Computed Tomography Colonography

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MSAC application 1095

Assessment Report

Electronic copies of the report can be obtained from the Medical Service Advisory Committee's Internet site at http://www.msac.gov.au/

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The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

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The procedure

Computed tomography colonography (CTC) is a minimally invasive radiological technique for imaging the colon and rectum. It involves the use of a spiral CT scanner to acquire multiple simultaneous tomographic sections ('slices') of the colon and rectum during one rotation of the x-ray source. A computer software program reformats these data to produce two dimensional images or three-dimensional reconstructions of the bowel (also referred to as 'virtual colonoscopy'). Patients require a bowel preparation the day before the procedure. At the time of scanning, the colon is insufflated with air or carbon dioxide via a catheter placed in the rectum. The patient does not require sedation.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of evidence is thus the basis of decision making when funding is sought under Medicare. A team from the NHMRC Clinical Trials Centre was engaged to conduct a systematic review of literature on CTC. An advisory panel with expertise in this area then evaluated the evidence and provided advice to MSAC.

MSAC's assessment of computed tomography colonography

Clinical need

Colorectal cancer is the most common cancer (excluding non-melanoma skin cancer) and the third most common cause of cancer death reported to Australian cancer registries. In 2001, there were 12,844 new cases of colorectal cancer reported and 4,754 deaths, accounting for 14.5% of all new cases of cancer and 13.1% of cancer deaths (Australian Institute of Health & Welfare (AIHW) & Australasian Association of Cancer Registries (AACR) 2004).

CTC has been proposed as a minimally invasive alternative to double contrast barium enema (DCBE) and colonoscopy in patients requiring investigation or surveillance for the detection of colorectal neoplasia (cancers and polyps). CTC does not allow biopsy like colonoscopy, but can be used in patients in whom colonoscopy is contraindicated or cannot be completed.

Reimbursement for CTC has been available as an interim item under the Medicare Benefits Schedule since May 2005 for two indications: (i) following an incomplete colonoscopy; and (ii) in patients with fistulous disease, obstructed colon, or megacolon in whom colonoscopy is contraindicated. Over the 6-month period, May to October 2005, 665 CTC were billed under these items in Australia with a trend of increasing CTC

requests over this period. This figure does not include the number of CTCs performed for other indications, nor the number of CTCs performed on public patients treated in public hospitals. It is difficult to estimate the potential magnitude of CTC use should it be funded for the diagnosis or exclusion of colorectal neoplasia under wider indications because data about the number of DCBE and colonoscopies performed in Australia each year do not record the indication for testing.

Review methods

This review addresses two research questions to determine the potential value of CTC for the diagnosis or exclusion of colorectal neoplasia in Australia.

Review question 1

What is the safety, effectiveness and cost-effectiveness of CTC versus DCBE and versus colonoscopy for the diagnosis or exclusion of colorectal neoplasia in symptomatic patients or in patients that are asymptomatic but at high risk of colorectal neoplasia due to a personal or family history of colorectal polyps or cancer?

Review question 2

What is the safety, effectiveness and cost-effectiveness of CTC versus DCBE for the diagnosis or exclusion of colorectal neoplasia in symptomatic or high-risk patients who are ineligible for colonoscopy due to patient contraindications or the inability to perform or complete the test?

Secondary analyses were conducted to assess the safety, effectiveness and cost-effectiveness of CTC versus DCBE and versus colonoscopy to detect other specific colorectal abnormalities and all colorectal abnormalities.

Literature search

A systematic review of the medical literature was undertaken using MEDLINE, Pre-MEDLINE, EMBASE, Current Contents, the Cochrane Library and Health Technology Assessment databases to identify relevant studies and systematic reviews published between January 1994 and June 2005.

This search did not identify any studies comparing overall health outcomes following the use of CTC, DCBE or colonoscopy. Conclusions about the safety and effectiveness of CTC are based on four systematic reviews and 24 clinical studies that reported on CTC and/or DCBE safety and accuracy with or without comparisons with colonoscopy and 11 studies that reported on patient preferences or quality of life outcomes associated with these tests.

Safety

CTC is a relatively safe procedure compared to DCBE and as least as safe as, or safer than, diagnostic colonoscopy. Both CTC and DCBE expose patients to ionizing radiation and are associated with a very small risk of colonic perforation.

