowel spasm, diverticulitis or diverticulosis, ischemic colitis, colonic configuration due to previous surgery, obstructive tumors, external compression from masses or hernia. (14)

The advantage of colonoscopy is that it allows detection, biopsy, and removal of the lesions identified. Therefore, a single session detection and treatment would be more convenient for the patients. In addition, the longer interval between screening colonoscopy (10 years) enables a eduction in cost compared to other methods.

The drawback of the technique is that it is invasive and is associated with clinically important complications such as bleeding and/or perforation. However, these risks are small and are more commonly associated with polypectomy and/or biopsy. (15) A study conducted among the United States Medicare population examined the risk of colonic perforation following colonoscopy and sigmoidoscopy. (16) Overall, there were 77 perforations after 39,286 colonoscopies (incidence = 1.96/1,000 procedure). The risk of perforation for those who underwent screening colonoscopy (n = 20,163) was 1.3/1,000.

A large Swedish study (17) involving 6,066 diagnostic and therapeutic colonoscopies demonstrated that bleeding and perforation occurred in 0.2% and 0.1% respectively with no colonoscopy related mortality. Bleeding was confined to therapeutic colonoscopy and occurred immediately, mainly after removal of large polyps with thick stalks. Perforation at diagnostic colonoscopy occurred in the left colon and was diagnosed sooner than perforations due to therapeutic colonoscopy where the cecum was the most frequent site. The bleeding was correlated to the experience of endoscopist.

The risk of perforation is higher in the presence of conditions such as active colitis, inflammation, diverticular or ischemic disease, and prior irradiation. Although colonoscopy is not routinely indicated for patients with inflammatory bowel disease, it may be indicated for patients with ulcerative colitis of more than 10 years' duration because of an increased risk of carcinoma.

Though there are no published randomized trials, there is indirect evidence that the technique can reduce the overall incidence and mortality of CRC. Colonoscopy was an integral part of the FOBT clinical trials that demonstrated reduction in mortality through colorectal cancer screening.

Existing techniques for CRC screening generally fall into the following three categories:

Endoscopic techniques:

- Optical colonoscopy
- Flexible sigmoidoscopy (FS)

Stool-based techniques:

- Fecal occult blood test (FOBT)
- Fecal Immunological Test (FIT)
- Fecal DNA testing

Imaging techniques:

- Virtual colonoscopy techniques using:
  a) Computed tomographic colonography (CT colonography)
  b) Magnetic resonance colonography (MR colonography)
- Wireless capsule endoscopy (PillCam Colon)
- Double-contrast barium enema (DCBE)

CT Colonography Technique

CT colonography, which uses computed tomographic data to acquire images of the colon, falls under the umbrella of 'virtual colonoscopy', which also includes MR colonography. It's a relatively new technique that uses a helical (spiral) CT scanner and specialized software to generate a continuous image of the entire colon for the identification of colonic cancers and polyps.

The success of the technique depends on a number of factors such as the CT scanning parameters, colonic preparation, colonic distension, the software package used, the image viewing method, and the interpretive approach. These factors cannot compensate for one another and, therefore, failure in any of these can lead to poor results. Imaging via CT colonography is a stepwise process consisting of a prescan, scanning and image acquisition, and image processing and viewing (as detailed below).

Prescanning

Patient preparation for CT colonography is more or less identical to preparation for conventional colonoscopy. The CT colonographic prescan is itself a sequential process consisting of four steps: bowel cleansing, administration of antispasmodics, administration of a contrast agent, and air insufflation.

Bowel Cleansing

A meticulous cleansing of the bowel is required for optimal results during colonography. Retained fecal matter or fluid can lead to significant perceptual errors. Sodium phosphate is commonly used in a standard laxative preparation and is generally well tolerated in adults without known or suspected renal or cardiac insufficiency, or elderly patients taking angiotensin-converting enzyme inhibitors for treatment of hypertension. (18) For nearly all patients in whom sodium phosphate is contraindicated, magnesium citrate is an acceptable substitute. For severely compromised patients who cannot tolerate even moderate fluid or electrolyte shifts, polyethylene glycol can be used. This preparation is, however, associated with poorest compliance because of its consistency and large volume. (18)

Administration of Antispasmodics

Prior to scanning, the patient is asked to empty the bowels to ensure that the rectum contains as little fluid as possible and then a spasmolytic agent may be administered. Antispasmodic medications help to maximize colonic distension, reduce colonic movement, and improve patient comfort.

Butylscopolamine (Buscopan®) is widely used in barium enema studies and has been shown to significantly improve bowel distension in CT colonography. Since the effect of IV Buscopan lasts about 15 min, the injection should be given just before insufflation to allow enough time to acquire images in both the supine and prone position. (19) It should be used with caution in patients with a history of cardiac events, due to its antimuscarinic effects. Buscopan is contraindicated in patients with angle-closure glaucoma. Glucagon (GlucaGen®) can be used when Buscopan is contraindicated. (19)

Administration of Contrast Agent

Visualization of polyps is possible because of the high contrast between soft tissue and the air-filled colon. Studies have shown that the use of contrast materials improves the diagnostic accuracy of CT colonography in the detection of colorectal polyps and cancer by assisting radiologists in the interpretation of acquired images. (20;21) Orally ingested contrast materials include diluted barium sulphate for tagging any solid stool and iodinated contrast medium (diatrizoate) for opacification of luminal fluid. (18;22) Fecal tagging also reduces the need for bowel cleansing before CT colonography.

Several studies have investigated the feasibility of performing CT colonography without any bowel purgation (Prepless CT colonography). (23;24) Image analysis is performed after subtracting the high attenuation labelled stool from the colonic lumen using simple threshold or specific subtraction computer software. (22)

The use of intravenous iodinated contrast material may further help in the detection of local and distant metastases. Although their use is not advised in the asymptomatic colorectal screening population, there is argument for their use in symptomatic patients in whom detailed examination of extracolonic organs is often of clinical benefit. (19) Disadvantages of intravenous contrast materials include added cost, patient discomfort, and occasional adverse effects such as nephrotoxicity and anaphylactoid reactions.

Air Insufflation

Adequate colonic distension is crucial for high-quality images and a fundamental prerequisite for CT colonography. Prior to scanning, an enema tip is inserted into the rectum and air or pressure-controlled carbon dioxide is insufflated to the near maximum patient tolerance. The degree of distension can be assessed on the CT pilot view and the colon can be reinflated and reimaged. Patients should be informed that distension may result in feeling of cramping or bloating, which usually improves when they turn from the supine to the prone position. (19) Whether automated or manual insufflation is used, it is essential that those administering the gas into the patient's bowel are aware of the risk of colonic perforation. (19;25)

Scanning and Image Acquisition

Although most of the initial work on CT colonography was performed using single detector spiral CT, it is now generally accepted that high performance of CT colonography is achieved through the use of multi detector scanners that allow thin slice thickness and minimal movement artifact. (19) Today, much thinner beam collimation is used with 16- and 64-detector scanners. With the multi-detector CT scanners, the entire abdomen and pelvis can be scanned within one breath hold of as little as 20 to 30 seconds as multi-slice CT scanners are capable of scanning up to eight times faster than the single-slice CT scanners.

Patient Positioning

There is almost universal agreement that patients must be imaged in both supine and prone positions to maximize the distension of the dependent parts of the colon. The use of additional prone images improves the sensitivity of CT colonography for colorectal polyps by approximately 15%, primarily by improving distension in the rectosigmoid colon. (26) Generally, colonic segments that are located posteriorly, including the sigmoid and descending colon, show better distension with prone scanning, whereas the transverse colon, which is located anteriorly, shows better distension with supine scanning. Supine, followed by prone imaging, is the generally accepted sequence. (27)

Technical Parameters

The optimal settings for image acquisition aim to increase image quality and decrease both scanning time and radiation exposure. A smaller slice thickness improves image quality, a higher pitch[1] value decreases the scanning time, and a lower tube current reduces radiation exposure. (28) With 16 detector and 64 detector scanners, thinner submilimeter slice thickness is preferable. Scanning with a 64 detector scanner and a detector configuration of 64 x 0.6 mm, allows the entire abdomen to be scanned in about 6-7 s. (29)

The selected tube current and tube voltage determine the radiation dose. Higher tube current reduces image noise and thus improves sensitivity for visualization of soft tissues, in which the contrast is low.

[1] a parameter defined as the quotient between the table feed per rotation (*d*) and the slice thickness (*s*): $p = d/s$.

Generally, useful settings are a 120 kVp tube voltage and a 50-100 mAs tube current in each position. (29) A recent survey of different institutions performing CT colonography for colorectal cancer screening has shown that such institutions mostly use 16-64 detector scanners, collimation in the range of 0.6-1.25 mm, pitch of 0.5 or 0.75, tube current in the range of 10-100 mAs, and a tube voltage of 120 kVp. (30)

Image Processing and Viewing

Two-dimensional and Three-dimensional Viewing

Two-dimensional (2D) multiplanar images are oriented in an axial, coronal, sagittal, or oblique direction in relation to body anatomy. Three-dimensional (3D) fly through images are generated by a variety of computer algorithms. There is a consensus that combined 2D and 3D viewing (one as the primary and the other as problem solving) is the most accurate way of detecting and measuring polyps. (28) The use of 3D viewing without 2D may result in false positive findings due to residual stool, diverticuli, or the ileocecal valve. The radiologist has the choice between primary 2D versus primary 3D image interpretation.

Computer-aided Detection

Computer-aided detection (CAD) for CT colonography refers to a computerized scheme that automatically detects polyps and masses in the images and reveals their location. CAD assists the radiologist where many images need to be interpreted rapidly to find suspicious lesions in a population where the prevalence of polyp is low.

Exposure to Ionizing Radiation

CT scanning involves exposure to ionizing radiation. Ionizing radiation consists of high energy waves that can penetrate into the cells, ionize the atoms and moleculs, and produce free radicals that interact with nearby DNA. These series of events can cause damging effect in nearby tissues. In addition, resulting changes and mutations in DNA can lead to the development of cancer. The degree of damage is related to the amount of radiation the tissue has received.

Factors Affecting Radiation Dose in CT Scanning

In CT scanning, the radiation dose to the patient is a function of scan parameters including but not limited to the tube current, beam energy, the overlap between CT slices, and scanning time. Other factors such as the design of the scanner and patient size are also important factors that affect the radiation dose to the patient. With multi-slice scanners, the radiation dose is about 50% greater than with the single-slice, and scanning in both supine and prone position doubles the radiation dose to the patient.

Measures of Radiation Dose

A variety of measures have been used to describe the amount of radiation delivered by CT equipment, the most relevant measures to be effective dose, absorbed dose, and CT dose index (CTDI). (31) The effective dose is a quantity most relevant to the risk of cancer. The absorbed dose is the quantity that describes the effect of radiation in a tissue or organ and represents the amount of energy deposited per unit mass. The entrance skin dose is the dose absorbed by the skin and is proportional to the tube current, the length of exposure, and the square of the beam energy (kVp) used. The dose at any location is also inversely proportional to the square of the distance to the source (Inverse Square Law). (32) The organ dose refers to the dose absorbed by the organs during an imaging procedure. Organs which are more sensitive to radiation are thyroid, breasts, gonads, colon, and the lens of the eye. (32) The majority of the dose from a single scan is delivered to the thin volume of tissue exposed to the primary beam and tissues outside of this volume receive a dose from scattered radiation. (32)

Radiation Dose of CT Colonography

CT scanning involves the use of higher doses of radiation as compared to the other medical imaging procedures. For example, the effective dose for a typical plain-film chest X-ray is 0.02 mSv which is equivalent to the 2.4 days background radiation. The effective dose for a CT scan is 500 times higher than the dose used for a chest X-ray. A list of diagnostic procedures and associated doses posted on the United States Food and Drug Administration website is shown in Table 2.

Table 2: Radiation Dose Comparison

Procedure	Typical Effective Dose, mSv	Number of Chest X-rays (PA Film) for Equivalent Effective Dose†	Time for Equivalent Dose From Natural Background Radiation‡
Chest X-ray (PA film)	0.02	1	2.4 days
Skull X-ray	0.07	4	8.5 days
Lumbar spine	1.3	65	158 days
IV urogram	2.5	125	304 days
Upper GI	3	150	1 year
Barium enema	7	350	2.3 years
CT head	2	100	243 days
CT abdomen	10	500	3.3 years

CT refers to computed tomography; GI, gastrointestinal; IV, intravenous; mSv, millisieverts; PA, posterior-anterior.
†Based on the assumption of an average "effective dose" from chest X-ray (Posterior-anterior film) of 0.02 mSv.
‡Based on the assumption of an average "effective dose" from natural background radiation of 3 mSv per year in the United States.

Reproduced from: U.S.Food and Drug Administration. What are the radiation risks from CT? [Internet].[updated 2008; cited 2009 Jan 1]. Available from: http://www.fda.gov/Radiation-EmittingProducts/RadiationEmittingProductsandProcedures/MedicalImaging/MedicalX-Rays/ucm115329.htm

Currently, various professional organizations have differing image acquisition protocols for CT colonography. A survey of the research institutions investigating CT colonography showed that the median effective dose for CT colonography is significantly lower for screening than for daily practice protocol. (30) The median effective dose in 39 institutions for daily practice protocol was 9.1 mSv (range 2.8-22). The median effective dose for screening CT colonography was 5.6 mSv (range 2.6-14.7), which would be equal to 280 chest X-ray and 1.8 years background radiation.

Many authors have indicated that estimates of the effective dose from a diagnostic CT procedure can vary by a factor of 10 or more depending on the type of CT procedure, patient size, and the CT system and its operating technique. Thus the actual dose from a CT procedure could be two or three times larger or smaller than the estimate. (33)

Health Effects of x-Ray Radiation

Extensive information on the risk of radiation-induced cancer has been gained from long-term follow-up of several populations with radiation exposure. For example, studies conducted on Japanese atomic bomb survivors, persons exposed to radiation for medical reasons, persons working at nuclear plants, and medically exposed persons have greatly contributed to the current knowledge about the risk of radiation.

Among the supportive studies that show significant association between radiation dose and mortality from cancer is a 15-country collaborative cohort study (34), which provided direct estimates of cancer risk following protracted low doses of ionizing radiation in 407,391 nuclear industry workers. A significant association was found between radiation dose and all-cause mortality. The excess relative risk was mainly attributed to a dose related increase in all cancer mortality. Among 31 specific types of malignancies studied, a significant association was found for lung cancer.

Literature contains several reports of female populations being exposed to the ionizing radiation who developed breast cancer later in life. Examples of these studies are:

- Women who had multiple fluoroscopic examinations of the chest for the treatment of pulmonary tuberculosis (35-37)
- Women who received X-ray examinations in the treatment of scoliosis (38)
- Women who received radiation for treatment of acute postpartum mastitis (39)
- Women who had irradiation for the treatment of Hodgkin's disease (40)

Age at Exposure to Ionizing Radiation

The risk of radiation exposure is generally higher in younger compared to the older adults. Hancock et al. (41) have quantified the risk of breast cancer following exposure to ionizing radiation for treatment of Hodgkin's disease according to age at treatment and compared the risk with that in age and race matched general female population. The risk of developing breast cancer was four times higher in females in exposed group (RR, 4.1, 95% CI, 2.5-5.7). They showed that age at irradiation strongly influenced the risk; RR was 136 for women treated before 15 years of age (95% CI, 34–371). The risk of bereast cancer declined with age but remained significantly elevated in groups under 30 years old at the time of irradiation; for those 15-24, RR = 19 (95% CI = 10.3-32); for those 24-29, RR = 7 (95% CI = 3.2-14.4).

Risk of Radiation in Women

The potential for biological damage from radiation exposure is greater in women than in men. This issue is compounded by the fact that life expectancy is longer for women and may exceed the latent period of the carcinogenic effect of radiation.

The radiation dose received during CT colonography is about 50% higher for women than for men. For example, Macari et al. (42) calculated the effective dose for their study as 5.0 mSv for men and 7.8 mSv for women using WinDose software. In Thomeer's study, (43) the effective dose per patient was 7.03 mSv for men and 10.28 mSv for women. In women who undergo CT procedure, the skin of the breast is closer to the surface of the table and scanning in the prone position will expose the breasts to high amount of radiation. However, in CT colonography breasts are normally outside of the field of radiation if adequate shielding is provided to prevent scattered radiation. The ovaries unfortunately are exposed to X-ray radiation during the CT colonography since they are located in the pelvis area.

Literature Review of Effectiveness

Research Questions

1. What is the accuracy of CT colonography in the detection of CRCs and polyps in individuals 50 years of age and older compared with the gold standard optical colonoscopy?
2. How safe is the CT colonography in the context of CRC screening?

Primary Outcomes

- Detection of CRCs in patients 50 years of age and older
- Detection of colorectal polyps in patients 50 years of age and older

Methods

Outcome Measures

- Sensitivity for cancer detection.
- Per-patient sensitivity and specificity for large, medium, and small polyps
- Per-polyp sensitivity for large, medium, and small polyps

Inclusion Criteria

- Prospective studies comparing accuracy of CT colonography with optical colonoscopy (OC) for the detection of CRCs and polyps
- Studies comparing accuracy of CT colonography with the gold standard optical colonoscopy
- Studies reporting either per-patient or per-polyp sensitivities/specificities
- Studies reporting results in absolute numbers
- Studies including 20 or more patients

Exclusion Criteria

- Retrospective studies
- Studies on PET/CT colonography
- Studies of bodily areas other than the colon
- Studies addressing other diseases of the colon
- Studies addressing technical, educational, or other aspects of CT colonography
- Studies that did not report accuracy data

Data Extraction

The following data were extracted for analysis:

- Study characteristics
- Number of procedures completed
- Number of identified cancers
- Number of patients diagnosed with polyp(s) (separately for categories of polyp size)
- Number of individual polyps identified by CT colonography (separately for categories of polyp size)
- Technical parameters
- Image reviewing techniques
- The experience of the study radiologists

Data Analysis

Summary Receiver Operating Characteristic (SROC) methodology was used as a summary measure of the accuracy of CT colonography for identifying patients with different sizes of polyp. SROC curves and forest plots of sensitivities and specificities were produced using MetaDisc software. (44) Area under curve (AUC) and Index Q (a point on the curve where sensitivity equals specificity) were used as summary measures of the accuracy of CT colonography for the identification of patients with polyps of different size.

Pooled sensitivity and specificity and 95% CI, along with related forest plots, were constructed for per-polyp sensitivity for different size polyps. Pooled sensitivities were also used to demonstrate the accuracy of CT colonography for the identification of individual polyps of different size.

The cancer detection rate of CT colonography was calculated by dividing the total number of patients with CRC identified by CT colonography by the total number of patients with CRC identified by colonoscopy

Literature Search

A search of electronic databases including OVID MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, The Cochrane Library, and the International Agency for Health Technology Assessment (INAHTA/CRD) database was undertaken to identify relevant studies published from January 1, 2003, to January 30, 2008. The search was limited to English-language articles and human studies. The search strategy is detailed in Appendix 1. The literature search identified 620 citations, of which 38 met inclusion criteria. Retrospective studies, even large trial such as Kim et al. (45), were excluded from further analysis.

Two of the identified studies were community-based screening; one was an RCT (46) and one (47) was a prospective cohort study. However, the latter (47) was excluded from further analysis because the main objective of the study was participation and the sample size calculation was based on the hypothesis that a choice of tests increases participation rate in screening.

Since two studies on average risk people (48;49) became published after our search date, this report was updated in July 2009 to include the results of these studies.

Table 3 and 4 show the number of studies included in this report separately for the high risk and average risk people.

Table 3: Quality of Evidence of Included Studies*: High Risk People

Study Design	Level of Evidence	Number of Eligible Studies
Large RCT, systematic reviews of RCT	1	0
Large RCT unpublished but reported to an international scientific meeting	1(g)	0
Small RCT	2	0
Small RCT unpublished but reported to an international scientific meeting	2(g)	0
Non-RCT with contemporaneous controls (the same individual)	3a	37
Non-RCT with historical controls	3b	0
Non-RCT presented at international conference	3(g)	0
Surveillance (database or register)	4a	0
Case series (multisite)	4b	0
Case series (single site)	4c	0
Retrospective review, modeling	4d	0
Case series presented at international conference	4(g)	0

* RCT refers to randomized controlled trial; g indicates grey literature.

Table 4: Quality of Evidence of Included Studies*: Average Risk People

Study Design	Level of Evidence	Number of Eligible Studies
Large RCT, systematic reviews of RCT	1	0
Large RCT unpublished but reported to an international scientific meeting	1(g)	0
Small RCT	2	1
Small RCT unpublished but reported to an international scientific meeting	2(g)	0
Non-RCT with contemporaneous controls (the same individual)	3a	2
Non-RCT with historical controls	3b	0
Non-RCT presented at international conference	3(g)	0
Surveillance (database or register)	4a	0
Case series (multisite)	4b	0
Case series (single site)	4c	0
Retrospective review, modeling	4d	0
Case series presented at international conference	4(g)	0

* RCT refers to randomized controlled trial; g indicates grey literature.

Results of Literature Review

Trials Included in the Review

Thirty seven prospective cohort studies and one RCT in the literature search met the inclusion criteria. The 37 cohort studies originated from 16 different countries and comprised a total of 6,868 patients. These studies included mostly people at high risk of CRC. The study by Macari et al. (42) was the only one of the 37 to include people at average risk for CRC. Patients in this study had no colorectal symptoms; had negative FOBT; did not have family history of CRC in a first degree relative; had no prior history of colorectal polyp; and did not undergo prior colonoscopy, sigmoidoscopy, or double contrast barium enema. However, the results of the study by Macari et al. were not analyzed with other three studies on average risk people (which were more recent) because this study was conducted in 2001/2002 and prior to technical advancement of CT colonography.

The only RCT found through the literature search included people at average risk for CRC. In addition, two other studies on average risk people were identified after our search date; therefore, the results of the three studies on average risk people were analyzed separately.

Studies on Average Risk People

Three studies (46;48;49) were included in the analysis. One identified study (47) which was on average risk people was excluded from further analysis because the sample size calculation was based on the hypothesis that a choice of tests increases participation rate in screening. The study did not have sufficient power to detect differences in the yield between colonoscopy and CT colonography and detailed data for accuracy was not presented.

The Multicentre Australian Colorectal Neoplasia Screening Study (MACS)

A randomized comparative study conducted in Australia (46) compared participation rate, yield of advanced colorectal neoplasia, acceptability, and safety of 6 different screening strategies. It was hypothesized that providing a choice of screening test would significantly increase the participation rate. The study was planned to have a power of 80% based on a conventional 5% level of significance.

To be eligible for CRC screening, participants needed to be asymptomatic and at average risk for CRC. Participants with symptoms or strong family history of CRC were excluded. Exclusion criteria were:

- Having a single first degree relative under 55 years of age
- Two relatives of any age with bowel cancer
- Personal history of colorectal neoplasia
- Change in bowel habit
- Rectal bleeding
- Unexplained weight loss within last 12 months
- Colonoscopy, FS, or barium enema within the preceding 5 years
- FOBT within last 12 months
- Other serious comorbidities
- Inability to speak English

The study population was restricted to two age groups (50-54 years and 65-69 years). Sample groups were allocated by random number generation. A total of 1,679 people aged 50–54 or 65–69 years were randomly selected from the electoral roll in metropolitan Perth, Adelaide, and Melbourne. Invitation letters were sent to these people, and a total of 1,333 people were considered eligible. Sixty-eight percent responded to the first, and 32% to the second invitation letter. Overall, 278 were screened (Participation rate: 20.9%; 95% CI, 18.7%–23.1%).

Participants were not aware that there were other screening groups and were allocated to one of the six groups:

- Fecal immunochemical test (FIT)
- FIT negative & flexible sigmoidoscopy (FS)
- CT colonography (CTC)
- Optical colonoscopy (OC)
- A choice of these tests with FOBT kit mailed with the letter of invitation
- A choice of these tests with no FOBT kit but mailed upon request

Participants in whom FOBT result was positive were referred for colonoscopy and those with a negative FOBT were referred for FS after an enema preparation. Polyps identified through FS were biopsied and the screening test results were considered positive if any adenoma was present. Positive results in FS led to OC being recommended.

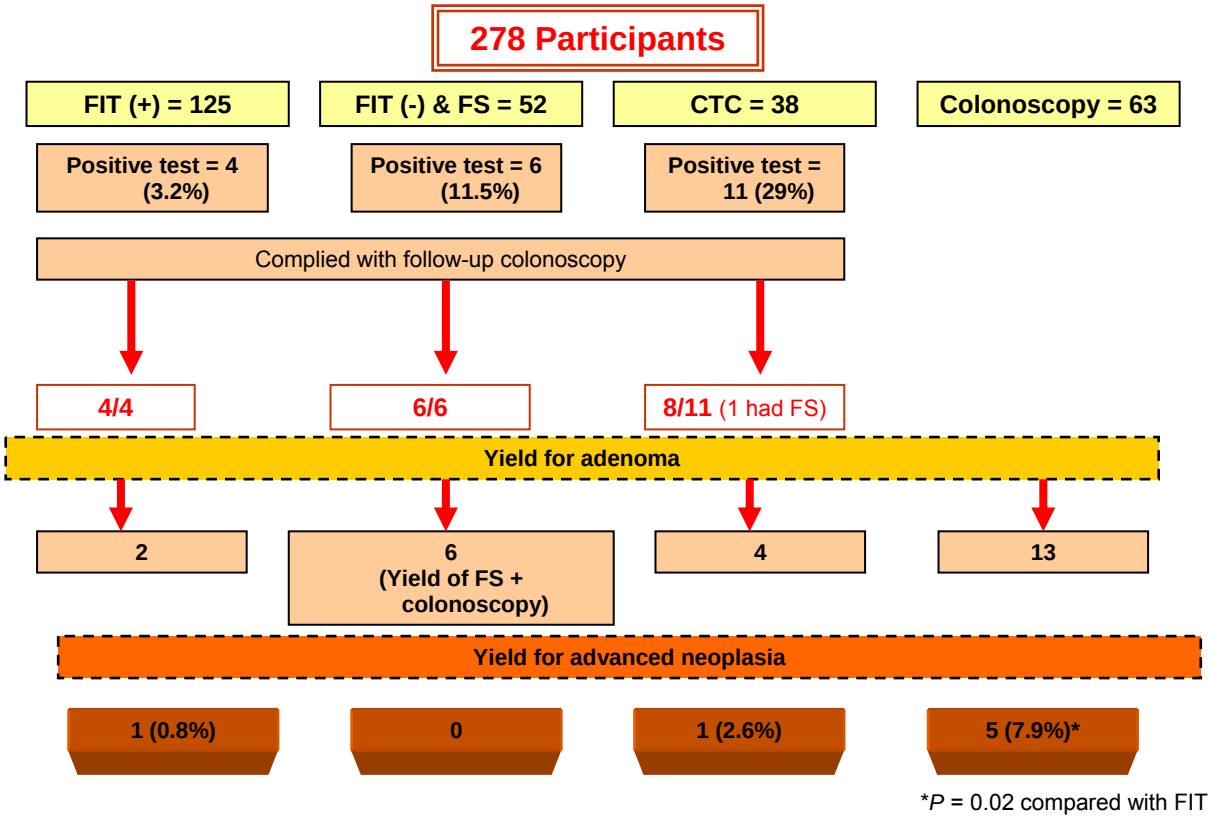
CT colonography was performed with a standard bowel preparation and same-day colonoscopy was provisionally booked. All participants with a positive CT colonography result underwent colonoscopy with the exception of 3 of 11 people. The total radiation dose was less than 5 mSv per person and examinations were performed by experienced radiologists who had performed more than 50 CT colonography examinations. Detection of any polyp > 5 mm or two or more polyps of any size led to colonoscopy being recommended.

All colonoscopies were performed by a gastroenterologist. Of 112 people undergoing colonoscopy either as primary screening or follow-up procedure), complete colonoscopy was achieved in 110 (98%).

Participants in FS, colonoscopy, and computed tomographic colonography were also given a questionnaire to evaluate 5 variables (perception of pain, tolerance, satisfaction, embarrassment, and readiness to have a repeat test).

Advanced neoplasia was defined as any adenoma larger than 10 mm in diameter, presence of villous histology, high-grade dysplasia, or cancer. The yield of advanced colorectal neoplasia was calculated as the number of participants with 1 or more such lesions per 100 people screened.

The results showed that the highest yield for advanced neoplasia was in participants having colonoscopy (7.9%). Yield of advanced neoplasis was 2.6% in CTC and 0.8% in the FIT group. The yield of advanced neoplasia was significantly higher in colonoscopy arm compared to FIT (P = .02). (see Figure 5)



CTC refers to computed tomographic colonography; FIT, fecal immunochemical test; FS, flexible sigmoidoscopy.

Figure 5: The Multicentre Australian Colorectal Neoplasia Screening (MACS) Study

The participation rate was calculated as the number of participants divided by the total number of eligible people. Participation in screening by FOBT/FS was defined as completion of the screening strategy. Participation was highest in screening by FOBT (64/234 [27.4%]). Participation for other screening strategies compared with FOBT was as follows: FOBT/FS 31/224 (13.7%; $P < .001$), CTC 35/215 (16.3%; $P = .005$), colonoscopy 38/214 (17.8%; $P = .02$), choice of test with FOBT kit 42/226 (18.6%; $P = .03$), choice of test without FOBT kit 50/220 (22.7%; $P = .3$) (see Table 5).

Table 5: Participation Rate for Colorectal Cancer Screening

	Participation Rate, %	P†
FOBT	27.4	
FS & FOBT	13.7	<.001
CTC	16.3	.005
OC	17.8	.02
Choice of screening With FOBT kit:	18.6	.03
Choice of screening Without FOBT kit:	22.7	.3

CTC, computed tomographic colonography; FOBT, fecal occult blood test; FS, flexible sigmoidoscopy; †Compared with FOBT.

When a choice of screening was offered to people, most chose FOBT (66%) or colonoscopy (27%). However, preference for FOBT was less marked in the choice without FOBT kit group: FOBT (58%), colonoscopy (36%).

Visual analogue scores for pain, tolerance, satisfaction, embarrassment, and readiness to repeat the test showed that all tests were well accepted.

There were no episodes of bleeding, perforation, or other serious complications arising from screening.

American College of Radiology Imaging Network (ACRIN) Multicentre Study

Johnson et al. (48), conducted a large multicentre study in which 2,600 asymptomatic people 50 years of age and older were recruited through 15 clinical sites. Participants were those who were scheduled to undergo routine colonoscopy at the participating sites between February 2005 and December 2006. Patients were excluded if they had any of the following symptoms:

- Melena or hematochezia for more than one occasion in the previous 6 months
- Lower abdominal pain
- Inflammatory bowel disease
- Familial polyposis syndrome
- Anemia (a hemoglobin level of less than 10 g per deciliter)
- Colonoscopy in the preceding 5 years
- Positive FOBT
- A serious medical condition that increases the risk of colonoscopy

Patients underwent both CT colonography and colonoscopy. Complete CT examination and colonoscopy results were available for 2,531 (97%) participants. The majority of participants had no known risk factor for CRC other than the age. Nine percent of the participants had a first degree relative with a history of colorectal polyp or cancer, 1% had personal history of polyp or cancer and less than 1% had both. All others were considered to be at average risk for CRC. The mean age of the participants was 58.3 years and 48% were male.

The preparation for CT colonography included a standard method of bowel purgation and the use of fluid and stool tagging. All examinations were performed with multidetector scanners (64- slice: in 1,308, 40-slice in 83, and 16-slice in 1,140 people) in both supine and prone positioning. Images were acquired with collimation of 0.5-1 mm, 50 mAs effective dose and peak voltage of 120 kVp. Images were reconstructed to slice thickness of 1-1.25 mm with a reconstruction interval of 0.8 mm. Images were randomly read with the use of either primary 2D image display with 3D for problem solving (n=1280) or a primary 3D endoluminal fly through with 2D for problem solving (n=1,251). The radiologists made their interpretations without knowledge of colonoscopy results and were instructed to record only lesions measuring 5 mm or more.

Same day CT and colonoscopy examinations were performed in 99% of the participants. Each participating radiologist had experience of at least 500 CT colonography examination or had participated in specialized 1.5 day training session in CT colonography. In addition, they all were required to complete a qualifying examination in which they achieved a detection rate of 90% or more for polyps measuring 10 mm or more in a reference image set. Of 20 radiologists who initially met entry criteria, 15 with the highest scores were invited to participate in the study. All colonoscopy examinations were performed or

directly supervised by an experienced endoscopist without knowledge of CT colonography results. If a lesion 10 mm or more was detected by CT colonography but not by colonoscopy, patients were advised to undergo a second colonoscopy within 90 days. Endoscopists who were performing the second colonoscopy were aware of the results of CT colonography.

Ten of the 2,531 participants did not have colonoscopy data documented to the cecum because of previous resection. A total of 547 lesions measuring 5 mm or more were detected. There were 128 large adenomas (>= 10 mm) or carcinomas in 109 of the 2,531 participants (prevalence of 4.3%). Seven adenocarcinomas 10 mm or more in diameter were detected in 7 patients. Non-adenomatous lesions included hyperplastic polyps (n= 136), lipoma (n=7), or other types (n=30). A total of 2.4% of patients had a flat lesion (height/weight ratio <=50%)

The sensitivity, specificity, positive predictive value and negative predictive value were similar for participants at increased risk for CRC and for those at average risk of CRC. Sensitivity of CT colonography for detection of large polyps ranged from 67% to 100% among radiologists with 7 of 15 radiologists identifying all the patients with large lesions.

The pooled sensitivities for detection of large lesions were similar for primary 2D and primary 3D.

CT colonography missed a 10 mm cancer in the low rectum and this lesion was not visible on a second CT review (Sensitivity for cancer, 85.7%). Overall, CT colonography detected 90% of large and 78% of medium to large adenomas or cancers.

Table 6 shows sensitivity, specificity, and area under the ROC curve for detection of patients with large and medium to large adenomas and cancers. However, for detection of patients with large lesions (>= 9 mm) regardless of histological type the sensitivity, specificity and AUC were 87%±3.5%, 86%±2.2%, and 88%±2%. A specificity of 86% for large lesions translates to a false positive rate of 14%. The sensitivity of CT colonography for detection of adenomas/cancers is shown in Table 7.

Table 6: Sensitivity and Specificity of CT Colonography For Detection of Patients With Adenomas and Cancers

>= 9 mm			>=6 mm		
Sensitivity % (95% CI)	**Specificity % (95% CI)**	**AUC % (95% CI)**	**Sensitivity % (95% CI)**	**Specificity % (95% CI)**	**AUC % (95% CI)**
90 (83-96)	86 (81.7-90.2)	89 (85-93)	78 (71-85)	88 (84-92)	84 (81-88)

AUC, Area under curve

Table 7: Sensitivity of CT Colonography For Detection of Adenomas and Cancers

>9 mm	>=6 mm
82±0.04	70±0.05

A total of 30 lesions 10 mm or larger in 27 patients were detected by CT colonography but not by colonoscopy. Fifteen of these people with 18 lesions underwent a repeat colonoscopy and 5 of the 18 lesions were confirmed.

Three adverse events were reported by the study centres. One person developed severe nausea and vomiting after CT colonography which lasted less than 24 hours. Hematochezia occurred in one patient after snare polypectomy requiring 2 days hospitalization. Bacteremia with Escherichia coli occurred in one patient 24 hours after both procedures.

Extracolonic findings were observed in 1,670 people (66%) and 405 (16%) were deemed to require additional evaluation or urgent care. The findings were in the chest (27%), genitourinary tract (45%), GI tract (18%), and musculoskeletal system (3%).

Study Conducted in Germany

The study by Graser et al. (49) was a prospective trial designed to compare the performance characteristics of five different screening tests for detection of advanced colonic neoplasia in average risk people. In this study, five different screening tests including CT colonography, colonoscopy, flexible sigmoidoscopy, fecal immunochemical stool testing, and FOBT were compared in the same patients. The study was powered to detect a 10% difference in colonoscopy and CT colonography sensitivity for detection of polyps >5 mm.

Patients were eligible to enter the study if they were 50 years of age or older and free of symptoms of colonic diseases such as melena, hematochezia, diarrhea, abdominal pain, and changes in bowel habit. Exclusion criteria included:

- Prior colonoscopy within the last 5 years
- Positive family history of CRC (one first degree relative diagnosed with CRC before age 60 or two first degree relatives diagnosed with CRC at any age)
- Hereditary colorectal cancer syndromes
- Inflammatory bowel disease
- Body weight more than 150 kg
- Severe cardiovascular or pulmonary disease

The study did not report how the study population was recruited. It is reported that a total of 311 consecutively enrolled people 50-81 years of age (mean age 60.5), in which 171 were men, were included in the study. Four people had to be excluded because of withdrawal from the trial or incomplete colonoscopy. Each participant was sent a prepared package including instruction for stool sampling and medication for bowel preparation. Stool samples for FIT were available for 285 and FOBT slides were available for 276 people. Before initiation of bowel lavage, stool samples were taken on three consecutive days. Bowel preparation was based on a standard “wet prep” regimen. Oral iodinated contrast agent was added to the last bowel preparation regimen to tag residual fluid.

CT colonography examinations were performed on a 64-channel multidetector scanner at a collimation of 0.6 mm. Images were constructed using a slice thickness of 0.75 mm and 0.5 mm reconstruction increment. The tube voltage was 120 kVp and the tube current was 70 mAs in the supine and 30 mAs in the prone position.

All scans were reviewed by one of the three experienced radiologists who had read more than 300 CT colonography examinations prior to the study. A primary 3D image display with 2D for problem solving was used to review the images. Immediately after CT colonography, patients were transferred to endoscopy unit to undergo optical colonoscopy which was performed by one of six experienced gastroenterologists who had performed more than 1,000 colonoscopies before the start of the study. If desired, Disoprivan (propofol) was administered intravenously to provide sedation.

A technique known as "segmental unblinding" was used to allow the exact correlation of CT colonography and OC findings. Segmental unblinding was performed in cases in which a discrepancy between CT colonography and colonoscopy were found in the first-look colonoscopy. In the endoscopy unit, the report form containing CT colonography results was revealed to the endoscopist after withdrawal of the endoscope from each colonic segment and a second look of the respective segment had to be performed if the findings of the two techniques were discrepant in that segment.

No separate sigmoidoscopy procedure was performed and the results from endoscopic examination of rectum and sigmoid colon were used to show the performance of FS.

All polyps were resected or biopsied and sent for histopathological examination. Advanced colorectal neoplasia was defined as invasive cancer or advanced adenomas. Advanced adenoma was defined as a lesion of adenomatous histology that meets one of the following criteria: a size of 10 mm or larger, the presence of villous component of at least 25%, or the presence of high grade dysplasia.

Overall, 511 lesions were detected, of which, 418 were <=5 mm, 56 were 6-9 mm, and 37 were >9 mm. From all polyps detected, 221 (43.2%) were adenomatous and 290 (56.8%) were non-adenomatous. A total of 248 of these polyps (48.6%) were located within the reach of FS (78 adenomatous and 170 non-adenomatous). The study did not report on the results of segmental unblinding. However, from the data presented in Table 3, page 245 of the report, it seems that one adenoma 6-9 mm was missed by colonoscopy.

Table 8 shows the reported sensitivities for CT colonography and colonoscopy for detection of colonic adenomas.

Table 8: Sensitivity of CT Colonography and Optical Colonoscopy for Detection of Colonic Adenomas

	Sensitivity % (95% CI)			
	>9 mm	**6-9 mm**	**<=5 mm**	**All sizes**
OC	100 (89.4-100)	92.7 (80.1-98.5)	94.6 (89.6-97.6)	95.9 (92.4-98.1)
CTC	93.9 (79.8-99.3)	90.2 (76.9-97.3)	59.2 (50.8-67.2)	70.1 (63.8-76.1)

The prevalence of large adenomas (> 9 mm) in this study was 8.1% (25/307), twice of that in Johnson's study. This rate was also twice of that in another large study by Pickhardt et al. (9) in which only asymptomatic people were included. Therefore, the generalizability of the results of this study to the screening populations in which the prevalence of large adenomas are much lower is questionable.

In Graser's study, colonoscopy reached the highest sensitivities for detection of patients with adenomas (100% of patients with adenomas 10 mm or larger, 97.8% of patients with adenomas 6 mm or larger, and 97.3% of patients with adenomas of all size categories). CT colonography was the next most sensitive technique in identifying patients with adenomas (92% of patients with adenomas 10 mm or larger and 91.3% of patients with adenomas 6 mm or larger). Flexible sigmoidoscopy had a sensitivity of 68% and 67% for detection of patients with adenomas 10 mm or larger and 6 mm or larger respectively. Sensitivity and specificity of different screening tests and combination of tests for detection of patients with colonic adenomas are shown in Table 9.

Table 9: Sensitivity and Specificity of Screening Tests For Detection of Patients With Colonic Adenomas

	>9 mm		>=6 mm	
Test	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
OC	100 (86.3-100)	98.6 (96.4-99.6)	97.8 (88.5-99.9)	95.8 (92.6-97.9)
CTC	92 (74-99)	97.9 (95.4-99.2)	91.3 (79.2-97.6)	93.1 (89.3-95.9)
FS	68 (46.5-85.1)	99.6 (98-100)	67.4 (52-80.5)	98.9 (96.7-99.8)
FS+FIT	71.4 (47.8-88.7)	85.2 (80.4-89.3)	80 (64.4-90.9)	87.8 (83-91.6)
FS+FOBT	76.2 (52.8-91.8)	89.4 (85-92.9)	70 (53.5-83.4)	89.4 (84.8-93)
FIT	33.3 (14.6-57)	85.6 (80.8-89.6)	40 (24.9-56.7)	88.2 (83.4-91.9)
FOBT	23.8 (8.2-47.2)	89.8 (85.4-93.2)	17.5 (7.3-32.8)	89.8 (85.2-93.4)

This study also reported on detection of advanced neoplasia. Forty six advanced lesions were detected in 30 patients, from which, 33 were at least 10 mm, 6 were 6-9 mm, and 7 were 5 mm or smaller. The largest advanced lesion was a 57 mm stage 3 carcinoma of the transverse colon. This lesion was identified by CT colonography, colonoscopy, FIT, and FOBT. However it was not detected by FS because, it was out of reach of sigmoidoscope. Colonoscopy identified all advanced neoplasia while CT colonography missed one 16 mm, one 10 mm, and one 4 mm lesion with villous component. On a per patient basis, the patient with a 4 mm advanced lesion had also two other lesions 14 mm and 11 mm in size. Therefore, this patient would be detected by CT colonography for further investigation while the other two patients would have remained undetected.

Table 10 shows sensitivity of CT colonography and colonoscopy for detection of advanced neoplasia. Sensitivity of different screening tests for detection of patients with advanced neoplasia are shown in Figure 6.

Table 10: Sensitivity of CT Colonography For Detection of Advanced Neoplasia

Technique	Number/total number	Sensitivity, %
OC	46/46	100
CTC	43/46	93.5

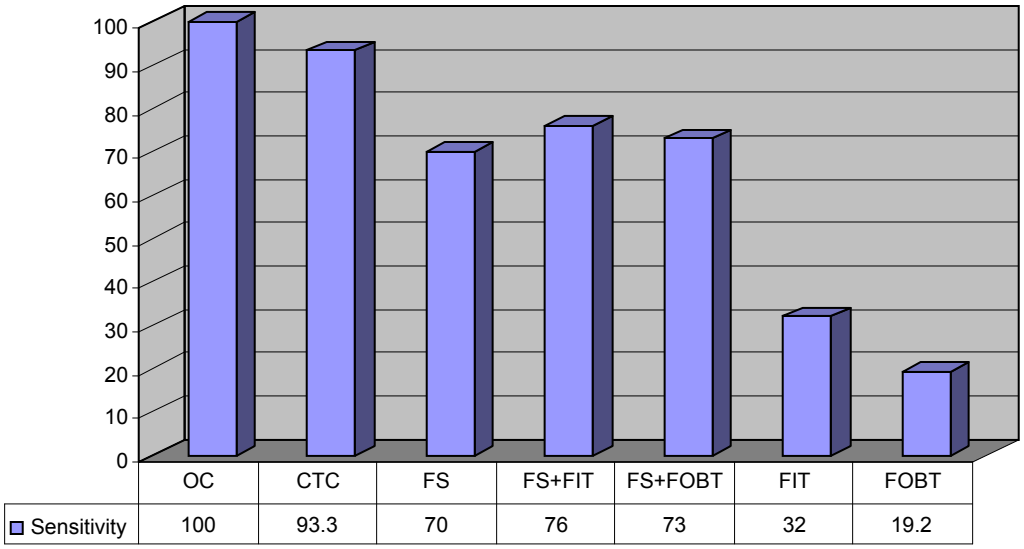


Figure 6: Sensitivity of Screening Tests for Detection of Patients with Advanced Naoplasia

In regards to radiation exposure, this study used low dose protocol and new dose modulation techniques. The mean radiation dose for CT colonography in this study was 4.5 (0.6) mSv (range 3.5-6.1 mSv). The supine scan contributed to a mean of 3.2 mSv and the prone scan to a mean of 1.3 mSv. The authors indicated that with dose modulation technique, they were able to maintain a high image quality even in the pelvis area, a region that is prone to image noise-induced artifacts in CT colonography.

Patients enrolled in this study also completed a questionnaire regarding their comfort level before and after CT colonography as well as after colonoscopy. A total of 256 people returned questionnaire from which, only 114 (44.5%) had received sedation for colonoscopy. Although no difference was found between CT colonography and colonoscopy for those who rated their comfort level as absent, very mild, or mild, the fact that sedation was not used for more than half of the colonoscopic examinations makes it difficult to make any judgment about the patient preference.

The study reported that there was no clinically relevant complication due to OC or CT colonography.

The reported specificity was based on the detection of adenomas; therefore, it is not an indicator of the proportion of false positive results of CT colonography.

Studies on High Risk People

Thirty seven studies reported the sensitivity and specificity of CT colonography for detection of colonic lesions. Table 11 shows study and patient characteristics. The inclusion/exclusion criteria of the prospective cohort studies on high risk people identified through the literature are summarized in a separate table in Appendix 2.

Table 11: Characteristics of the Studies on CT Colonography*

Study	Country	Patients	Gender Ratio M/F	Age, years, Mean (Range) or Mean ± SD	Segmental Unblinding/ Repeated Colonoscopy
Johnson et al., 2008 (24)	USA	114	76/38	65 (42–83)	VD
Taylor et al., 2008 (50)	UK	95 (89)†	39/50	64 (50–85)	SU
Johnson et al., 2007 (51)	USA	452	254/198	65 (41–82)	RC/VD
Arnesen et al., 2007 (52)	Denmark	231	130/101	60.2 (26–88)	SU
Graser et al., 2007 (53)	Germany	140	67/73	59 (50–77)	SU
Bose et al., 2007 (54)	UK	100 (90)†	37/63	63 (NR)	SU
Sallam et al., 2007 (55)	Poland	77	33/44	62 (NR)	No
Chaparro et al., 2007 (56)	Spain	50	26/24	62 (25–83)	SU
Reuterskiold et al., 2006 (57)	Sweden	111	66/45	66‡ (19–86)	VD
Kim et al., 2006 (58)	Korea	86	44/18	52.3 (26–68)	No
Yasumoto et al., 2006 (59)	Japan	50	37/13	64.8 (37–85)	No
Selcuk et al., 2006 (60)	Turkey	48	16/32	55 (27–83)	No
Karla et al., 2006 (61)	India	42	24/18	50‡ (10–84)	No
Juchems et al., 2006 (62)	Germany	21	9/12	58.1 (34–76)	No
Rockey et al., 2005 (63)	USA	614	428/186	57±10	SU
Arnesen et al., 2005 (64)	Denmark	100	61/39	61 (26–87)	VD/RC
Iannaccone et al., 2005 (65)	Italy	88	55/33	62.4 (50–70)	RC
Wessling et al., 2005 (66)	Germany	78	42/36	60.7 (NR)	No
Park et al., 2005 (67)	Korea	56	31/25	M: 60.2 (39–77) F: 56.8 (31–81)	No
Chung et al., 2005 (68)	Korea	51	32/19	63 (38–77)	No
Rottgen et al., 2005 (69)	Germany	48	22/26	57±21	No
Abdel Razek et al., 2005 (70)	Egypt	32	22/10	47 (10–74)	No
Cotton et al., 2004 (71)	USA	600§	270/330	61 ± 8.34	SU
Van Gelder et al., 2004 (72)	Netherlands	249	146 /103	56±13	RC
Iannaccone et al., 2004 (73)	Italy	203	141/62	60.5 (36–80)	SU
Cohnen et al., 2004 (74)	Germany	137	77/60	57.1±11.3	No
Hoppe et al., 2004 (75)	Switzerland	92	62/38	66 (20–91)	SU
Macari et al., 2004 (42)	USA	68	68/0	55 (50–67)	No
Pickhardt et al., 2003 (9)	USA	1233	728/505	57.8 (NR)	SU
Johnson et al., 2003 (76)	USA	703	442/261	64±7 (50–84)	VD
Pineau et al., 2003 (77)	USA	205	94/111	59.3 (38–83)	SU
Yee et al., 2003 (78)	USA	182	176/6	63 (37–88)	No
Iannaccone et al., 2003 (79)	Italy	158	88/70	M: 64 (52–80) F: 63 (48–80)	No
Thomeer et al., 2003 (43)	Belgium	150	88/62	58	No
Munikrishnan et al., 2003 (80)	UK	80	45/35	68‡ (29–83)	No
Ginnerup et al., 2003 (81)	Denmark	148	71/77	60 (25–86)	SU
Taylor et al., 2003 (82)	UK	54	22/32	69 ‡ (42–85)	SU

*F indicates female; M, male; NR, not reported; RC, repeated colonoscopy if necessary; SD, standard deviation; SU, segmental unblinding; VD, reviewed optical colonoscopy videotape if CT colonography revealed a convincing but previously unidentified lesion; †Number analyzed ‡Median age reported. §Sample size was estimated as 1,050 participants, but since recruitment was slower than expected, the study was stopped after 615 participants were enrolled

The gold standard in all the reviewed studies was colonoscopy. Due to the small risk of overlooking polyps at the initial colonoscopy, the technique of segmental unblinding was employed in many studies. In this technique, findings of CT colonography were revealed to the endoscopist after initial examination of each colonic segment. If a lesion was found at CT colonography but not at the initial colonoscopy, the endoscopist re-examined that segment to see whether the finding in CT colonography was a true positive or a false positive. The use of this trechnique led to additional true positive findings of CT colonography in some studies, increasing the sensitivity of CT colonography and decreasing the sensitivity of colonoscopy. Thirteen studies used the technique of segmental unblinding and in 7 studies, either the colonoscopy was repeated or the video images were reviewed again to identify the reason for discrepancy.