Effectiveness

CTC accuracy

CTC is generally highly sensitive and specific for the diagnosis or exclusion of cancers and polyps ≥ 10 mm in symptomatic patients and asymptomatic patients at high risk of colorectal neoplasia (11 studies of variable quality, median CTC sensitivity 84% (range 55-100%); median CTC specificity 97% (range 74-100%)). Estimates of CTC accuracy are higher for the detection of cancer alone (meta-analysis of four studies: CTC sensitivity 97% (95% CI 89-100%); CTC specificity 98% (95% CI 95-99%). These findings are consistent with results from three published systematic reviews.

CTC is only moderately sensitive for the detection of lesions 6-9 mm and poorly sensitive for lesions < 5 mm (lesions 6-9 mm: six studies, CTC sensitivity range 30-80%, CTC specificity range 93-99%; lesions ≤ 5 mm: four studies, CTC sensitivity range 14-57%, CTC specificity range 83-97%).

The variation observed between studies demonstrates that CTC is less accurate in some population subgroups or settings. The extent to which patient characteristics, prevalence of disease, CTC techniques, the experience of those performing and interpreting the tests or other factors may influence CTC performance has not yet been clearly defined.

Relative accuracy of CTC, DCBE and colonoscopy

Studies comparing CTC with DCBE and colonoscopy provide the best evidence to assess the relative accuracy of these tests. This evidence was limited to one study of fair quality (Rockey et al 2005) that found CTC and DCBE accuracy to be lower than noncomparative studies and systematic reviews of CTC accuracy. This study indicated that CTC is a more specific test than DCBE, but less sensitive and specific than colonoscopy for the detection of cancers and polyps ≥ 10 mm. This study also suggested that CTC may be a more sensitive test than DCBE; this difference did not reach statistical significance for lesions ≥ 10 mm, but was shown to be statistically significant for lesions 6-9 mm.

Relative accuracy of CTC, DCBE and colonoscopy for the detection of lesions ≥ 10mm (Rockey et al 2005)

Test	Sensitivity (95% CI)	p value[1]	Specificity (95% CI)	p value[1]
CTC	59% (46-71%)		96% (94-98%)	
DCBE	48% (35-61%)	0.11	90% (87-92%)	< 0.0001
colonoscopy	98.3% (91-100%)	< 0.0001	99.6% (99-100%)	< 0.0001

1   p value CTC versus comparator test.

Two studies of fair quality suggest that CTC may be more accurate than DCBE for the detection of all colorectal disease but less sensitive than colonoscopy; however, no studies have directly compared these tests (Munikrishnan et al 2003, Durdey et al 1987).

CTC patient preferences and quality of life

Three studies of fair to high quality have reported a statistically significant difference in patient preference, satisfaction and experience of pain or discomfort in favour of CTC versus DCBE (Gluecker et al 2003, Taylor et al 2005, Taylor et al 2003).

The evidence reviewed also suggests that CTC may be preferred over colonoscopy. However, comparison of pain and discomfort experienced by patients undergoing both tests have shown mixed results with three of eight studies reporting results in favour of colonoscopy.

Additional considerations

CTC is successful in visualising the entire colon in at least 90% of patients following an incomplete colonoscopy and may detect colorectal lesions in 18 to 27% of patients that were not identified at the initial incomplete colonoscopy (Neri et al 2002, Morrin et al 1999, Macari et al 1999, Minyue et al 2002).

CTC has an advantage over DCBE for visualising the proximal colon in patients with a distal obstruction. It also has an advantage over DCBE due to technical difficulties of coating the bowel wall with barium to conduct a DCBE following a colonoscopy.

CTC also offers the opportunity for detecting extracolonic lesions that cannot be identified at DCBE or colonoscopy. Rates of clinically significant extracolonic findings ranged between 1% and 13% in six studies reviewed. Incidental and clinically nonsignificant extra-colonic findings were reported in 19% to 63% of patients by three studies. The consequences of these findings have not been assessed. Clinically significant findings may be expected to change patient management, whereas insignificant findings may result in additional unnecessary investigations and patient distress.

No studies were designed to compare test failure rates for CTC versus DCBE and/or colonoscopy; however, the studies reviewed suggest that CTC failure rates are at least comparable to or better than DCBE and colonoscopy.

Cost-effectiveness

An economic model was developed to estimate the incremental cost-effectiveness of CTC compared to colonoscopy and compared to DCBE in the patients of interest. The analysis included one- and two-way sensitivity analyses of key parameters.

For the comparison of CTC with DCBE, the modelled analysis shows a cost per life year saved of $25,420 of CTC compared to DCBE in the base case scenario (CTC cancer sensitivity: 59%, DCBE cancer sensitivity: 48%) with cost-effectiveness widely varying in sensitivity analyses from $4,882 per life year saved to a situation where CTC is dominated by DCBE.