Three studies reported only on adenomatous polyps only (9;24;51); however, evidence shows that CT colonography has higher sensitivity for adenoma detection than for the detection of nonadenomatous polyps. This method may have thus resulted in a higher reported sensitivity for CT colonography. Table 12 shows sensitivity of CT colonography for all polyps versus adenomatous polyps only. (83)

Table 12: Comparison of Performance Characteristics of CT Colonography for Detection of All Polyps Versus Adenomatous Polyps

Lesion Size	Sensitivity for All Polyps, %	Sensitivity for Adenoma, %
≥10 mm	90.0	94.0
5–9 mm	80.1	82.0
<5 mm	59.1	66.9
Overall	69.7	77.5

Source: Yee et al., 2001. (83)

All but three of the studies performed CT colonography with dual positioning. Yasumoto et al. (59) and Cohnen et al. (74) performed CT scanning in the supine position only. In a study by Sallam et al. (55), the prone position was used only if bowel insufflation was incomplete. For a variety of reasons, colonoscopy was incomplete in the majority of studies (see Table 13). In most, the findings of patients who'd received an incomplete colonoscopy were compared between CT colonography and OC only in the segments of the colon that were visualized endoscopically.

The rate of incomplete colonoscopy was significantly higher in two studies. (60;61) In that by Karla et al., (61) the higher rate was due to occlusive cancers, and in the study by Celcuk et al., (60) the reasons for incomplete colonoscopy were poor patient tolerance, adhesion, occlusive carcinoma, and diverticulosis. In the latter study, however, colonic masses over 3 cm in diameter and those with mural thickening consistent with annular carcinoma were excluded from analysis. In the study by Park et al., (67) 40 patients in whom OC was incomplete were excluded from the analysis.

All the studies considered OC as the gold standard. If necessary, some studies also used the results of colonoscopy and additional information such as a review of clinical documentation (57), surgical and pathological findings (68), or results of additional tests (71). In addition, colonoscopy was performed on the same day as CT colonography in most studies. In a few, however, OC was performed a few days after CT colonography. In the study by Johnson et al. (24), barium sulphate was used as contrast agent and colonoscopy was performed within 7 days after CT colonography in 89% of the patients (range: 0–100 days). In the studies by Sallam et al. (55) and Rottgen et al. (69), OC was performed within 4 weeks after CT colonography.

Nine studies reported on extracolonic findings. (9;54;55;57;61;70;73;80;82)

Table 13: Percentages of Optical Colonoscopy and CT Colonography Completed*

Study	Optical Colonoscopy, %	CT Colonography, %
Johnson et al., 2008 (24)	96	NR
Taylor et al., 2008 (50)	89	100
Johnson et al., 2007 (51)	99	NR
Arnesen et al., 2007 (52)	100	100
Graser et al., 2007 (53)	100	NR
Bose et al., 2007 (54)	91	98
Sallam et al., 2007 (55)	NR	NR
Chaparro et al., 2007 (56)	100	100
Reuterskiold et al., 2006 (57)	91	NR
Kim et al., 2006 (58)	100	100
Yasumoto et al., 2006 (59)	100	100
Selcuk et al., 2006 (60)	65	NR
Karla et al., 2006 (61)	55	90
Juchems et al., 2006 (62)	NR	NR
Rockey et al., 2005 (63)	98.4	99.2
Arnesen et al., 2005 (64)	100	100
Iannaccone et al., 2005 (65)	94	100
Wessling et al., 2005 (66)	NR	NR
Park et al., 2005 (67)	100	100
Chung et al., 2005 (68)	78.5	NR
Rottgen et al., 2005 (69)	100	100
Abdel Razek et al., 2005 (70)	90.6	NR
Cotton et al., 2004 (71)	98.5	NR
Van Gelder et al., 2004 (72)	93	98
Iannaccone et al., 2004 (73)	96	100
Cohnen et al., 2004 (74)	100	100
Hoppe et al., 2004 (75)	94	99
Macari et al., 2004 (42)	100	100
Pickhardt et al., 2003 (9)	99.4	99.5
Johnson et al., 2003 (76)	98.2	NR
Pineau et al., 2003 (77)	100	100
Yee et al., 2003 (78)	100	100
Iannaccone et al., 2003 (79)	94.4	100
Thomeer et al., 2003 (43)	97	100
Munikrishnan et al., 2003 (80)	78	95
Ginnerup et al., 2003 (81)	91	76
Taylor et al., 2003 (82)	91	100

*NR indicates not reported.

Sensitivity of CT Colonography for Cancer Detection

A total of 225 cancers were found among 6,868 patients and, overall, CT colonography detected 94% of the cancers. The prevalence of cancer in these studies ranged from 0.2% to 43.8%. In some studies, the high prevalence of CRC led to a higher rate of incomplete colonoscopy. For example, in Karla et al. 2006 (61), 14 of 19 patients with incomplete colonoscopy had occlusive colonic lesions and in the study by Chung et al. (68) OC could not be used to explore the entire colon of 11.5% of the patients because of the presence of CRCs. Table 14 shows the number and percentages of cancers detected by CT colonography.

Table 14: Number of Cancers Detected by CT Colonography*

Study	Patients	Patients With Cancer	Prevalence of Cancer (%)	Cancers Detected by CTC, No. (%)
Johnson et al., 2008 (24)	114	0	0	0 (N/A)
Taylor et al., 2008 (50)	95	2	2.1	2 (100)
Johnson et al., 2007 (51)	452	5	1.1	5 (100)
Arnesen et al., 2007 (52)	231	5	2.2	4 (80)
Graser et al., 2007 (53)	140	0	0	0 (N/A)
Bose et al., 2007 (54)	100	3	3	3 (100)
Sallam et al., 2007 (55)	77	13	16.9	13 (100)
Chaparro et al., 2007 (56)	50	4	8	3 (75)
Reuterskiold et al., 2006 (57)	111	10	9	10 (100)
Kim et al., 2006 (58)	86	1	1.2	NR (NR)
Yasumoto et al., 2006 (59)	50	0	0	0 (N/A)
Selcuk et al., 2006 (60)	48	2	4.2	2 (100)
Karla et al., 2006 (61)	42	18	42.9	18 (100)
Juchems et al., 2006 (62)	21	1	4.8	1 (100)
Rockey et al., 2005 (63)	614	9	1.5	7 (78)
Arnesen et al., 2005 (64)	100	1	1	0 (0)
Iannaccone et al., 2005 (65)	88	5	5.6	NR (NR)
Wessling et al., 2005 (66)	78	3	3.8	3 (100)
Park et al., 2005 (67)	56	5	8.9	3 (60)
Chung et al., 2005 (68)	51	21	41.2	21 (100)
Rottgen et al., 2005 (69)	48	0	0	0 (N/A)
Abdel Razek et al., 2005 (70)	32	14	43.8	14 (100)
Cotton et al., 2004 (71)	600	8	1.3	6 (75)
Van Gelder et al., 2004 (72)	249	0	0	0 (N/A)
Iannaccone et al., 2004 (73)	203	0	0	0 (N/A)
Cohnen et al., 2004 (74)	137	0	0	0 (N/A)
Hoppe et al., 2004 (75)	92	8	8.7	7 (87.5)
Macari et al., 2004 (42)	68	0	0	0 (N/A)
Pickhardt et al., 2003 (9)	1233	2	0.2	2 (100)
Johnson et al., 2003 (76)	703	3	0.4	NR (NR)
Pineau et al., 2003 (77)	205	10	4.9	NR (NR)
Yee et al., 2003 (78)	182	0	0	0 (N/A)
Iannaccone et al., 2003 (79)	158	22	13.9	22 (100)
Thomeer et al., 2003 (43)	150	7	4.7	NR (NR)
Munikrishnan et al., 2003 (80)	80	29	36.3	28 (96.6)
Ginnerup et al., 2003 (81)	148	11	7.4	11 (100)
Taylor et al., 2003 (82)	54	6	11.1	5 (83)
Total	**6868**	**228**	**N/A**	**190 (94)**

*NR indicates not reported; N/A, not applicable

Sensitivity for Polyp Detection

Studies reported separately for lesions ≥10 mm, 6–9 mm, and ≤5 mm, as well as for a combination of these categories with slight variances in cut-off threshold. Therefore, in our review, the three categories of large, medium, and small were used for identified polyps. Where sufficient data was available, additional size categories were calculated (e.g. for medium to large size or all size polyps) by grouping other size categories if such were not reported.

It is generally agreed that polyps ≤5 mm have a very low likelihood of malignancy, to the extent that some investigators ignored documenting polyps ≤5 mm. The significance of polyps 6–9 mm has generated debate not only because sensitivity and specificity are affected, but also because the interval at which the examination should be repeated will change. For the sake of completeness, all types of polyps were included in this study. In terms of pathology, most of the studies reported polyps regardless of their nature, while three studies reported adenomatous polyps only (9;24;51) and two studies reported lesions (cancer and/or polyp) (71;77).

CT colonography results were analyzed in two different ways, a) identification of patient(s) with polyps, or b) the identification of individual polyps. From a screening perspective, focusing the analysis on per-patient data is more important than per-polyp data. While per-polyp data emphasizes the ability of CT colonography to identify colonic lesions, per-patient data emphasizes the utility of CT colonography as a screening tool.

Sensitivity and Specificity of CT Colonography for Identifying Patients with Polyps

For per-patient analysis, only studies that reported both sensitivity and specificity were included in the analysis. Further, for the economic evaluation and cost effectiveness analysis, it is reasonable to consider the accuracy of CT colonography reported as per-patient rather than per-polyp.

Per-patient sensitivity for CT colonography varied from 48% to 100% for large polyps, from 30% to 81% for medium polyps, and from 6% to 91% for small polyps. Per-patient specificity for CT colonography was more homogenous across studies being 92% to 100% for large polyps, 80% to 95% for medium polyps, and 86% to 100% for small polyps. Details of the sensitivity and specificity of CT colonography for the identification of patients with polyps of different size, by study, can be found in Appendix 3.

Summary Receiver Operating Characteristic

A meta-analysis using SROC methodology was conducted to summarize the results of the studies on the performance of CT colonography. The SROC method was developed by Moses et al. through a logistic transformation and linear regression of diagnostic accuracy data. (84) With diagnostic technology, the threshold for a positive test varies in different studies and the trade-off between sensitivity and specificity is often not well defined. Therefore, the full picture of the test accuracy cannot be obtained, giving rise to uncertainty in the value of the test. These problems can be resolved through logistic regression.

First the true positive rate (TPR) and false positive rate (FPR) are transformed into their corresponding logits. The logit of the true positive rate is a natural log of TPR/(1 − TPR), and the logit of the false positive rate is the natural log of FPR/(1 − FPR). The parameters of D and S, defined as the difference of the logits or the sum of the logits, are then calculated. By converting the TPR and FPR from each study to their logistic transform and plotting the sum and differences of the logistic transforms, one generates a curve and fits a linear model. The ideal position of a SROC curve on a SROC space is near the upper left corner, which would indicate a perfect test or a perfect technique in differentiating diseased and nondiseased individuals. In a SROC curve, studies appear in the SROC space as a set of points and the SROC curve is fitted through them. (85)

The area under curve (AUC) has been proposed as a summary measure of the overall performance of the test. A perfect test would have an AUC=1, whereas a completely random test would have an AUC of 0.5. Index Q is another method to summarize the accuracy data. The index Q corresponds to the point on the curve in which sensitivity equals specificity. The SE (AUC) is the standard error of the AUC and SE (Q) is the standard error of the Index Q.

Table 15 summarizes results of SROC analysis for CT colonography for detecting polyps of different sizes. Since many studies did nor report on per-patient sensitivity and specificity for small polyps, an SROC could not be constructed for this size category. Figures 7 to 10 show the resulting SROC curves for the different polyp sizes along with 95% CIs and related data points.

Table 15: Area Under Curve and Index Q for Detecting Patients with Different Size Polyps*

Polyp size	AUC	SE (AUC)	Index Q	SE (Index Q)
Large	0.9816	0.0068	0.9403	0.0133
Medium	0.8937	0.0372	0.8246	0.0390
Large & medium	0.8883	0.0210	0.8189	0.0216
All sizes	0.8139	0.0599	0.7481	0.0534

*All values generated SROC curves; AUC, area under curve; SE, standard error.

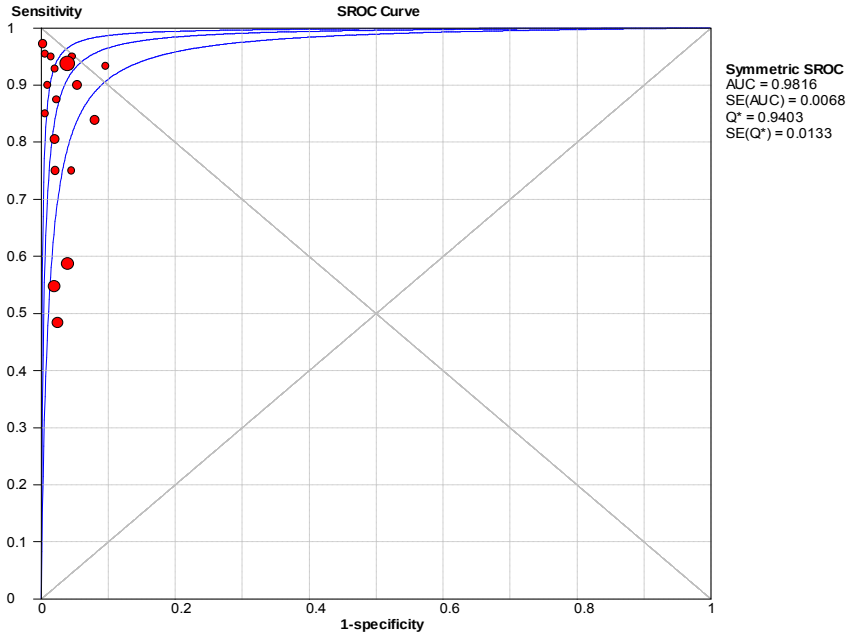


Figure 7: SROC Curve for Detecting Patients with Large-Size Polyps

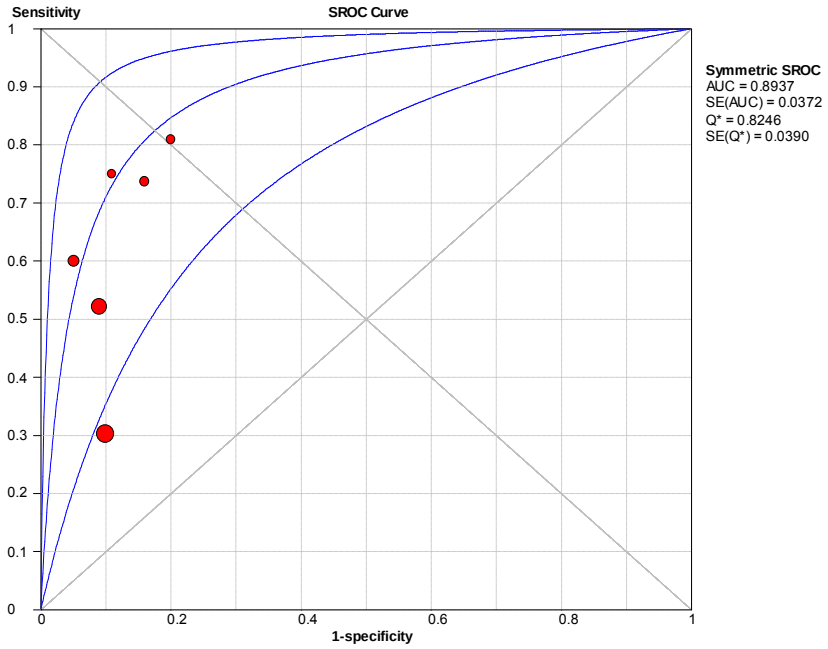


Figure 8: SROC Curve for Detecting Patients with Medium Polyps

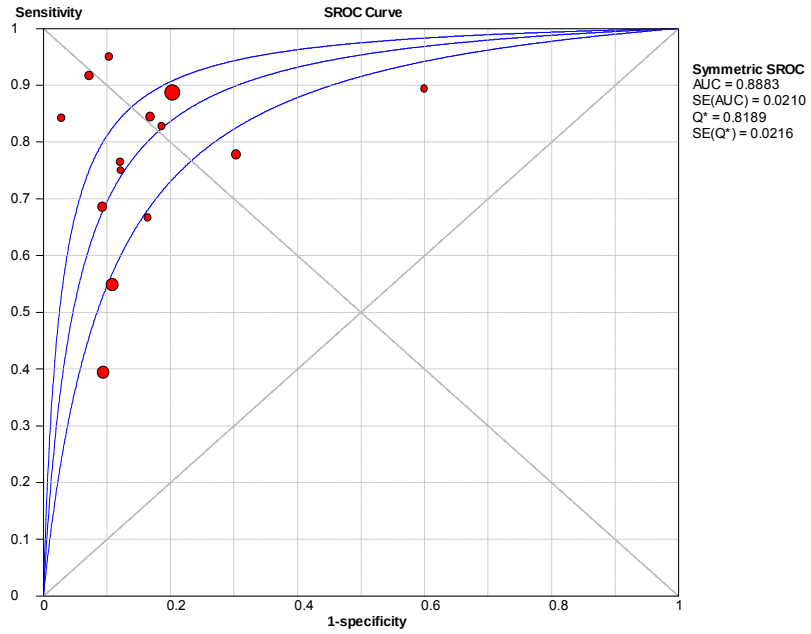


Figure 9: SROC Curve for Detecting Patients with Medium- to Large Polyps

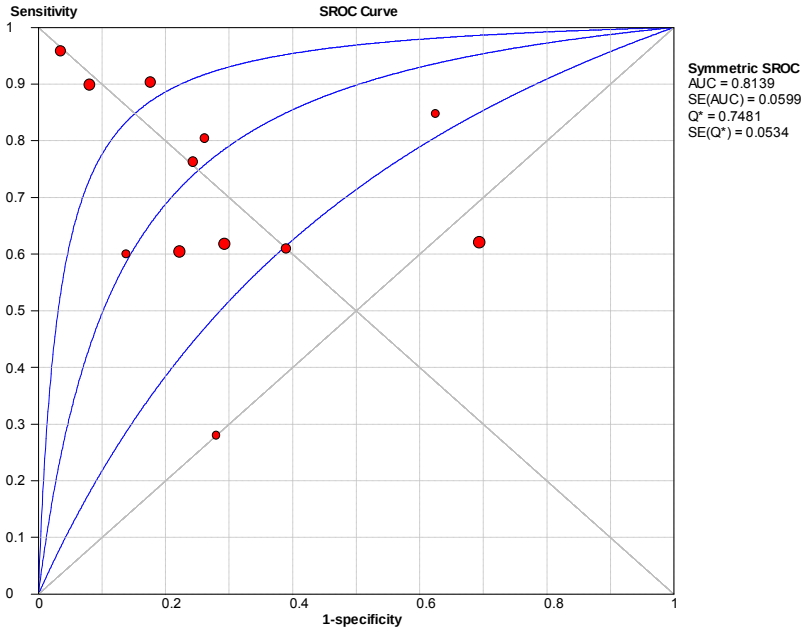


Figure 10: SROC Curve for Detecting Patients with Polyps of Any Size

As can be seen in Figures 7 to 9, the AUC and index Q increased with increasing polyp size. Excluding the three studies that did not use standard bowel preparation did not affect the SROC curve for patients who had medium to large polyps (AUC=0.8860).

Studies in which there was a high prevalence of cancer did not report per-patient data; therefore, the studies contributing to the SROC exhibited a prevalence of cancer between 0% and 11%. Studies contributing to the SROC for medium to large polyps exhibited a prevalence of between 0% and 8%.

Overall, the performance of CT colonography in the identification of large polyps was excellent. The SROC curve was located close to the top left corner and AUC was 0.98% (SE, 0.01); however, studies were heterogeneous in per-patient sensitivity (Figure 11). In contrast, per-patient specificity was more homogenous among the studies (Figure 12). Forest plots showed that per-patient pooled sensitivity and specificity were 79% and 97%, respectively (Figures 11–12). The higher, homogenous specificity contributed greatly toward a higher AUC value on the SROC curve.

Figures 13 and 14 display the sensitivity and specificity of CT colonography, respectively, for the detection of medium to large polyps.

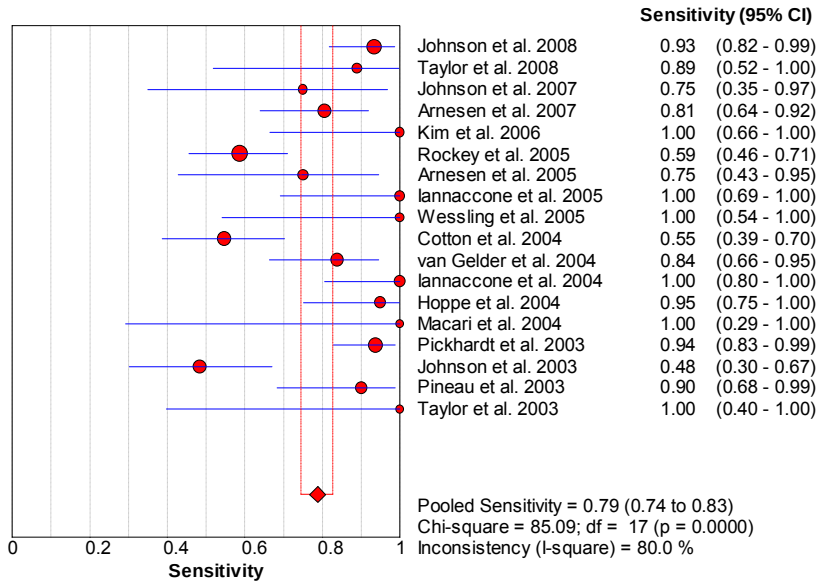


Figure 11: Sensitivity of CT Colonography for Detecting Patients with Large Polyps

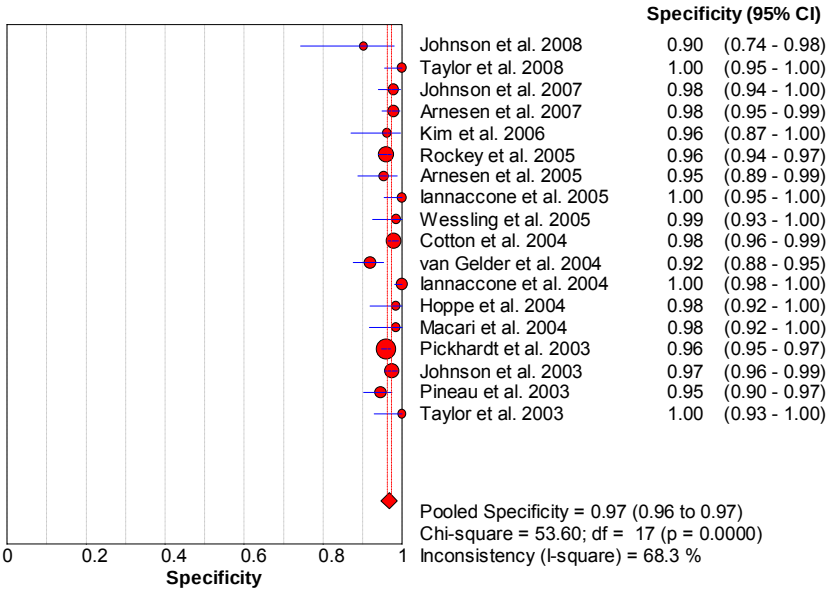


Figure 12: Specificity of CT Colonography for Detecting Patients with Large Polyps

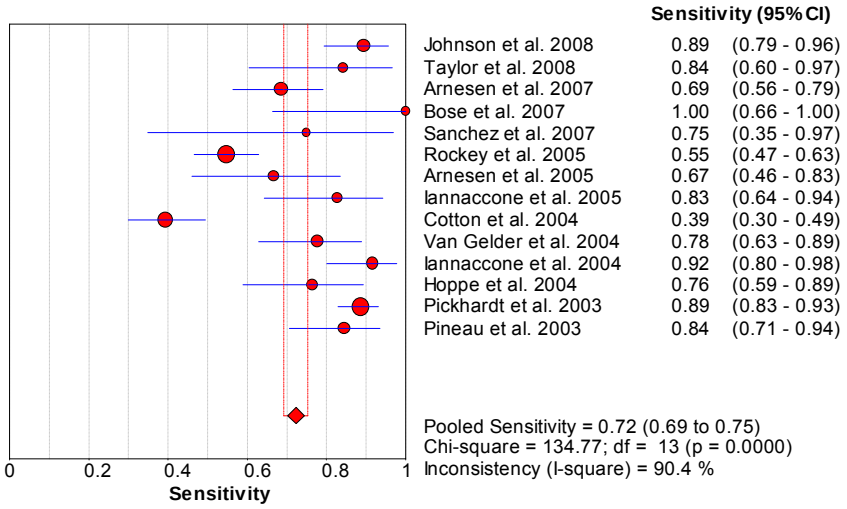


Figure 13: Sensitivity of CT Colonography for Detecting Patients with Medium to Large Polyps

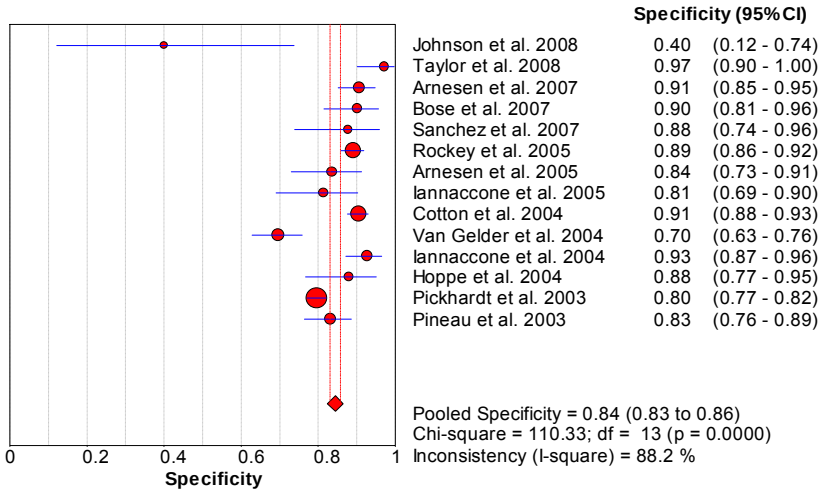


Figure 14: Specificity of CT Colonography for Detecting Patients With Medium to Large Polyps

Sensitivity of CT Colonography for Detection of Individual Polyps

Per-polyp sensitivity for CT colonography varied from 46% to 100% for large polyps, from 23% to 97% for medium polyps, and from 8% to 82% for small polyps. Pooled sensitivity for detection of different size of polyps was:

- Large polyps: 79% (95% CI, 75%–82%)
- Medium to large polyps: 71% (95% CI, 69%–73%)
- Medium polyps: 63% (95% CI, 60%–66%), and
- Small polyps: 35% (95% CI, 33%–37%).

Details of the sensitivity of CT colonography for the identification of polyps of different size are supplied in Appendix 4. Pooled sensitivity of CT colonography for detection of different size polyps and the related forest plots can be found in Appendix 5.

Heterogeneity of Reported Sensitivities

We found several technical variations as potential sources for heterogeneity among the reported sensitivities, specifically the viewing parameters, image acquisition parameters, and the use of a contrast agent.

Viewing Parameters

Since controversy exists about the best image display for accurate interpretation, we analyzed data separately for primary 2D versus primary 3D image display techniques and found that the sensitivity of CT colonography was nearly equal between studies employing a primary 2D image display with 3D for problem solving and those using a primary 3D endolunial fly through with 2D for problem solving. Table 16 shows different viewing methods used in these studies.

One of the parameters that resulted in higher reported sensitivity was the method of image reviewing. Sensitivity increased when images were reviewed in both antegrade and retrograde fashion. Figures 15 to 20 show sensitivity of CT colonography for identifying polyps of different size for studies that did and did not perform both antegrade and retrograde viewing.

Table 16: CT Colonography Studies: Viewing Parameters

Study	Antegrade and Retrograde Viewing	Modes Primary Viewing (Problem Solving)†
Johnson et al., 2008 (24)	No	2D
Taylor et al., 2008 (50)	No	2D (3D)
Johnson et al., 2007 (51)	No	2D (3D) or 3D virtual dissection (2D)
Arnesen et al., 2007 (52)	No	2D (3D)
Graser et al., 2007 (53)	No	3D (2D)
Bose et al., 2007 (54)	No	3D (2D)
Sallam et al., 2007 (55)	No	2D & 3D
Chaparro et al., 2007 (56)	No	2D (3D)
Reuterskiold et al., 2006 (57)	No	NR
Kim et al., 2006 (58)	No	2D (3D)
Yasumoto et al., 2006 (59)	Yes	3D (2D)
Selcuk et al., 2006 (60)	Yes	2D & 3D
Karla et al., 2006 (61)	Yes	2D & 3D
Juchems et al., 2006 (62)	Yes	3D & colon dissection
Rockey et al., 2005 (63)	No	2D (3D)
Arnesen et al., 2005 (64)	No	2D & 3D
Iannaccone et al., 2005 (65)	No	2D (3D)
Wessling et al., 2005 (66)	No	2D (3D)
Park et al., 2005 (67)	No	2D (3D)
Chung et al., 2005 (68)	Yes	2D (3D)
Rottgen et al., 2005 (69)	No	2D & 3D
Abdel Razek et al., 2005 (70)	Yes	2D & 3D
Cotton et al., 2004 (71)	No	2D (3D)
Van Gelder et al., 2004 (72)	No	3D (2D)
Iannaccone et al., 2004 (73)	No	2D (3D)
Cohnen et al., 2004 (74)	No	2D & 3D
Hoppe et al., 2004 (75)	No	2D & 3D
Macari et al., 2004 (42)	No	2D (3D)
Pickhardt et al., 2003 (9)	No	3D (2D)
Johnson et al., 2003 (76)	Yes	2D (3D)
Pineau et al., 2003 (77)	No	2D & selective 3D
Yee et al., 2003 (78)	Yes	2D & 3D
Iannaccone et al., 2003 (79)	No	2D (3D)
Thomeer et al., 2003 (43)	No	2D (3D)
Munikrishnan et al., 2003 (80)	No	2D (3D)
Ginnerup et al., 2003 (81)	No	2D (3D)
Taylor et al., 2003 (82)	No	2D (3D)

†The primary mode, either 2D or 3D, was used for initial viewing, while some investigators used an alternative mode when interpreting ambiguous results.

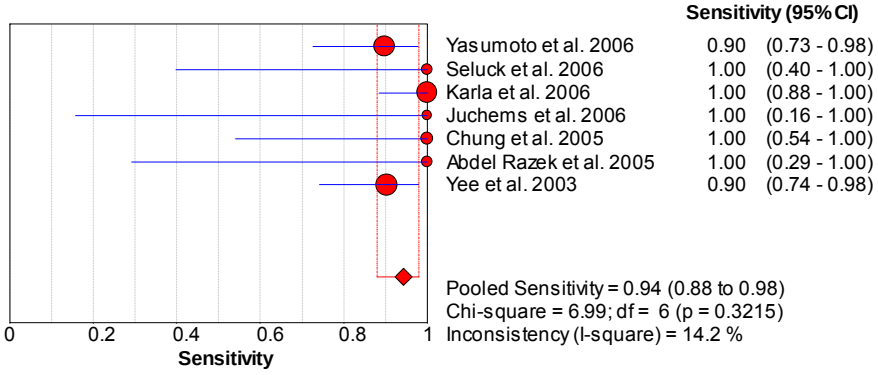


Figure 15: Sensitivity of CT Colonography for the Detection Large Polyps – Studies Performing Antegrade/Retrograde Viewing

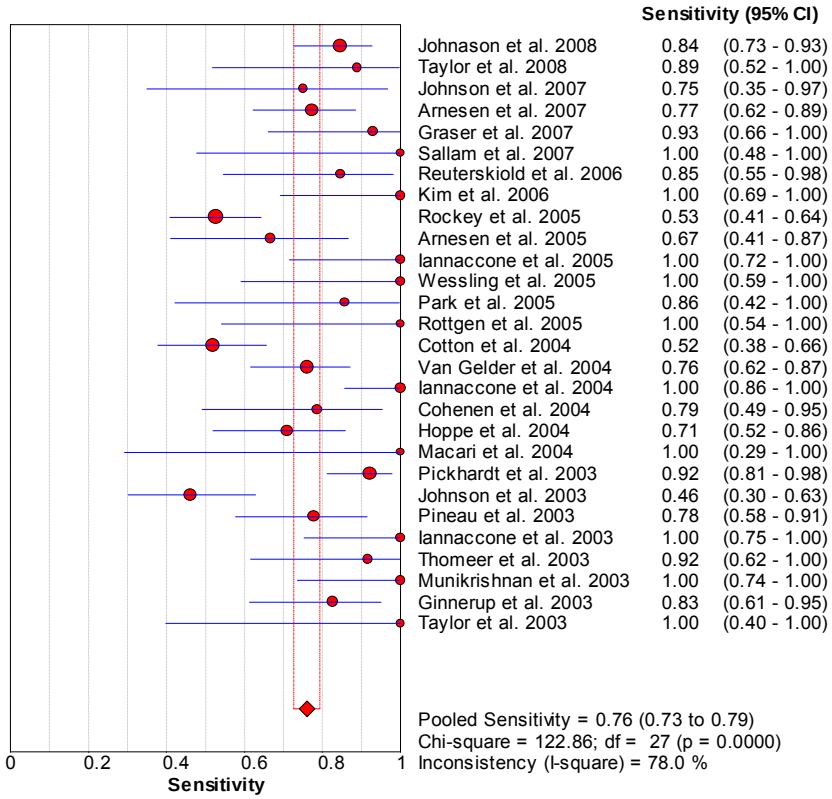


Figure 16: Sensitivity of CT Colonography for the Detection of Large Polyps – Studies Not Performing Antegrade/Retrograde Viewing

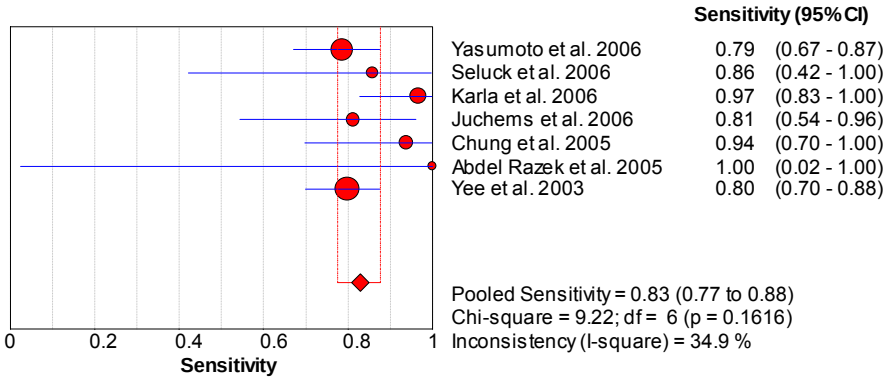


Figure 17: Sensitivity of CT Colonography for the Detection of Medium Polyps – Studies Performing Antegrade/Retrograde Viewing

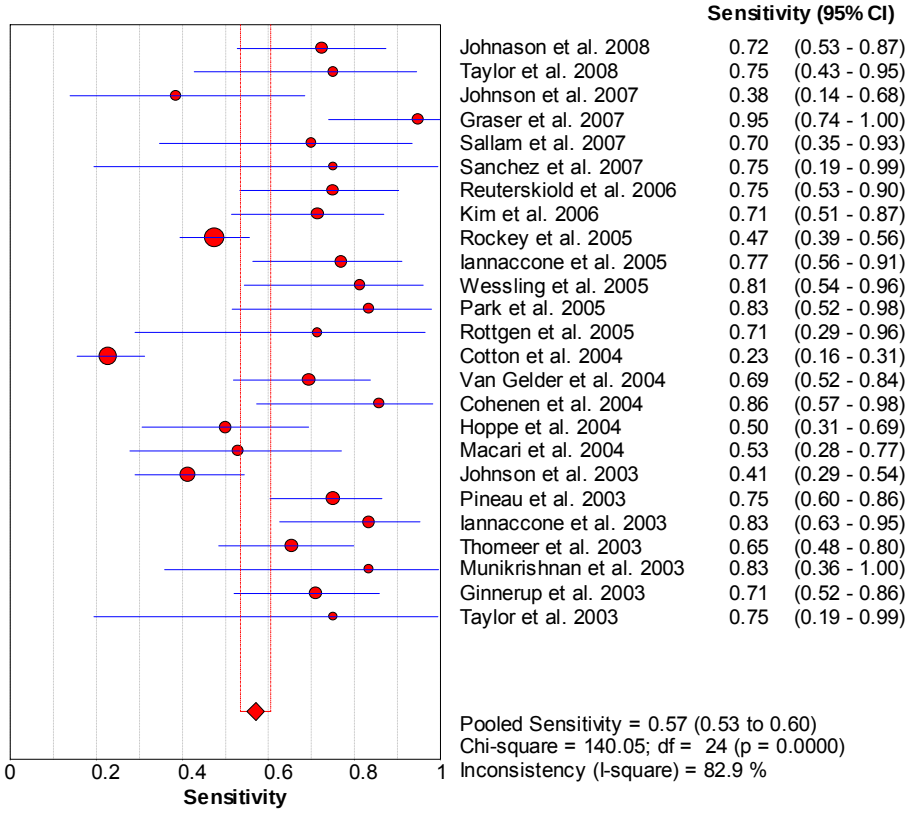


Figure 18: Sensitivity of CT Colonography for the Detection of Medium Polyps – Studies Not Performing Antegrade/Retrograde Viewing

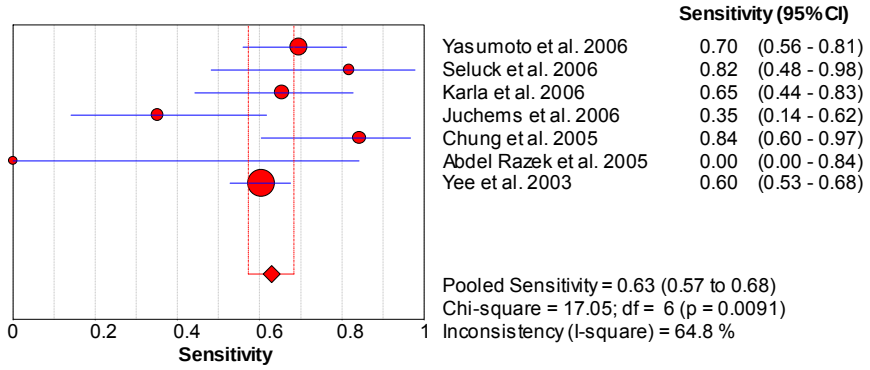


Figure 19: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Performing Antegrade/Retrograde Viewing

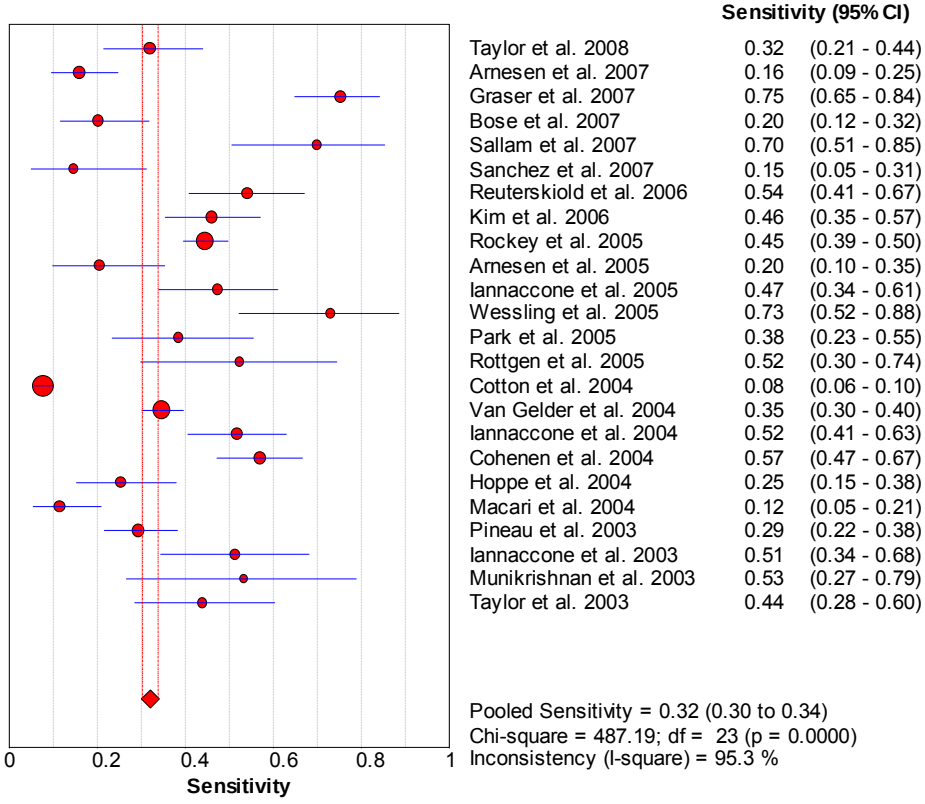


Figure 20: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Not Performing Antegrade/Retrograde Viewing

Acquisition Parameters

We found that some acquisition parameters contributed to the heterogeneity of reported sensitivities, specifically beam collimation and X-ray tube current.

Beam Collimation

Studies using narrower collimation (3 mm or less) demonstrated higher sensitivity compared to those using collimation of 5 mm. Sensitivity and 95% CI for detection of different size polyps separately for studies that used a narrower collimation (≤3 mm) versus those that used a thicker collimation (5 mm) was as follows:

- Large polyps: 83% (79%–86%) versus 69% (62%–75%)
- Medium to large polyps: 77% (74%-79%) versus 57% (53%-61%)
- Medium polyps: 69% (65%–72%) versus 48% (42%–54%)
- Small polyps: 43% (41%–45%) versus 16% (13%–18%)

Figures 21 to 28 show pooled sensitivity of CT colonography for detection of different size polyps according to the size of collimation.

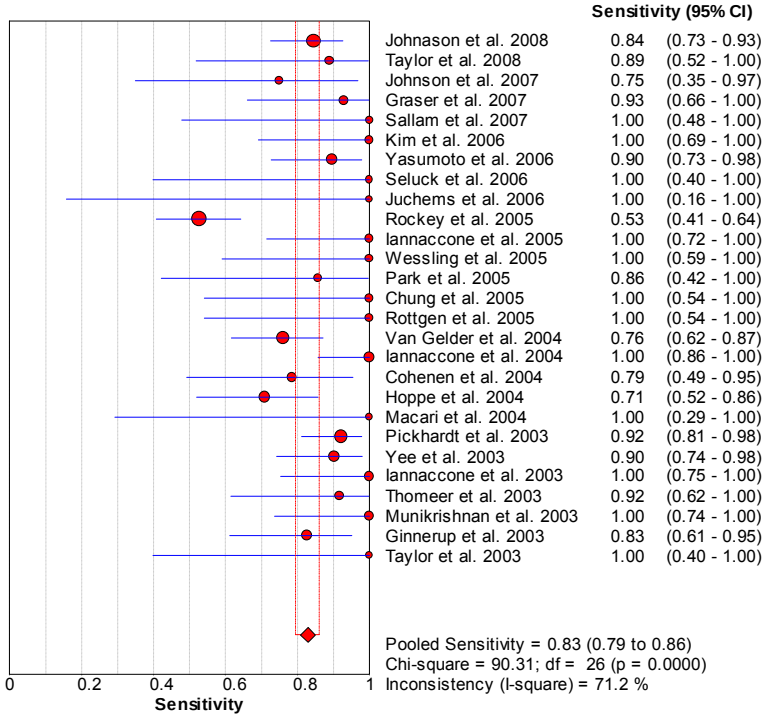


Figure 21: Sensitivity of CT Colonography for the Detection of Large Polyps – Studies Using Collimation ≤ 3 mm

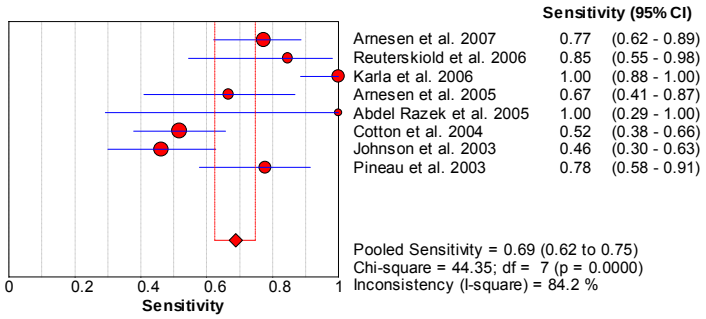


Figure 22: Sensitivity of CT Colonography for the Detection of Large Polyps – Studies Using 5 mm Collimation

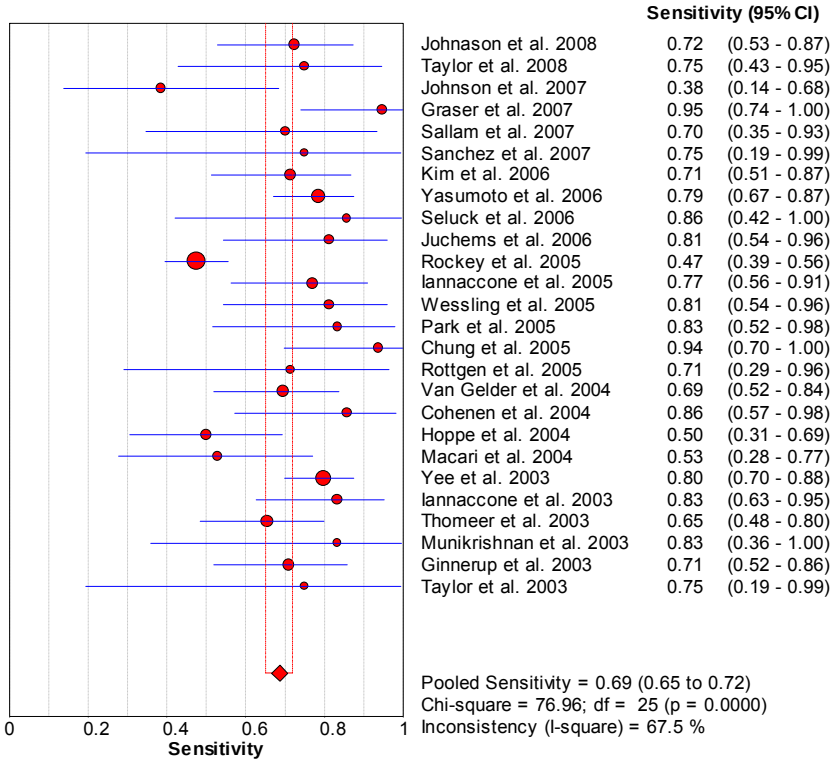


Figure 23: Sensitivity of CT Colonography for the Detection of Medium Polyps – Studies Using Collimation ≤3 mm

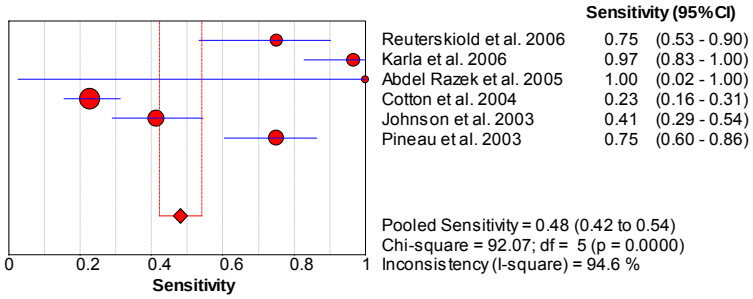


Figure 24: Sensitivity of CT Colonography for the Detection of Medium Polyps – Studies Using 5 mm Collimation

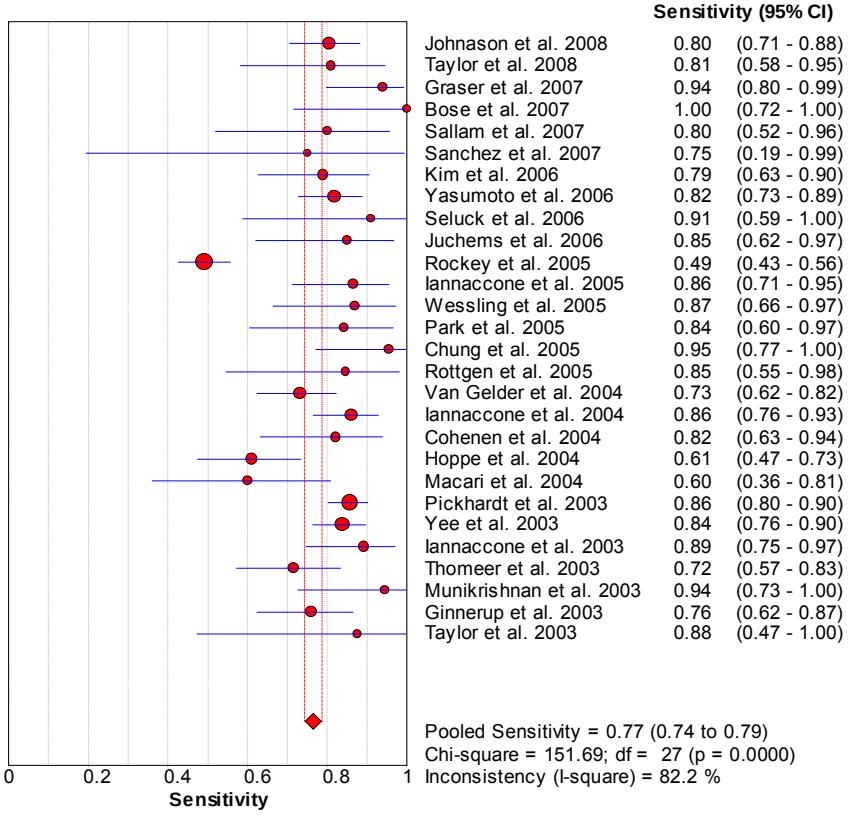


Figure 25: Sensitivity of CT Colonography for the Detection of Medium to Large Polyps – Studies Using Collimation ≤3 mm

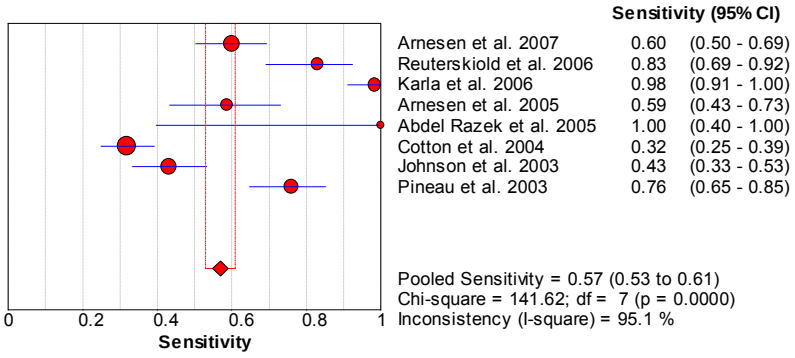


Figure 26: Sensitivity of CT Colonography for the Detection of Medium to Large Polyps – Studies Using Collimation 5 mm

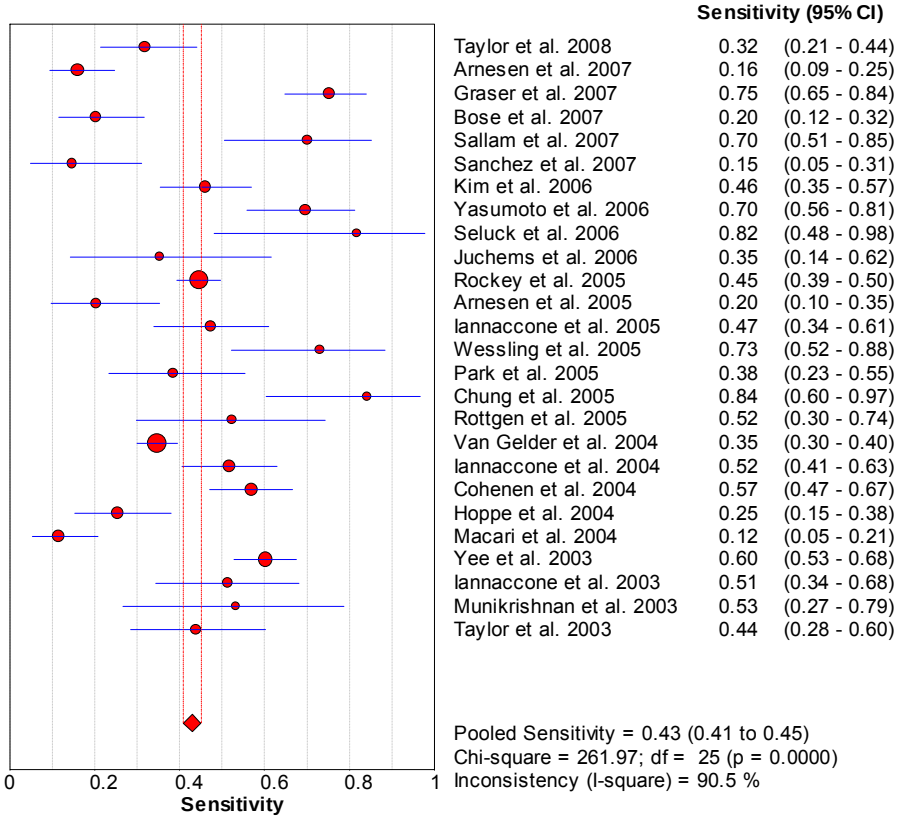


Figure 27: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Using Collimation ≤3 mm

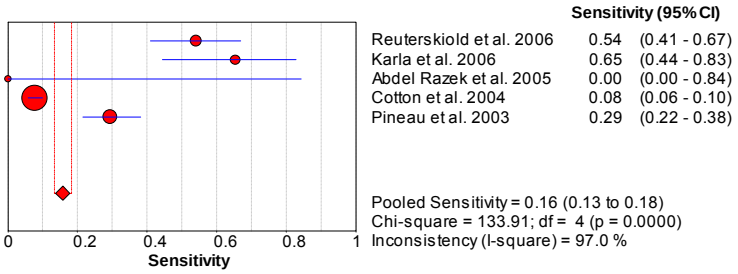


Figure 28: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Using 5 mm Collimation

Studies using 5 mm collimation generally demonstrated lower sensitivity for polyp detection, with the exception of two studies. (61;70) Karla et al. (61) achieved higher sensitivity because they performed both antegrade and retrograde viewing, used an intravenous contrast agent, and a higher tube current. Abdel Razek et al. (70) performed both antegrade and retrograde viewing, reporting high sensitivity for polyp detection.

All studies employing a four-detector scanner used a collimation of 1 to 2.5 mm, with the exception of three studies in which a 5 mm collimation was adopted (61;71;76) In two of these, those by Cotton et al. (71) and Johnson et al. (76), polyp detection sensitivity was very low, but in the third by Karla et al. (61), it was higher due to the above described factors.

A survey of the research institutions investigating CT colonography (30) showed that currently, the majority of organizations performing CT colonography use a scanner with 16 or more detectors and choose a collimation of 1 mm or less.

Phantom studies have shown that beam collimation is an important acquisition parameter affecting polyp visualization. (27;86;87) Taylor et al. (27) determined the optimal scanning parameters for polyp detection using a human colectomy specimen. Polyp detection significantly increased with a decrease in collimation size and pitch, but tube current had no significant effect on polyp detection. On average, 50% more polyps were detected at a collimation of 1.25 mm compared to that at 2.5 mm, while 30% more polyps were detected at a pitch of 3 compared to that achieved with a pitch of 6.

Most studies using a single detector employed 5 mm collimation, a set up that was originally based on the results of phantom studies. Based on current evidence, however, most investigators recommend a collimation of no more than 2.5 mm when using a multidetector CT scanner. (22)

Table 17 is a summary of scanning parameters according to the number of detectors used.

Table 17: Relationship Between the Number of Detectors and Width of Collimation in CT Colonography Studies*

Detectors, N	Collimation, mm	Tube current, mA	Tube Voltage, kVp	Study
1	5	70	120	Arnesen et al., 2007 (52)
	5	125	110	Reuterskiold et al., 2006 (57)
	5	70	120	Arnesen et al., 2005 (64)
	5	70–140	120	Abdel Razek et al., 2005 (70)
	5	70	120	Johnson et al., 2003 (76) (17%)‡
	5	200	120	Pineau et al., 2003 (77)
	3	150	120	Yee et al., 2003 (78)
2	3	200–400	120	Sallam et al., 2007 (55)
	2.5 and 5†	NR	NR	Cotton et al., 2004 (71)
4	1	40	120	Cohnen et al., 2004 (74)
	1	50	120	Macari et al., 2004 (42)
	1	60	120	Thomeer et al., 2003 (43)
	1	120–200	120	Munikrishanan et al., 2003 (80)
	1	140	120	Wessling et al., 2005
	1.25	50	120	Bose et al., 2007 (54)
	1.25	50	120	Chaparro et al., 2007 (56)
	1.25	100	120	Pickhardt et al., 2003 (9)
	1.25	50–100 (n=46)	120	Taylor et al., 2003 (82)
	2	200	120	Hoppe et al., 2004 (75)
	2.5	50	120	Taylor et al., 2008 (50) (86%)‡
	2.5	150–200	120	Juchems et al., 2006 (62)
	2.5	NR	NR	Rockey et al., 2005 (63) (61.5%)‡
	2.5	10	140	Iannaccone et al., 2005 (65)
	2.5	160	120	Park et al., 2005 (67)
	2.5	25–70 (n=219), 100 (n=30)	120	Van Gelder et al., 2004 (72)
	2.5	10	140	Iannaccone et al., 2004 (73)
	2.5	100	120	Pickhardt et al., 2003 (9)
	2.5	10	140	Iannaccone et al., 2003 (79)
	2.5	70	120	Ginnerup et al., 2003 (81)
	2.5	50–100 (n=8)	120	Taylor et al., 2003 (82)
	2.5 and 5†	NR	NR	Cotton et al., 2004
	5	Supine: 250, prone: 70	120	Karla et al., 2006 (61)
	5	80	120	Johnson et al., 2003 (76) (83%)‡
8	1.25	70	120	Johnson et al., 2007 (51)
	1.25 (n=24)	150	120	Kim et al., 2006 (58)
	1.25	120	120	Yasumoto et al., 2006 (59)
	1.25	100	120	Pickhardt et al., 2003 (9)
	2.5	NR	NR	Rockey et al., 2005 (63) (38.5%)‡
16	0.625	200–400	120	Sallam et al., 2007 (55)
	0.625	160	120	Rottgen et al., 2005 (69)
	0.75 (n=63)	150	120	Kim et al. 2006 (58)
	0.75	50	120	Selcuk et al., 2006 (60)
	0.75	Maximum 175	120	Juchems et al., 2006 (62)
	0.75	120–160	120	Chung et al., 2005 (68)
64	0.6	50	120	Taylor et al., 2008 (50) (14%)‡
	0.6	Supine: 120, prone: 40	120	Graser et al., 2007 (53)

*NR indicates not reported.

†Data for each scanner type not available

‡Percentage of people in the study who underwent the procedure using this particular scanner.

Studies performed CT colonography using a 16-detector or 64-detector CT scanner, which generally use a collimation of less than 1 mm, reported high sensitivity for the detection of large polyps (pooled sensitivity 98%; 95% CI, 87%–100%; see Figure 34). Pooled sensitivity for medium polyps was 81% (95% CI, 72%–88%; see Figure 35).

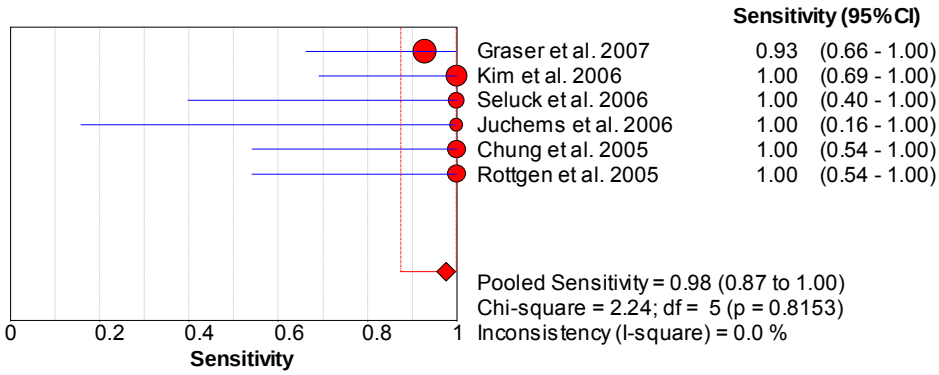


Figure 29: Sensitivity for the Detection of Large Polyps Using 16-Detector and 64-Detector Scanners

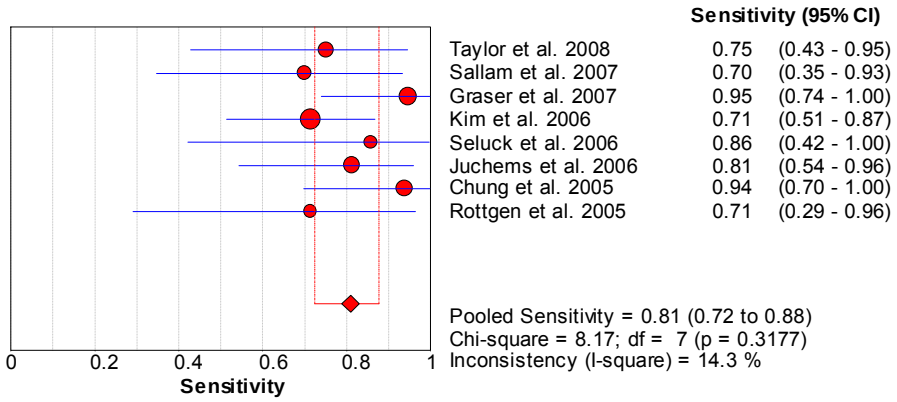


Figure 30: Sensitivity for the Detection of Medium Polyps Using 16-Detector and 64-Detector Scanners

X-ray Tube Current

Studies using a higher tube current (≥100 mA) reported higher sensitivities; however, most of these studies used also a narrow collimation. Sensitivity for different size polyps in studies that used higher tube current (≥100 mA) versus those that used lower tube current (<100 mA) was as follows:

- Large polyps: 90% (86%–93%) versus 72% (67%–76%)
- Medium to large polyps: 83% (81%–86%) versus 61% (58%–64%)
- Medium polyps: 79% (74%–82%) versus 52% (48%–56%)
- Small polyps: 53% (49%–56%) versus 28% (26%–30%)

Figures 31 to 38 show sensitivity of CT colonography for detection of polyps of different size according to tube current.

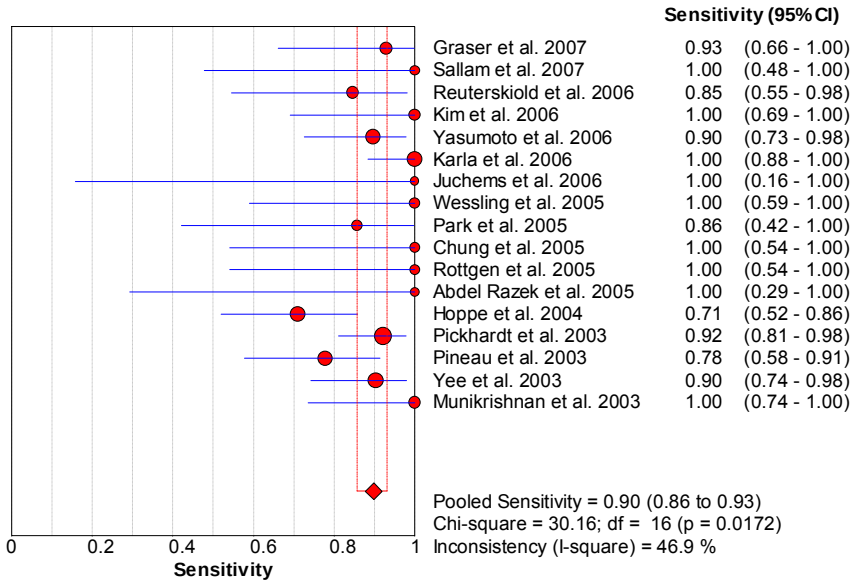


Figure 31: Sensitivity of CT Colonography for the Detection of Large Polyps – Studies Using ≥100 mA

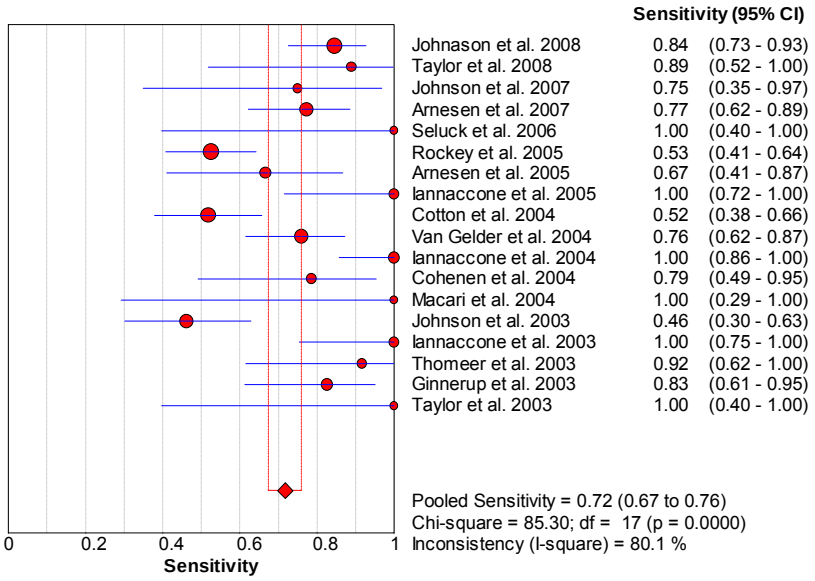


Figure 32: Sensitivity of CT Colonography for the Detection of Large Polyps – Studies Using <100 mA

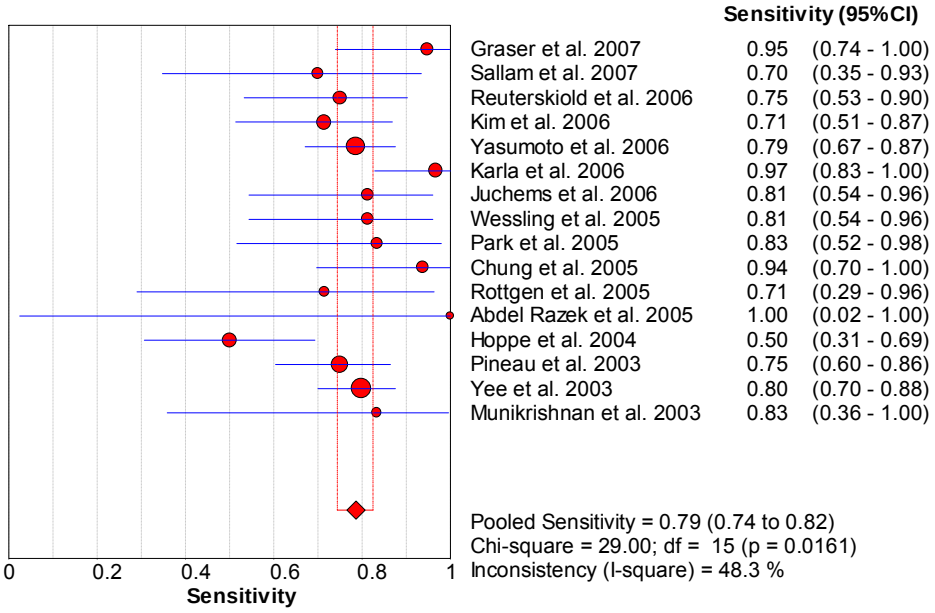


Figure 33: Sensitivity of CT Colonography for the Detection of Medium Polyps – Studies Using ≥100 mA

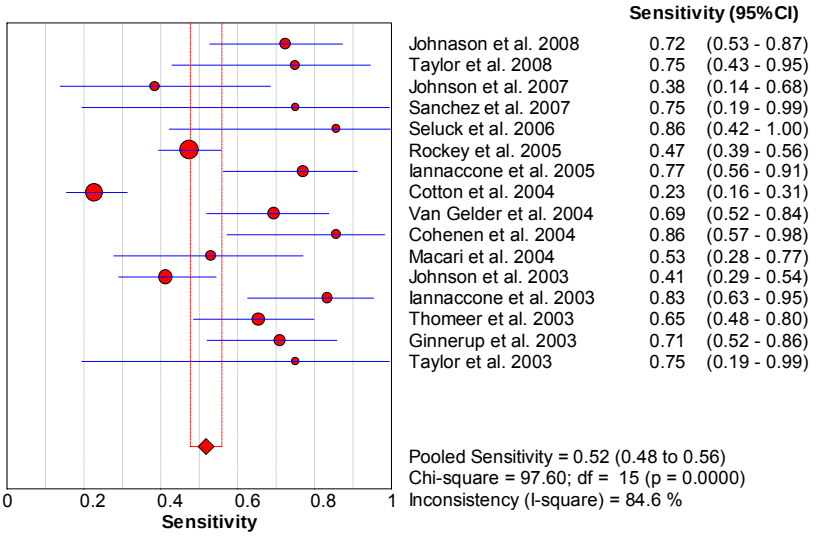


Figure 34: Sensitivity of CT Colonography for the Detection of Medium Polyps – Studies Using <100 mA

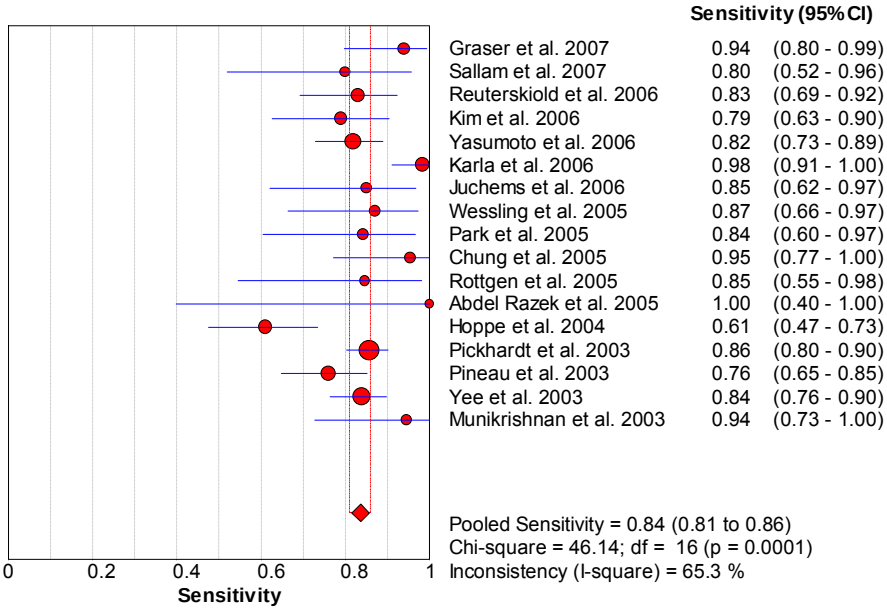


Figure 35: Sensitivity of CT Colonography for the Detection of Medium to Large Polyps – Studies Using ≥100 mA

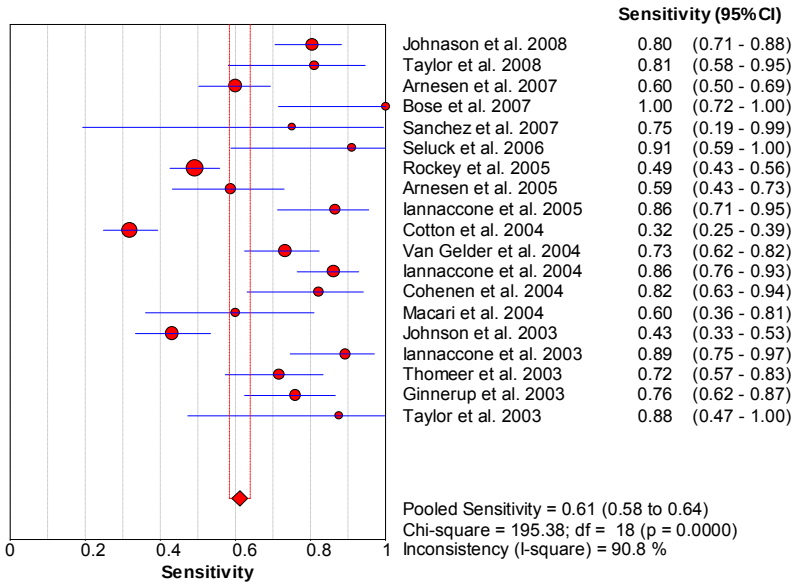


Figure 36: Sensitivity of CT Colonography for the Detection of Medium to Large Polyps – Studies Using <100 mA

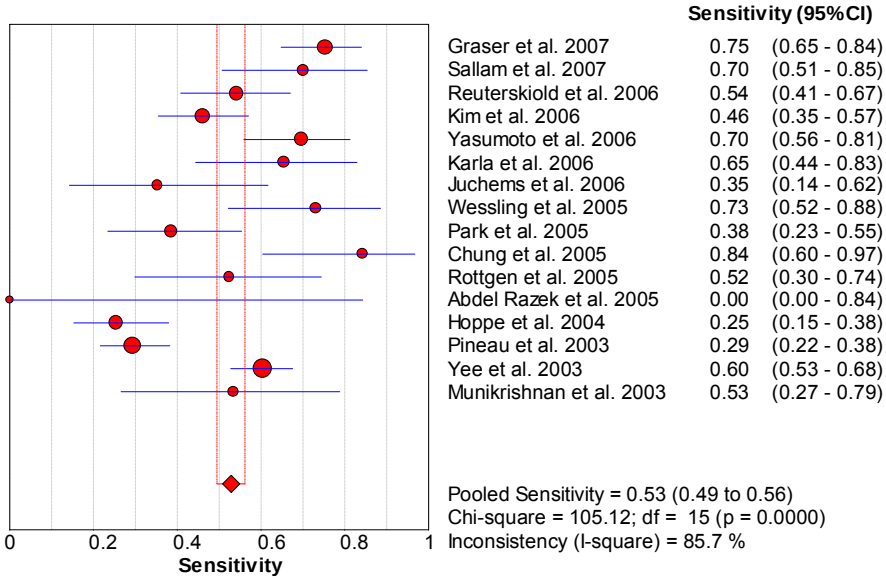


Figure 37: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Using ≥100 mA

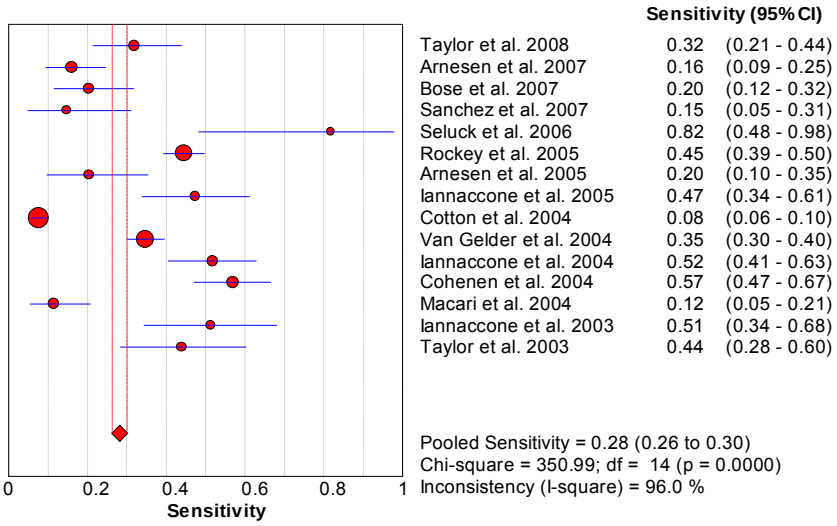


Figure 38: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Using <100 mA

Use of Contrast Agents

The use of a contrast agent resulted in improved in sensitivity for the detection of polyps of different sizes. Overall, oral contrast agents were used in seven studies (9;24;43;50;54;73;77) and intravenous administration of iodinated contrast agents was carried out in nine studies (55;58;61;67-69;75;80;82). In the study by Taylor et al. (82), administration of a contrast agent was performed in cases in which an abnormality was seen in the images taken while subjects were in the prone position.

As displayed in Figures 39 to 46, sensitivity for polyps among those studies that used and did not use a contrast agent was:

- Large polyps: 89% (95% CI, 85%–93%) versus 72% (67%–76%),
- Medium to large polyps: 83% (95% CI, 80%–85%) versus 64% (95% CI, 61%–66%)
- Medium polyps: 74% (95% CI, 68%–79%) versus 59% (95% CI, 55%–62%), and
- Small polyps: 40% (95% CI, 37%–44%) versus 33% (95% CI 32%–36%).

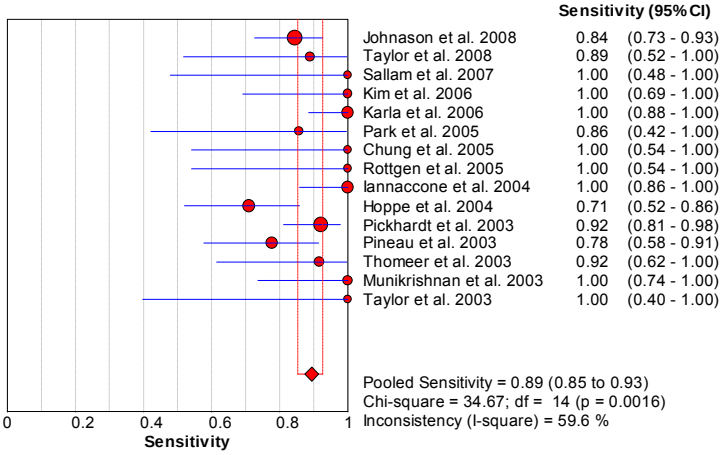


Figure 39: Sensitivity of CT Colonography for the Detection of Large Polyps – Studies Using Contrast Agent

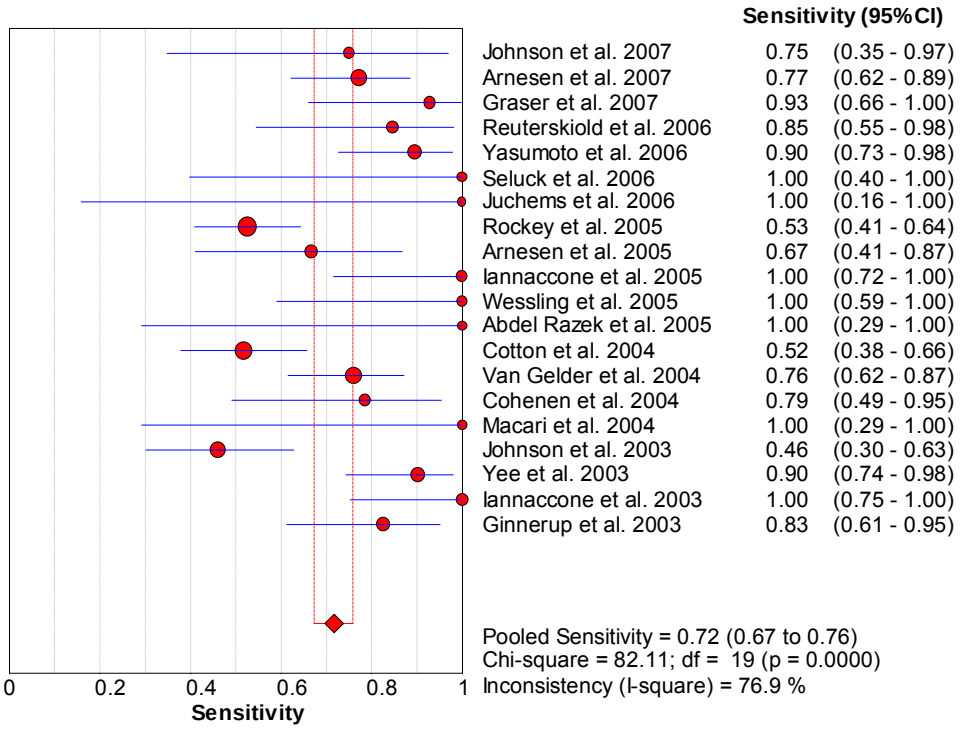


Figure 40: Sensitivity of CT Colonography for the Detection of Large Polyps – Studies Not Using Contrast Agent

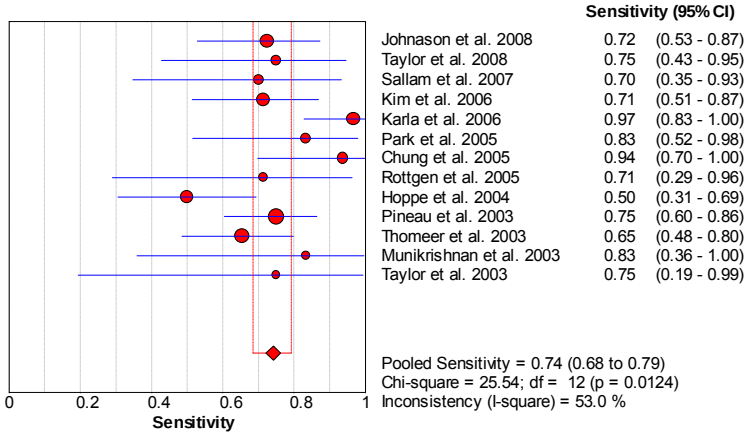


Figure 41: Sensitivity of CT Colonography for the Detection of Medium Polyps – Studies Using Contrast Agent

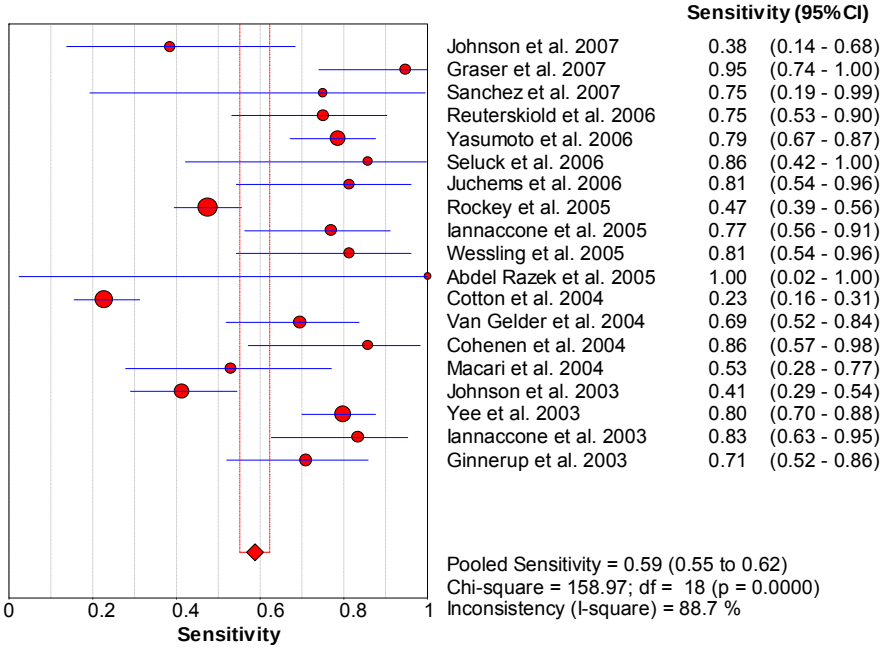


Figure 42: Sensitivity of CT Colonography for the Detection Medium Polyps – Studies Not Using Contrast Agent

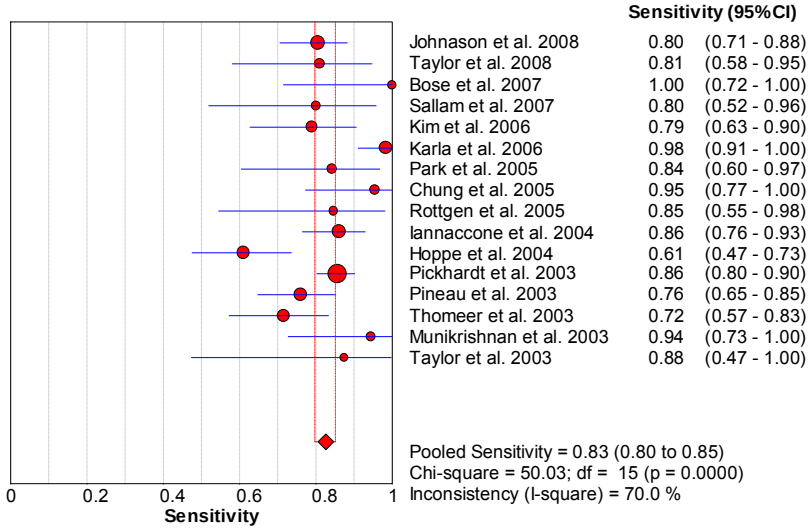


Figure 43: Sensitivity of CT Colonography for the Detection of Medium to Large Polyps – Studies Using Contrast Agent

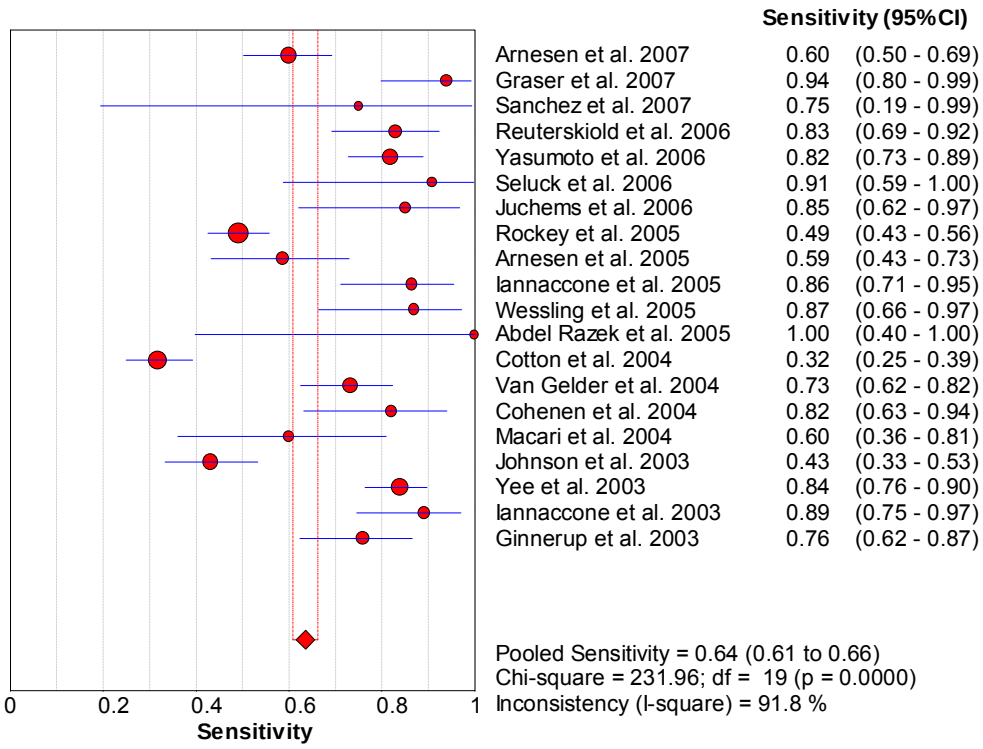


Figure 44: Sensitivity of CT Colonography for the Detection of Medium to Large Polyps – Studies Not Using Contrast Agent

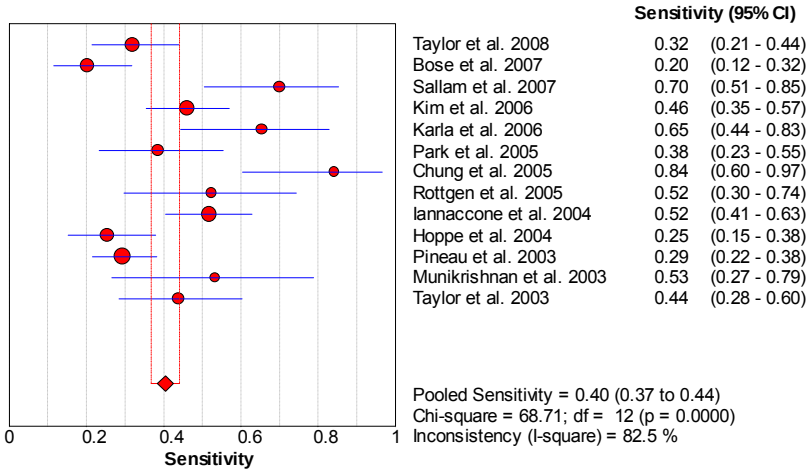


Figure 45: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Using Contrast Agent

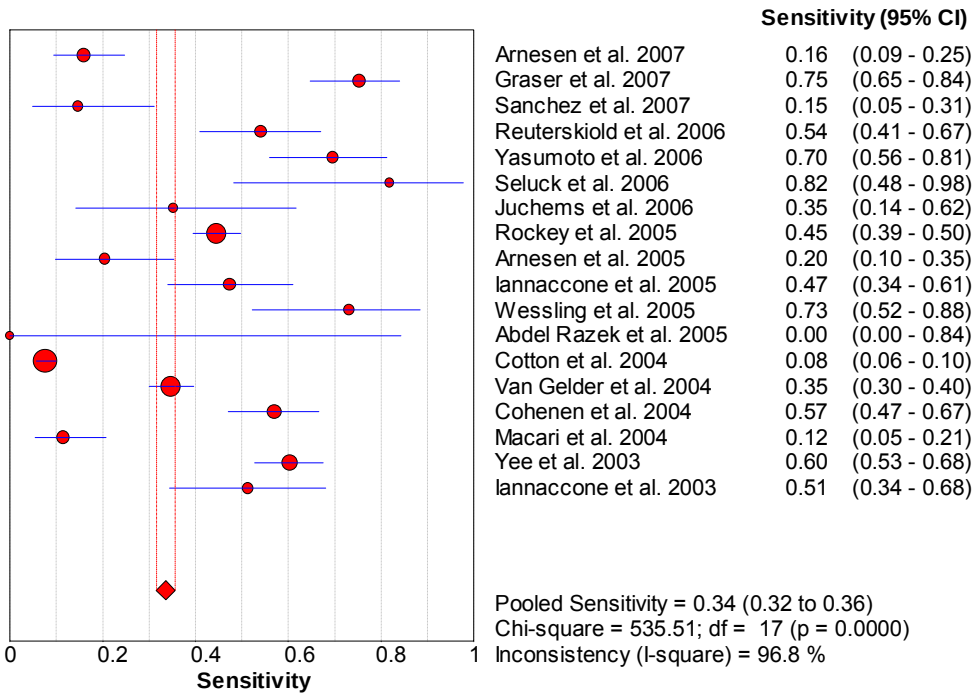


Figure 46: Sensitivity of CT Colonography for the Detection of Small Polyps – Studies Not Using Contrast Agent

With regards to the appearance of images taken with a contrast agent, it appears that the addition of an agent is helpful in differentiating real lesions from false ones, which positively influences the overall accuracy of the scan. It is well known that fecal residue and fluid remain present in the colon and mimic the appearance of polyps, while submerged polyps may remain invisible. This increases the number of false negative and false positive results. One approach to overcome these drawbacks is to increase the signal intensity of fecal residue and fluid via fecal tagging.

Although use of a contrast agent might have had affected sensitivity, it is difficult to determine the contribution this has on the rate of polyp detection because of the interrelationship of technical factors. For example, some of the studies that used a contrast agent also used a narrow collimation.

Orally ingested barium sulphate and/or iodinated radiopaque contrast media can be administered for fecal tagging or opacification of luminal fluid. The use of dense barium sulphate could interfere with the endoscopy examination that is performed subsequent to CT colonography. (43) Three (9;50;54) of four studies that used barium sulphate for fecal tagging performed the colonoscopy the same day, while in one study colonoscopy was performed within 7 days (89% of the patients; range, 0–100 days). (24) Although diluted barium (2%) was used in these studies to avoid interference with subsequent colonoscopy, Pickhardt et al. reported a lower sensitivity for colonoscopy than CT colonography for identification of polyps ≥10 mm. (9) In this study, 12.5% of the adenomas ≥10 mm were not identified by colonoscopy while the literature indicates that miss rate of colonoscopy for large lesions is about 6%. (12) The pooled sensitivities of CT colonography for the identification different sizes of polyps according to acquisition parameter and contrast agent use are shown in Table 18.

Table 18: Pooled Sensitivities for the Detection of Colorectal Polyps According to Technical Parameters*

Technical Parameters	Sensitivity, % (95% CI)		
	Large Polyps	Medium Polyps	Small Polyps
Antegrade/retrograde viewing			
Yes	94 (88–98)	83 (77–88)	63 (57–68)
No	76 (73–79)	57 (53–60)	32 (30–34)
Beam Collimation			
≤3 mm	83 (79–86)	69 (65–72)	43 (41–45)
5 mm	69 (62–75)	48 (42–54)	16 (13–18)
Tube current			
≥100 mA	90 (86–93)	79 (74–82)	53 (49–56)
<100 mA	72 (67–76)	52 (48–56)	28 (26–30)
Contrast agents			
Used	89 (85–93)	74 (68–79)	40 (37–44)
Did not use	71 (67–75)	59 (55–62)	34 (32–36)

*CI indicates confidence interval.

Experience of the Image Reviewer

CT colonography technique is associated with a steep learning curve and successful interpretation of images is dependent on the experience of the image viewer. Most of the studies reported that one or more experienced radiologists reviewed images. However, the minimum required experience with CT colonography varied across studies from having performed at least 10 CT colonographies in the study by Cotton et al. (71), to more than 1,000 CT colonographies in Johnson et al. (24) (see Table 19).

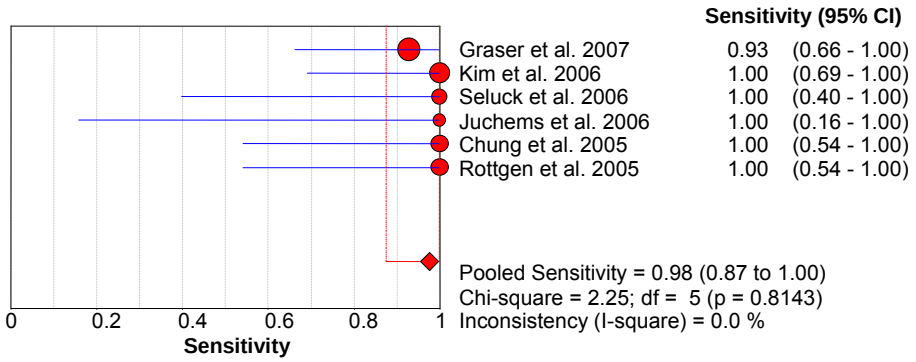
Table 19: CT Colonography Studies: Image Interpretation*

Study	Image Reviewers	Reviewer Experience
Johnson et al., 2008 (24)	3 radiologists	>1,000 CTCs (20 noncathartic method)
Taylor et al., 2008 (50)	3 radiologists	300 CTCs
Johnson et al., 2007 (51)	3 radiologists	>1,000 CTCs
Arnesen et al., 2007 (52)	1 GI radiologist	12 pilot CTCs & 12 paired video recorded OCs
Graser et al., 2007 (53)	1 abdominal radiologist	>700 CTCs
Bose et al., 2007 (54)	1 GI radiologist	
Sallam et al., 2007 (55)	>1 radiologists	5 years experience
Chaparro et al., 2007 (56)	NR	
Reuterskiold et al., 2006 (57)	2 reviewers	
Kim et al., 2006 (58)	1 radiologist	>300 CTCs
Yasumoto et al., 2006 (59)	3 radiologists	200 CTCs
Selcuk et al., 2006 (60)	1 abdominal radiologist	
Karla et al., 2006 (61)	2 radiologists	≥8 years experience in GI radiology
Juchems et al., 2006 (62)	1 radiologist	Previous experience with both display methods
Rockey et al., 2005 (63)	Radiologists	About half had experience with >50 CTCs
Arnesen et al., 2005 (64)	1 reviewer	12 pilot CTCs and 12 paired video recorded OC
Iannaccone et al., 2005 (65)	3 GI radiologists	
Wessling et al., 2005 (66)	2 radiologists	At least 40 CTC
Park et al., 2005 (67)	2 GI radiologists	>50 CTC
Chung et al., 2005 (68)	2 radiologists	5 years experience with abdominal CT
Rottgen et al., 2005 (69)	2 radiologists	
Abdel Razek et al., 2005 (70)	3 radiologists	
Cotton et al., 2004 (71)	2 independent radiologists	At least 10 CTCs
Van Gelder et al., 2004 (72)	1 abdominal radiologist and one research fellow	Both >50 CTCs
Iannaccone et al., 2004 (73)	3 GI radiologists	100, 200, and 300 CTCs
Cohnen et al., 2004 (74)	2 radiologists and 1 gastoenterologist	
Hoppe et al., 2004 (75)	3 radiologists	30–60 CTCs
Macari et al., 2004 (42)	1 radiologist	5 years experience in CTCs
Pickhardt et al., 2003 (9)	6 radiologists	4 with 25 CTC training, 2 with >100 CTCs
Johnson et al., 2003 (76)	3 abdominal radiologists	150 CTCs
Pineau et al., 2003 (77)	1 diagnostic radiologist	
Yee et al., 2003 (78)	2 radiologists	
Iannaccone et al., 2003 (79)	2 GI radiologists	4 years experience with CTCs
Thomeer et al., 2003 (43)	2 independent readers	1 with 30 CTCs in single-detector, 1 with 50 CTCs in single/multi-detector
Munikrishnan et al., 2003 (80)	2 GI radiologists	
Ginnerup et al., 2003 (81)	1 radiologist	100 CTCs
Taylor et al., 2003 (82)	1 radiologist	

*CTC indicates computed tomographic colonography; GI, gastrointestinal; NR, not reported; OC, optical colonoscopy.

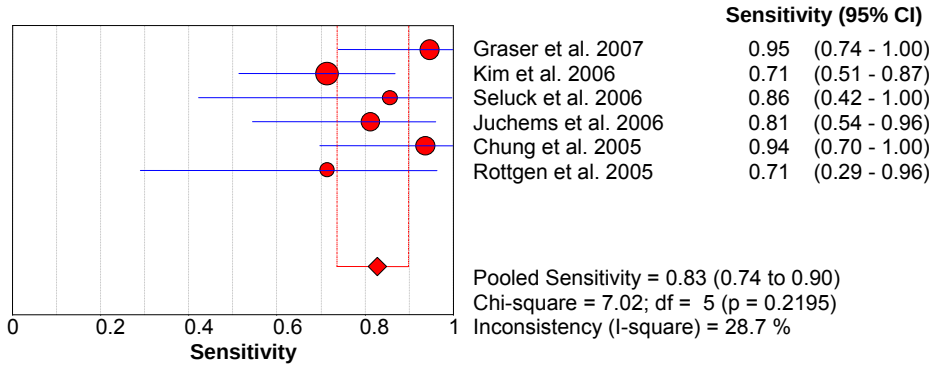
Sensitivity of Ct Colonography Compared With MR Colonography

Studies on CT colonography with 16-slice or 64-slice CT equipment have reported higher sensitivity for detection of large and medium polyps than those using 1-, 4-, or 8-slice equipment (Figures 47 and 48). Figure 49 shows pooled sensitivity of both CT colonography and MR colonography for detection of cancer and different sized polyps.



Studies used 16-slice or 64-slice scanners.

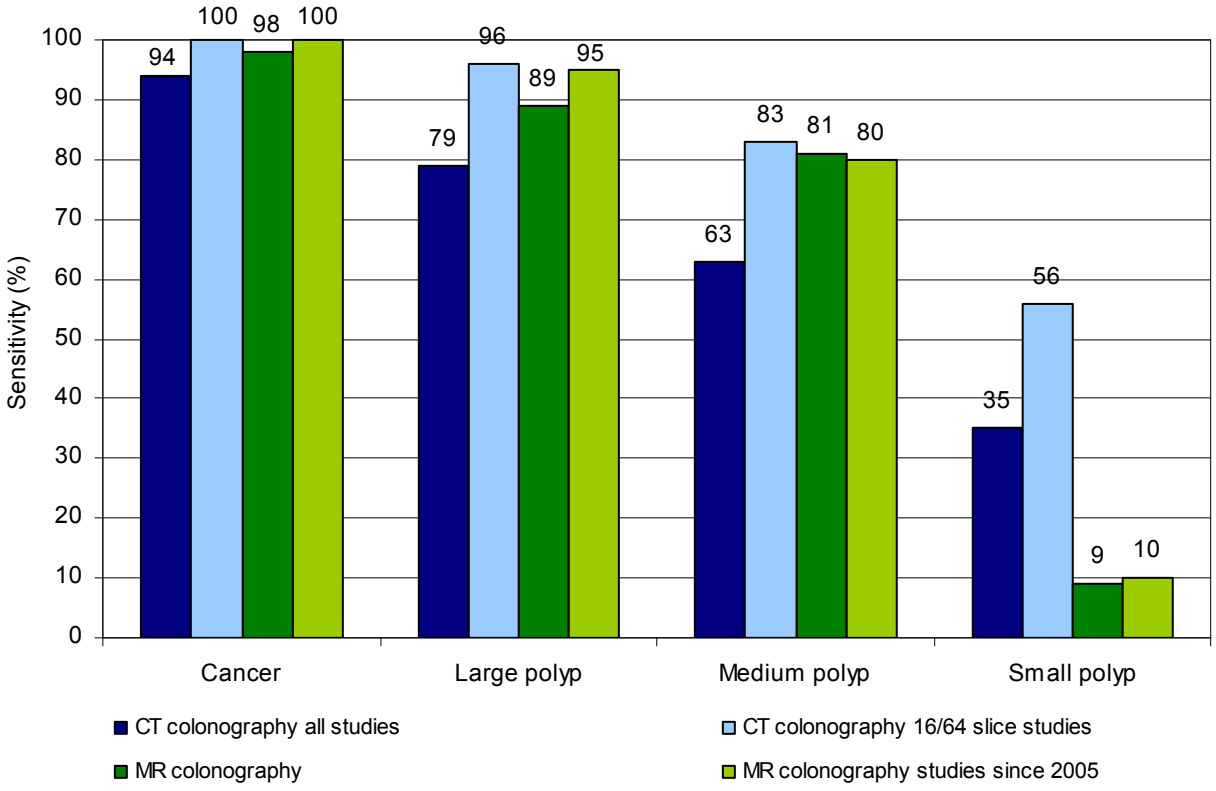
Figure 47: Sensitivity of CT Colonography for the Detection of Large Polyps



Studies used 16-slice or 64-slice Scanners

Figure 48: Sensitivity of CT Colonography for the Detection of Medium Polyps

Figure 49: Pooled Sensitivity of CT Colonography Compared With MR Colonography



Conclusions

- MR colonography and CT colonography with 16-slice or 64-slice scanners have equal sensitivity for the detection of CRC, as well as for the detection of large and medium sized polyps; however, MR colonography does not carry the associated risks of ionizing radiation.
- MR colonography and CT colonography with 16-slice or 64-slice scanners can reliably detect most CRCs and large colorectal polyps; however, about 20% of medium-sized colorectal polyps will be missed by both techniques.
- None of the techniques can reliably detect small polyps and MR colonography has a much lower sensitivity for the detection of small polyps compared with CT colonography.

Patient Safety

Estimation of Risk of Cancer from Exposure to Ionizing Radiation

Compared with plain-film radiography, CT scanning involves much higher doses of X-ray radiation, resulting in a marked increase in radiation exposure in the population. It is estimated that 1.5% to 2% of all cancers in the US can be attributed to the radiation from CT scanning. (31)

Several recent reports from international organizations have presented cancer risk estimates for exposure to ionizing radiation. The recent report of the committee on Biological Effects of Ionizing Radiation (BEIR VII)[2] (88) provided the most up-to-date and comprehensive risk estimate for exposure to low dose radiation in human subjects. The BEIR VII includes detailed estimates for both cancer incidence and mortality since new and more extensive data have become available since their previous report in 1990.

The BEIR VII report concludes that the current scientific evidence is consistent with the hypothesis that, at the low-LET radiation [3]such as X-rays and gamma rays, there is a linear dose-response relationship between exposure to ionizing radiation and the development of solid cancers in humans and that there is no threshold, meaning that the smallest dose has the potential to cause a small increase in risk of cancer. Low dose radiation is defined as doses ranging from nearly zero to 100 mSv.

The BEIR VII has provided the estimated number of cancer cases and deaths expected to arise in 100,000 people exposed to 100 mSv. The report also provides estimates for cancers of specific sites. The estimated incidence of all solid cancers per 100,000 persons is 800 (400-1600) for males and 1,300 (690-2,500) for females. The estimated incidence of leukemia per 100,000 persons is 100 (30-300) for males and 70 (20-250) for females. About half of the solid cancers and 2/3 of leukemia cases will result in death.

According to the American Cancer Society, the average natural lifetime incidence of cancer in the US is 42 per cent; meaning that 42 out of 100 people will develop some sort of cancer in their lifetime. The BEIR VII lifetime risk model predicts that approximately one individual in 100 people would develop cancer from exposure to radiation with a dose of 100 mSv and approximately one individual in 1,000 would develop cancer from an exposure to 10 mSv. The International Commission on Radiological Protection (ICRP) (89) has estimated the risk of fatal radiogenic cancer caused by CT colonography with a dose of 8 mSv as 0.04% or 1 in 2,500, or 40 in 100,000 individuals.

Although the risk of developing a radiogenic cancer due to exposure to CT colonography is relatively small (0.04%) in comparison to the natural incidence of cancer (42%), it should be borne in mind that the natural incidence of colon cancer as indicated in BEIR VII is 4,200 in 100,000 people (4.2%) and the fatality from such cancer is about 40 percent (according to the data from Cancer Care Ontario).

Individual risk from exposure to ionizing radiation of CT examination varies significantly depending upon many factors including the age and sex of the patient, absorbed dose, and the expected lifespan. (90) Based on BEIR data, the International Atomic Energy Agency (IAEA) (90) has provided risk estimate of dying from radiogenic cancers caused by exposure to the radiation during CT colonography procedure at various ages. (see Table 20) The risk of dying from such cancer declines as people become older but is always higher in female than male.

[2] The seventh in a series of reports from the Ntional Research Council prepared to advise the US government on the health effects of exposure to ionizing radiation

[3] Low linear energy transfer ionizing radiation

Table 20: Potential Lifetime Radiogenic Fatal Cancer Risk for CT colonography at Various Ages

Gender	Age at Exposure	Fatal Radiogenic Cancer/Leukemia Risk (%)
Male	30	0.030
	40	0.030
	50	0.029
	60	0.026
	70	0.020
	80	0.012
Female	30	0.043
	40	0.041
	50	0.038
	60	0.033
	70	0.026
	80	0.015

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The International Commission on Radiological Protection (ICRP) has recommended dose limits for ionizing radiation for those working with radiation and for the public. According to ICRP, the recommended dose limit for occupational exposure is 20 mSv, averaged over 5 years, with the condition that there will be no more than 50 mSv in any single year. For members of the public, the recommended limit is 1mSv per a year. Exceptionally, a higher value of effective dose could be allowed in a year provided that the average over 5 years does not exceed 1 mSv in a year. (91)

Risk of Complications due to Bowel Insufflation

The advantages of CT colonography compared to colonoscopy are the lower rate of colon perforation and the ability to use scout CT images to identify the presence of gas following perforation in the peritoneum. Recent data from Sosna et al. and Burling et al. show a perforation rate of 0.05% and 0.06% during CT colonography. In the study by Sosna et al. (25), a total of 11,870 CT colonography examinations performed in 11 medical centres between January 2001 and December 2004 were reviewed. There were seven cases of colorectal perforation, yielding a risk ratio of 0.059%. The mean age of patients who had perforation was 77.8 years. Six of these cases occurred in symptomatic patients at high risk for colorectal neoplasia and one in an asymptomatic average risk individual. Five cases of perforation occurred in the sigmoid colon and one occurred in the rectum. Six cases of perforation occurred in patients in whom a rectal tube was inserted and in five of them, a ballon was inflated. Four patients required surgical treatment. Possible underlying diseases that contributed to perforation were left inguinal hernia containing colon (n=3), diverticulosis (n=3), and obstructive carcinoma (n=1).

In the study by Burling et al. (92), the frequency of serious adverse events associated with CT colonography performed in symptomatic patients were collected through a national survey of 50 centres in UK. From a total of 17,067 CT colonography examinations that were performed, 13 patients (0.08%) had a potentially serious adverse event related to the procedure. Of these, there were 3 self limiting vasovagal episodes and one episode of cardiac angina. There were 9 (0.05%) colonic perforations in which 4 did not have any symptom of perforation. One patient required laparatomy.

Appendices

Appendix 1: Search Strategy – Virtual Colonoscopy

Search date: January 30, 2008
Databases Searched: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library, INAHTA/CRD
Database: Ovid MEDLINE(R) <1996 to January Week 3 2008>
Search Strategy:

1 exp Colonography, Computed Tomographic/ (727)
2 (virtual colonoscopy or virtual colonography).mp. (364)
3 ((ct or computed tomographic or mr or mri or magnetic resonance) adj2 (colonography or colonoscopy)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (956)
4 or/1-3 (1076)
5 exp Colorectal Neoplasms/ (51853)
6 exp Colonic Polyps/ (2221)
7 ((colon$ or colorectal or rectal or rectum) adj5 (precancer$ or pre-cancer$ or polyp$ or neoplasm$ or adenoma$ or cancer$ or dysplasia$ or neoplasia$ or tumo?r$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (62656)
8 exp Precancerous Conditions/ (10419)
9 or/5-8 (74178)
10 4 and 9 (845)
11 limit 10 to (humans and english language and yr="2002 - 2008") (596)
12 (meta analy$ or metaanaly$ or pooled analysis or random$ or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (376626)
13 exp Technology Assessment, Biomedical/ or exp Evidence-Based Medicine/ (30570)
14 11 and (12 or 13) (68)
15 11 (596)
16 limit 15 to (case reports or comment or editorial or letter or "review") (236)
17 15 not 16 (360)
18 14 or 17 (390)

Database: EMBASE <1980 to 2008 Week 04>
Search Strategy:

1 exp Computed Tomographic Colonography/ (1026)
2 (virtual colonoscopy or virtual colonography).mp. (348)
3 ((ct or computed tomographic or mr or mri or magnetic resonance) adj2 (colonography or colonoscopy)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1275)
4 or/1-3 (1386)
5 exp Colorectal Cancer/ (31930)
6 exp Colorectal Tumor/ (1892)
7 exp Colon Polyp/ (6733)
8 exp Colon Adenoma/ (2353)
9 ((colon$ or colorectal or rectal or rectum) adj5 (precancer$ or pre-cancer$ or polyp$ or neoplasm$ or adenoma$ or cancer$ or dysplasia$ or neoplasia$ or tumo?r$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (103335)
10 exp "Precancer and Cancer-In-Situ"/ (21099)
11 or/5-10 (123356)
12 4 and 11 (982)
13 limit 12 to (human and english language and yr="2002 - 2008") (688)
14 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or random$ or data extraction or cochrane).ti,ab. (401281)
15 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (277742)
16 13 and (14 or 15) (95)
17 13 (688)
18 limit 17 to (editorial or letter or note or "review") (280)
19 Case Report/ (975460)
20 17 not (18 or 19) (381)
21 16 or 20 (423)

Appendix 2: Inclusion and Exclusion Criteria of the Studies Reviewed

Study Country	Inclusion Criteria	Exclusion Criteria
Johnson et al., 2008 (24) USA	Patients with a known or suspected colorectal neoplasm scheduled for colonoscopy	
Taylor et al., 2008 (50) UK	Patients scheduled to undergo diagnostic colonoscopy for symptoms suggestive of colorectal neoplasia	▪ Age <50 years ▪ Known diagnosis of IBD
Johnson et al., 2007 (51) USA	Asymptomatic patients ≥40 years old who were scheduled to undergo screening colonoscopy	▪ Melena ▪ Hematochezia ▪ IBD ▪ Familial polyposis ▪ Symptomatic patients
Arnesen et al., 2007 (52) Denmark	Patients ≥18 years of age referred for colonoscopy	▪ Acute symptoms ▪ Recent abdominal surgery ▪ Colostomy ▪ Pregnancy ▪ Failure to fulfill bowel preparation
Graser et al., 2007 (53) Germany	Patients without symptoms of colonic disease	▪ Positive FOBT in the last 5 years ▪ Prior OC in the last 5 years ▪ History of IBD ▪ Rectal bleeding or hematochezia ▪ Abdominal pain
Bose et al., 2007 (54) UK	Patients ≥50 judged to have indication for colonoscopy	▪ Incapability to complete CTC study ▪ Inflammatory bowel disease
Sallam 2007 (55) Poland	Patients with clinical suspicion of large bowel disease	
Chaparro et al., 2007 (56) Spain	Patients referred for colonoscopy	▪ Age <18 years ▪ IBD ▪ Contraindication for OC
Reuterskiold et al., 2006 (57) Sweden	Patients referred for colonoscopy	▪ Women < 50 years of age ▪ Acute colitis ▪ Colostomy
Kim et al., 2006 (58) Korea	Group 1 (n=24) were patients suspected of having polyps by recent flexible sigmoidoscopy or colonoscopy and were scheduled for endoscopic polypectomy with colonoscopy. Group 2 were patients referred for CTC for screening purposes (n=62).	

Study Country	Inclusion Criteria	Exclusion Criteria
Yasumoto et al., 2006 (59) Japan	Screening patients with average risk of CRC, personal or family history of colorectal polyps, family history of CRC, follow-up of an abnormal screening test, iron deficiency anaemia, hematochezia, abdominal pain, weight loss	▪ History of familial adenomatous polyposis or hereditary non-polyposis cancer syndromes ▪ Prior colorectal surgery ▪ Suspected diagnosis of IBD ▪ Bowel obstruction ▪ Acute diverticulitis ▪ A medical condition that precluded the use of bowel preparation ▪ Rejection of CTC or OC ▪ Pregnancy
Selcuk et al., 2006 (60) Turkey	Patients eligible for screening (hematochezia, positive FOBT, iron deficiency, personal or family history of colonic neoplasms)	
Karla et al., 2006 (61) India	Patients with symptoms of colonic disease (lower abdominal pain, weight loss, altered bowel habits, diarrhea, or rectal bleeding), past history of surgery for colonic carcinoma	
Juchems et al., 2006 (62) Germany	Patients who had received conventional colonoscopy after CTC	
Rockey et al., 2005 (63) USA	Patients with positive FOBT, hematochezia, iron deficiency anaemia, family history of CRC	
Arnesen et al., 2005 (64) Denmark	Patients aged ≥18 years referred for colonoscopy (polyp surveillance, CRC surveillance, rectal bleeding, change in bowel habits, abdominal pain, possible polyp on barium enema, other)	▪ Patients presenting with acute symptoms ▪ Recent abdominal surgery ▪ Colostomy ▪ Pregnancy ▪ Failure to observe bowel preparation regimen
Iannaccone et al., 2005 (65) Italy	Asymptomatic patients (n=38 [43%]) ▪ screening ▪ personal history of polyps ▪ family history of CRC ▪ abnormal screening test result Symptomatic patients (n=50 [57%]) ▪ hematochezia ▪ change in bowel movement habit ▪ weight loss ▪ abdominal pain ▪ iron deficiency anaemia	
Park et al., 2005 (67) Korea	Patients in whom colon cancer was suspected or had been newly diagnosed and were scheduled to undergo colonoscopy	

Study Country	Inclusion Criteria	Exclusion Criteria
Chung et al., 2005 (68) Korea	History of altered bowel habits, anaemia of unknown cause, abdominal pain, positive FOBT, hematochezia	
Rottgen et al., 2005 (69) Germany	Abdominal pain, positive FOBT, change in bowel habit, family history of CRC	▪ Previous history of CRC
Abdel Razek et al., 2005 (70) Egypt	Rectal bleeding, weight loss, altered bowel habit, abdominal pain, constipation, easy fatigability, sensation of anorectal fullness	
Cotton et al., 2004 (71) USA	Patients aged 50 years or older scheduled for a clinically indicated elective colonoscopy (reasons for colonoscopy: overt and occult rectal bleeding, change in stool habit, abdominal pain, and surveillance after polypectomy)	▪ Patients who had undergone colonoscopy within 3 years
Van Gelder et al., 2004 (72) The Netherlands	Patients at high risk for CRC scheduled for colonoscopy because of a personal or family history of colorectal polyp or CRC	▪ Patients younger than 18 years ▪ Impossibility of understanding patient information/informed consent/refusal to sign the consent form ▪ Colorectal polyp/cancer diagnosed during recent examination of colon ▪ Colostomy after colorectal surgery
Iannaccone et al., 2004 (73) Italy	Patients 35 years of age or older scheduled to undergo colonoscopy Asymptomatic patients (51.7%) ▪ average-risk CRC screening (22.6%) ▪ family history of colorectal CRC (15.8%) ▪ personal history of polyps (9.3%) ▪ an abnormal screening test (3.9%) Symptomatic patients (48.3%) ▪ hematochezia (18.7%) ▪ change in bowel habits (11.3%) ▪ iron deficiency anaemia (7.4%) ▪ abdominal pain (5.9%) ▪ weight loss (2.1%)	▪ Familial adenomatous polyposis or hereditary nonpolyposis cancer syndromes ▪ Prior colorectal surgery ▪ A suspected diagnosis of IBD ▪ Bowel obstruction ▪ Acute diverticulitis ▪ A medical condition that precluded the use of bowel preparation ▪ Rejection for colonoscopy for any reason ▪ Contraindications to the ingestion of iodinated-containing agents
Cohnen et al., 2004 (74) Germany	Patients referred for colonoscopy for evaluation of abdominal complaints including changing bowel habits (22.6%) abdominal pain (31.4%) blood in stool (19%) control colonoscopy after polypectomy (27%) Family history of CRC (0%)	▪ NR

Study Country	Inclusion Criteria	Exclusion Criteria
Hoppe et al., 2004 (75) Switzerland	Patients referred for colonoscopy to evaluate symptoms including Hematochezia, positive FOBT, iron deficiency anaemia, positive personal or family history of colonic neoplasm None of the patients were known to have polyps beforehand.	▪ NR
Macari et al., 2004 (42) USA	Asymptomatic patients older than 50 years of age scheduled to undergo screening colonoscopy (had no colorectal symptoms, had negative FOBT, did not have family history of CRC in a first-degree relative, had no prior history of colorectal polyp, did not undergo prior colonoscopy, sigmoidoscopy, or double contrast barium enema)	
Pickhardt et al., 2003 (9) USA	Asymptomatic patients referred for screening colonoscopy: ▪ average risk of CRC between 50 and 79 years of age (n=32 [2.6%]) ▪ higher than average risk between 40 and 79 years who had either a first degree relative with CRC diagnosed before 60 years of age or two first-degree relatives with CRC diagnosed at any age (n=1201 [97.4%])	▪ Positive FOBT (guaiac-based) within 6 months before referral ▪ Iron deficiency anaemia within previous 6 months ▪ Rectal bleeding or hematochezia within previous 12 months ▪ Unintentional weight loss of more than 10 pounds within previous 12 months ▪ OC within previous 10 years ▪ Barium enema within previous 5 years ▪ History of adenomatous polyp, CRC, or IBD ▪ History of familial adenomatous polyposis or hereditary nonpolyposis cancer syndromes ▪ Rejection of OC for any reason ▪ Medical condition that precludes the use of sodium phosphate preparation ▪ Pregnancy
Johnson et al., 2003 (76) USA	Patients >50 years of age who were prescheduled for colonoscopy and at a higher than average risk for CRC (prior history of CRC or colorectal polyp, strong family history of CRC, new onset of iron deficiency anaemia)	▪ Melena, hematochezia ▪ IBD ▪ Known familial polyposis
Pineau et al., 2003 (77) USA	Patients scheduled to undergo a clinically indicated colonoscopy: Average-risk CRC screening, a personal or family history of colorectal polyps or cancer, follow-up of an abnormal screening test, iron deficiency anaemia, minor gastrointestinal symptoms	▪ Personal or family history of a genetic polyp syndrome ▪ Prior colonic surgery ▪ Suspected diagnosis of IBD ▪ Bowel obstruction ▪ Diverticulitis ▪ Inability to tolerate bowel preparation ▪ Pregnancy ▪ Severe congestive heart failure ▪ Chronic renal failure

Study Country	Inclusion Criteria	Exclusion Criteria
Yee et al., 2003 (78) USA	Hematochezia, positive FOBT, iron deficiency anaemia, history of colonic polyps (n=110) Asymptomatic patients scheduled for routine colonic screening (n=72)	
Iannaccone et al., 2003 (79) Italy	Patients referred for CRC screening (n=31), positive FOBT, history of polyps, history of CRC, hematochezia, iron deficiency anaemia	▪ IBD ▪ Acute diverticulitis ▪ Pregnancy ▪ Inability to provide written consent
Thomeer et al., 2003 (43) Belgium	Patients scheduled for colonoscopy including primary CRC screening, secondary CRC screening, follow-up of polyposis coli, follow-up of colorectal tumour, bleeding, abdominal pain, change in stool habits, primary tumour search, weight loss, anaemia, other reasons	▪ IBD ▪ Pregnancy
Munikrishnan et al., 2003 (80) UK	Patients referred for colonoscopy (change in bowel habit, rectal bleeding, abdominal pain, loss of weight, rectal mass)	▪ Large bowel obstruction ▪ Pregnancy ▪ Barium studies within the previous 14 days
Ginnerup et al., 2003 (81)	Polyp/cancer surveillance, rectal bleeding, altered bowel habits, abdominal pain, CRC, preoperative colonoscopy, mucus per rectum, weight loss, anaemia	
Taylor et al., 2003 (82) UK	Rectal bleeding with change in bowel habits, change in bowel habit alone (>60 years of age), rectal bleeding without anal symptoms (>60 years of age), abdominal mass, iron deficiency anaemia	

*CRC indicates colorectal cancer; CTC, CT colonography; FOBT, fecal occult blood test; IBD, inflammatory bowel disease; NR, not reported; OC, optical colonoscopy.

Appendix 3: Sensitivity and Specificity of CT Colonography for Detection of Patients According to Polyp Size

Study, Subgroup Details (where applicable)	≥10 mm		6–9 mm		≤5 mm		≥6 mm		Any size	
	True positive	True negative	True positive	True negative	True positive	True negative	True positive	True negative	True positive	True negative
Johnson et al., 2008†					NR	NR			NR	NR
Without stool subtraction	41/45	30/31	14/21	49/55			55/66	3/10		
With and without stool subtraction	42/45	28/31	17/21	44/55			59/66	4/10		
Double reading	65/68	41/46	27/31	64/83			92/99	91/115		
Taylor et al., 2008			NR	NR	NR	NR			NR	NR
Regimen A	3/4	19/19					3/4	18/19		
Regimen B	3/3	20/20					7/7	16/16		
Regimen C	1/1	22/22					3/3	20/20		
Regimen D	3/3	17/17					5/7	12/13		
Overall	8/9	80/80					16/19	68/70		
Johnson et al., 2007 (Ad)†										
Slice thickness										
2.5 mm	2D: 6/8 3D: 6/9	2D: 137/140	2D: 5/10 3D: 6/10	2D: 129/138						
1.25 mm	2D: 6/8 3D: 6/9	3D: 137/140	2D: 6/10 3D: 6/11	3D: 131/142						
Double reading		2D:		2D:						
2.5 mm	16/19	138/141	9/14	132/139						
1.25 mm	8/19	3D: 138/141	10/14	3D: 132/140						
		205/210		194/215						
		205/210		196/215						
Arnesen et al., 2007 (52)	29/36	191/195	NR	NR	10/26 (<5 mm)	190/205 (<5 mm)	48/70 (≥5 mm)	146/161 (≥5 mm)	58/96	105/135
Graser et al., 2007 (53)	9/9 (>9 mm) CAD: 9/9	NR	16/16 CAD: 15/16	NR	25/31 CAD: 17/31	NR	25/25 CAD:24/25	NR	50/56 CAD: 41/56	NR
Bose et al., 2007 (54)	NR	NR	NR	NR	NR	NR	9/9	73/81	NR	NR
Sallam et al., 2007 (55)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Study, Subgroup Details (where applicable)	≥10 mm		6–9 mm		≤5 mm		≥6 mm		Any size	
	True positive	True negative	True positive	True negative	True positive	True negative	True positive	True negative	True positive	True negative
Chaparro et al., 2007 (56)	0/0	45/45	3/4 (5-10 mm)	41/46 (5–10 mm)	1/17 (<5 mm)	32/34 (<5 mm)	6/8 (≥5 mm)	36/41 (≥5 mm)	7/25	18/25
Reuterskiold et al., 2006 (57)	8/9	NR	5/9	NR	10/17	NR	13/18 (≥5 mm)	NR	23/35	NR
Kim et al., 2006 Patients with lesions: Wet Dry Overall	 12/13 9/9 21/22	 9/11 51/53 60/64	NR	NR	NR	NR	NR	NR	 23/24 39/46 62/70	 0/0 6/16 6/16
Yasumoto et al., 2006 (59)†	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Selcuk et al., 2006 (60)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Karla et al., 2006 (61)	NR	NR	NR	NR	NR	NR	NR	NR	NR	10/13
Juchems et al., 2006 (62)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rockey et al., 2005 CTC DCBE	 37/63 30/63	 529/551 496/551	 59/116 41/116	NR	 167/375	NR	 85/155 71/155	 409/459 376/459	NR	NR
Arnesen et al., 2005 (64)	9/12	84/88	NR	NR	NR	NR	18/27 (≥5 mm)	61/73 (≥5 mm)	25/41	36/59
Iannaccone et al., 2005 (65) Ad†‡	10/10	78/78	14/19	58/69	13/17	71/71	24/29	48/59	37/46	31/42
Wessling et al., 2005 (66)	6/6	71/72	NR	NR	NR	NR	NR	NR	NR	NR
Park et al., 2005 (67)	NR	NR	NR	NR	NR	NR	NR	NR	NR	19/26
Chung et al., 2005 (68)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rottgen et al., 2005 (69)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Abdel Razek et al., 2005 (70)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Cotton et al., 2004 (71) (L) 2D 3D	 23/42 25/42	 535/558 547/558	 23/76 27/76	 488/524 495/524	 37/274 48/274	 295/326 295/326	 41/104 47/104	 449/496 462/496	 NR NR	 NR NR
Van Gelder et al., 2004 (72)	26/31	200.5/218	NR	NR	NR	NR	35/45	142/204	87.5/141	33/108
Iannaccone et al., 2004 (73)†	17/17	186/186	NR	NR	27/31	172/172	44/48	128/138	71/79	114/124

Study, Subgroup Details (where applicable)	≥10 mm		6–9 mm		≤5 mm		≥6 mm		Any size	
	True positive	True negative	True positive	True negative	True positive	True negative	True positive	True negative	True positive	True negative
Cohnen et al., 2004 (74)	NR	NR	NR	NR	NR	NR	NR	NR	45/59	59/78
Hoppe et al., 2004 (75)	19/20‡	65/66	NR	NR	NR	NR	26/34‡	51/58	NR	NR
Macari et al., 2004 (42)	3/3	64/65	NR	NR	NR	NR	NR	NR	NR	NR
Pickhardt et al., 2003 (9)(Ad)	45/48	1138/1185	NR	NR	NR	NR	149/168	848/1065	NR	NR
Johnson et al., 2003 (76)† Individual reading Double reading	 15/31‡ 30/47‡	 426/437 625/656	(5–9 mm) 24/46 45/69	(5–9 mm) 385/423 542/634	NR	NR	NR	NR	NR	NR
Pineau et al., 2003 (77) (L)	18/20	175/185	NR	NR	NR	NR	38/45	133/160	55/89	82/116
Yee et al., 2003 (78) Supine Prone Combined supine and prone	NR	NR	NR	NR	NR	NR	NR	NR	 73/114 68/114 103/114	 58/68 66/68 56/68
Iannaccone et al., 2003 (79)	NR	NR	NR	NR	NR	NR	NR	NR	69/72	83/86
Thomeer et al., 2003 (43)†	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Munikrishnan et al., 2003 (80)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Ginnerup et al., 2003 (81)	12/17 (10-19mm)	NR	19/25	NR	NR	NR	40/44§	101/104	NR	NR
Taylor et al., 2003 (82)‖	4/4	50/50	1/2	NR	10/19	25/29	5/6	NR	15/25	25/29

*2D indicates 2-dimensional; 3D, 3-dimensional; Ad, reported adenomas; CAD, computer-aided detection [algorithm]; CTC, CT colonography; DCBE, double contrast barium enema L, reported lesions; NR, not reported.

†Mean of different readers.

‡Including cancers.

§Includes masses/cancer.

‖Cancers were manually excluded.

Appendix 4: Sensitivity of CT Colonography for Detection of Polyps According to Polyp Size

	≥10 mm	6–9 mm	≤5 mm	≥6 mm	Any Size
	True Positive	True Positive	True Positive	True Positive	True Positive
Johnson et al., 2008 (24)†‡			NR		NR
Without stool subtraction	47/58	16/29		63/87	
With and without stool subtraction	49/58	21/29		70/87	
Double reading	76/87	35/44		111/131	
Taylor et al., 2008 (50)					
Regimen A	1/2	N/A	3/10		
Regimen B	3/3	5/6	10/30		
Regimen C	1/1	2/2	6/20		
Regimen D	3/3	2/4	4/12		
Overall	8/9	9/12	23/72	17/21	40/93
Johnson et al., 2007 (51) (Ad)†‡			NR	NR	NR
Slice thickness					
2.5 mm	2D: 6/8 3D: 6/9	2D: 5/13 3D: 5/13			
1.25 mm	2D: 6/8 3D: 6/9	2D: 5/13 3D: 6/13			
Double reading					
2.5 mm	16/19	9/20			
1.25 mm	18/19	11/20			
Arnesen et al., 2007 (52)§		NR	(<5 mm)	(≥5 mm) 66/110	
	34/44		16/100		82/210
Graser et al., 2007 (53)					
	(>9 mm)				
Radiologist	13/14	18/19	64/85	31/33	95/118
CAD	12/14	17/19	43/85	29/33	72/118
Bose et al., 2007 (54)	NR	NR	14/69	11/11	25/80
Sallam et al., 2007 (55)	5/5	7/10	21/30	12/15	33/45
Chaparro et al., 2007 (56)‖		(5–10 mm)	(<5 mm)	(≥5 mm)	
	0/0	¾	5/34	3/4	8/38
Reuterskiold et al., 2006 (57)‖		(5–9 mm)	(<5 mm)	(≥5 mm)	
	11/13	18/24	33/61	39/47	72/108

	≥10 mm	6–9 mm	≤5 mm	≥6 mm	Any Size
	True Positive	True Positive	True Positive	True Positive	True Positive
Kim et al., 2006 (58)		(5–9 mm)		(≥5 mm)	
Wet	12/13	19/26	11/24	31/39	40/61
Dry	10/10	20/28	41/89	30/38	71/127
Overall	22/23	39/54	52/113	61/77	111/188
Yasumoto et al., 2006 (59)†					
One-way	26/29	55/70	39/56	81/99	120/155
Two-way	28/29	61/70	48/56	89/99	137/155
Selcuk et al., 2006 (60)	4/4	6/7	9/11	10/11	19/22
Karla et al., 2006 (61)	30/30	29/30	17/26	59/60	76/86
Juchems et al., 2006 (62)¶		(5–10 mm)	(<5 mm)	(≥5 mm)	
Conventional endoluminal	2/2	13/16	6/17	17/20	23/37
Colon dissection	3/4	9/16	8/17	12/20	20/37
Rockey et al., 2005 (63)					
CTC	40/76	75/158	167/375	115/234	282/609
DCBE	34/76	47/158	120/375	81/234	201/609
Arnesen et al., 2005 (64)		NR		≥5 mm	
	12/18		9/44	27/46	36/90
Iannaccone et al., 2005 (65)†§					
	11/11	20/26	27/57	32/37	58/94
Wessling et al., 2005	7/7	13/16	19/26	20/23	39/49
Park et al., 2005 (67)‖	6/7	10/12	15/39	16/19	31/58
Chung et al., 2005 (68)	6/6	15/16	16/19	21/22	37/41
Rottgen et al., 2005 (69)		(5–9.9 mm)		(>5 mm)	
2D axial CTC	6/6	5/7	11/21	11/13	22/34
3D virtual CTC	6/6	7/7	18/22	13/13	31/35
3D colon dissection	6/6	7/7	20/22	13/13	33/35
Abdel Razek et al., 2005 (70)	3/3	1/1	0/2	4/4	4/6
Cotton et al., 2004 (71)					
2D(L)	28/54	27/119	50/654	55/173	105/827
Cotton et al., 2004 (71)					
3D(L)	30/54	33/119	39/561	63/173	102/734
Van Gelder et al., 2004 (72)			< 6 mm		
	36.5#/48	25/36	140.5#/405	61.5#/84	202/489
Iannaccone et al., 2004 (73)†	24/24	NR	43/83	68/79	104/162
Cohnen et al., 2004 (74)	11/14	12/14	61/107	23/28	84/135
Hoppe et al., 2004 (75) (L)	22/31	14/28	16/63	36/59	52/122

	≥10 mm	6–9 mm	≤5 mm	≥6 mm	Any Size
	True Positive	True Positive	True Positive	True Positive	True Positive
Macari et al., 2003 (42)	3/3	9/17	9/78	12/20	21/98
Pickhardt et al., 2003 (9) (Ad)	47/51	NR	NR	180/210	NR
Johnson et al., 2003 (76)†		(5–9 mm)	NR	(≥5 mm)	NR
Single reading	18/39	26/63		44/102	
Double reading	37/59	51/94		88/153	
Pineau et al., 2003 (77) (L)	21/27	36/48	37/126	57/75	94/201
Yee et al., 2003 (78)		(5–9.9 mm)		(≥5 mm)	
Supine	24/41	42/89	65/179	66/130	131/309
Prone	21/41	37/89	54/179	58/130	112/309
Combined	38/41	71/89	108/179	109/130	217/309
Iannaccone et al., 2003 (79)§	13/13	20/24	19/37	33/37	52/74
Thomeer et al., 2003 (43)†		(5–9 mm)	NR	(≥5 mm)	NR
	11/12	25.5#/39		36.5#/51	
Munikrishnan et al., 2003 (80)	12/12	5/6	8/15	17/18	25/33
Ginnerup et al., 2003 (81)	(10–19 mm)		NR	(6–19 mm)	NR
	19/23	22/31		41/54	
Taylor et al., 2003 (82)‖	4/4	3/4	18/41	7/8	25/49

*2D refers to 2-dimensional; 3D, 3-dimensional; CAD, computer-aided detection [algorithm]; CTC, computed tomographic colonography; DCBE, double contrast barium enema; L, reported lesions; NR, not reported.
†Mean of different readers were calculated.
‡Reported adenomas.
§Including cancers.
‖Cancers were manually excluded.
¶Per lesion for colon dissection report.
#A nonintegral value is a mean calculated in the original report.

Appendix 5: Forest Plots and Pooled Sensitivities of CT colonography for Polyps of Different Sizes

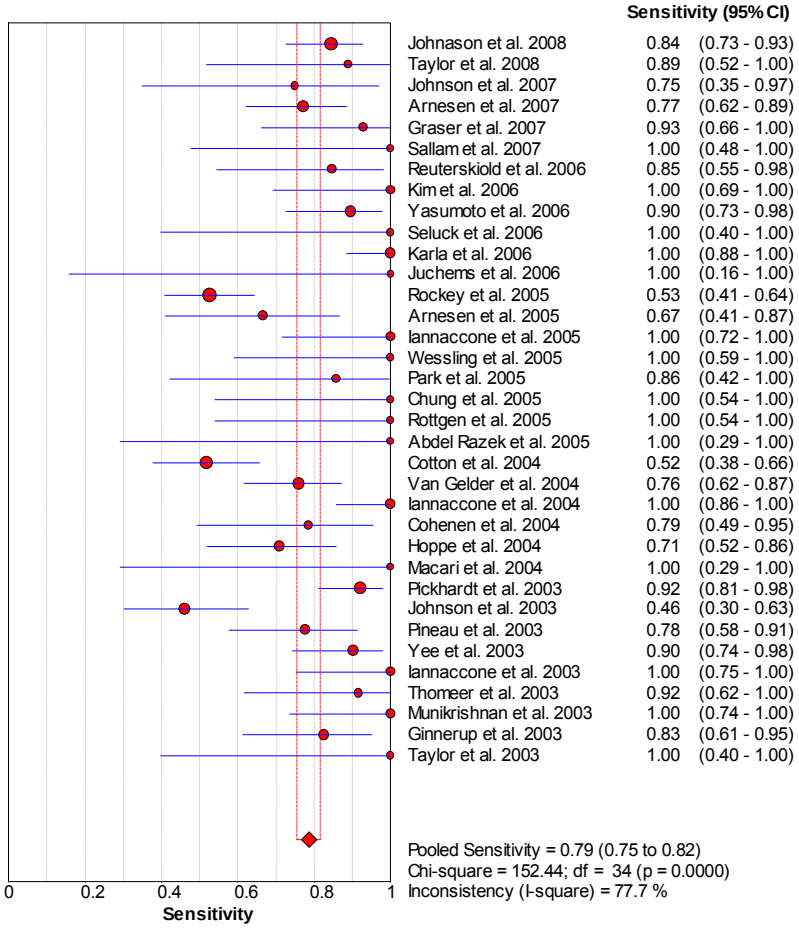

Figure 50: Sensitivity of CT Colonography for the Detection Large-Size Polyps

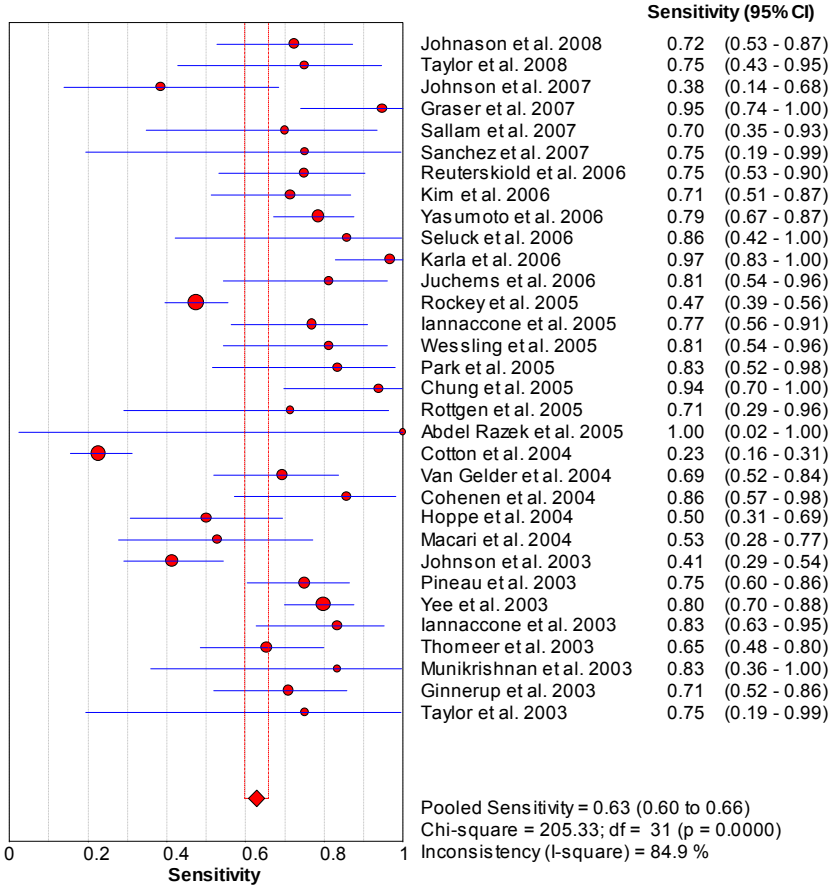

Figure 51: Sensitivity of CT Colonography for the Detection of Medium-Size Polyps

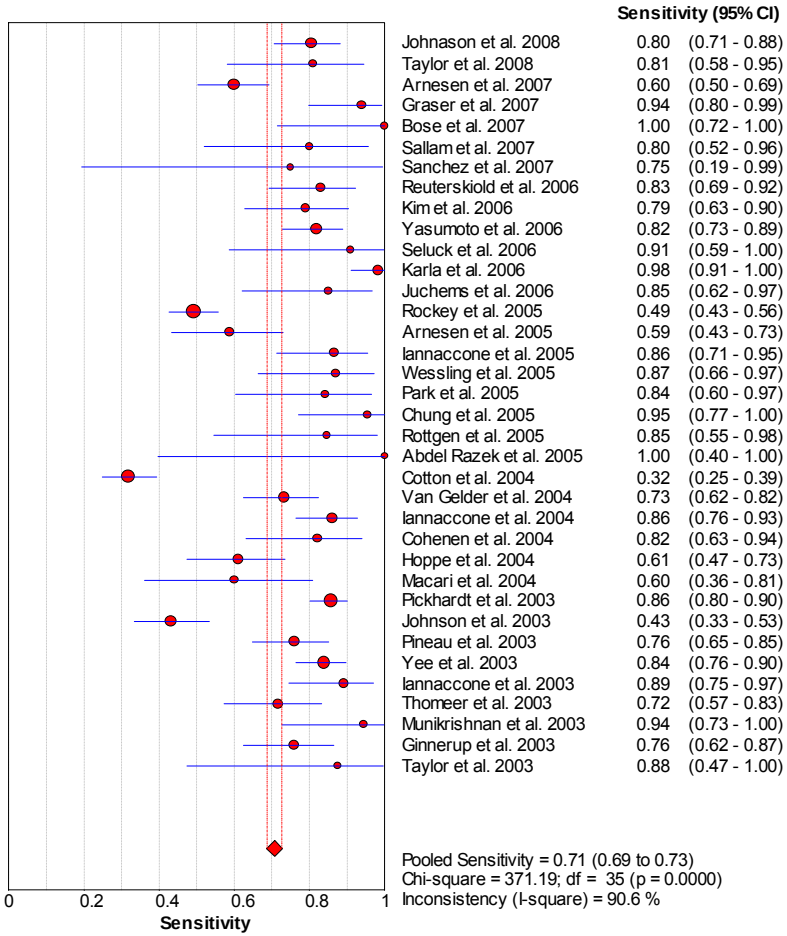

Figure 52: Sensitivity of CT Colonography for the Detection Medium- to Large-Size Polyps

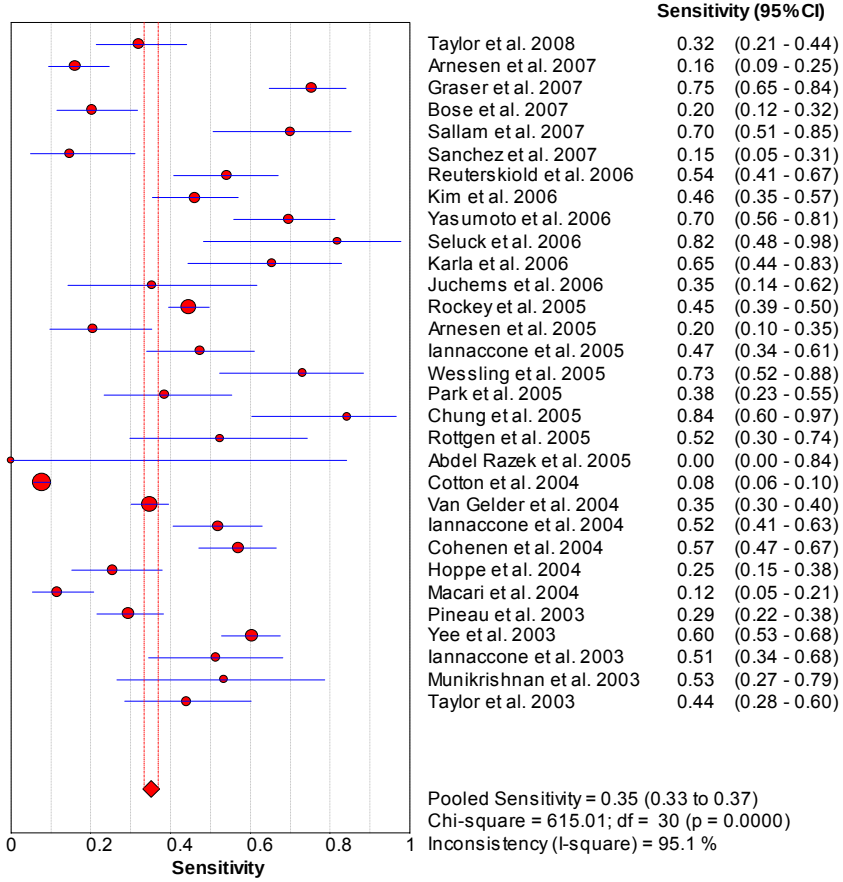

Figure 53: Sensitivity of CT Colonography for the Detection of Small-Size Polyps

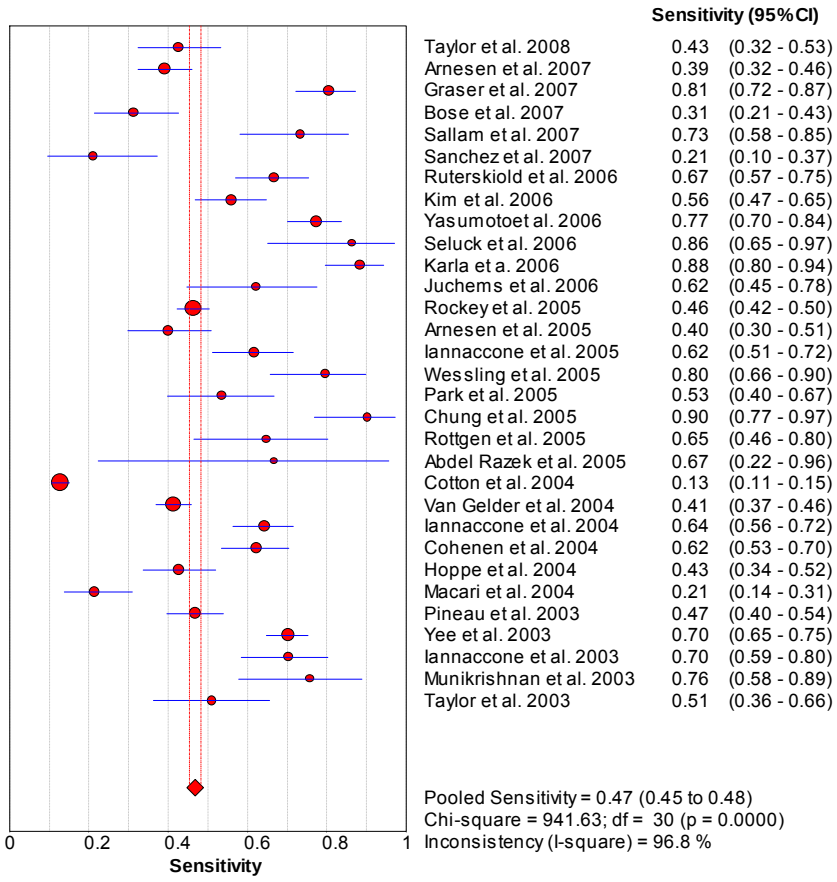

Figure 54: Sensitivity of CT Colonography for the Detection of Polyps of Any Size

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Ref Type: Generic

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