The base case economic analysis further indicates that CTC is less costly, but also less effective than colonoscopy. The incremental cost of colonoscopy versus CTC per life year saved is $1,659 for the base case (CTC sensitivity for cancer=59%, colonoscopy sensitivity for cancer=98%). In sensitivity analyses, the cost per life year saved for colonoscopy ranged between $13,955 and a situation where colonoscopy is more effective and associated with less costs than CTC.

The results of the economic analysis must be interpreted with caution due to uncertainties around model parameters, in particular the uncertainty around the estimates of test sensitivity for cancer.

Review Question 1: CTC versus DCBE and versus colonoscopy

CTC is a relatively safe test compared to DCBE and colonoscopy.

Evidence about CTC accuracy for the detection of cancers and polyps $\geq$ 10 mm compares favourably with DCBE. There is also some evidence to suggest that patients prefer CTC over DCBE. CTC is more costly than DCBE and an economic model suggests a base case incremental cost per life year saved for CTC compared to DCBE of $25,420; results of the sensitivity analysis ranged from a cost per life year saved of $4,882 for CTC compared to DCBE to a situation where CTC is dominated by DCBE (more costly and less effective).

CTC is less accurate than colonoscopy for the detection of cancers and polyps $\geq$ 10 mm. There is also some evidence to suggest that patients prefer CTC over colonoscopy. CTC is less costly than colonoscopy and an economic model found a base case incremental cost per life year saved of $1,659 for colonoscopy compared to CTC. The cost per life year saved for colonoscopy in sensitivity analyses ranged between $13,955 and a situation where colonoscopy is more effective and associated with less costs than CTC.

Review Question 2: CTC versus DCBE in patients with a contraindication to colonoscopy

There is little evidence for a comparison of CTC versus DCBE accuracy in patients following an incomplete colonoscopy. The evidence available indicates that CTC is successful in visualising the entire colon in at least 90% of patients following an incomplete colonoscopy. CTC also has demonstrated advantages over DCBE in visualising the proximal colon in patients with a distal obstruction, the detection of extracolonic disease, and patient preferences and tolerance of testing. Another consideration favouring the use of CTC is that it can be performed immediately after a failed colonoscopy, whereas coating the bowel wall with barium can be difficult to achieve after colonoscopy.

CTC is more costly than DCBE. An economic analysis based on a general model of CTC compared to DCBE in symptomatic patients found a base case incremental cost per life year saved for CTC compared to DCBE of $25,420; results of the sensitivity analysis ranged from a cost per life year saved of $4,882 for CTC compared to DCBE to a situation where CTC is more costly and less effective than DCBE.

Recommendation

Computed tomography colonography (CTC) is a relatively safe procedure. CTC, double contrast barium enema (DCBE) and colonoscopy are associated with a small risk of complications.

Evidence in relation to the comparison of CTC with colonoscopy indicates that CTC is less effective. MSAC recommends that public funding for CTC as a substitute investigation for colonoscopy should not be supported.

On the basis of the strength of evidence pertaining to the effectiveness and cost-effectiveness, MSAC recommends that public funding for CTC for exclusion of colorectal neoplasia in symptomatic or high risk patients who are either ineligible for colonoscopy due to patient contraindications or where there is an inability to perform or complete a colonoscopy, should be supported.

- The Minister for Health and Ageing accepted this recommendation on 24 August 2006.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of Computed Tomography Colonography (CTC) as a diagnostic test for the detection of colorectal disease, in particular polyps and cancer. MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's terms of reference and membership are at Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence for CTC for the diagnosis or exclusion of colorectal neoplasia in symptomatic patients or in asymptomatic patients at high risk of colorectal neoplasia. CTC is compared to double contrast barium enema (DCBE) and to colonoscopy. It is also compared to DCBE in patients who are not eligible for colonoscopy due to patient contraindications or the inability to perform or complete the test.

Background

The procedure

Computed tomography colonography (CTC) is a minimally invasive radiological technique that is used to provide images of the colon and rectum (large bowel). A spiral CT scanner is used to acquire multiple simultaneous tomographic sections ('slices') of the colon and rectum during one rotation of the x-ray source. Software programs are used to reformat these data and display two-dimensional images (in axial, sagittal or coronal planes) or three-dimensional reconstructions of the bowel (also referred to as 'virtual colonoscopy'). In addition to these technological requirements, the bowel must be cleansed and distended prior to testing. Patients are asked to use a bowel preparation the day before the procedure to empty the bowel. At the time of the procedure, the patient is positioned on the CT scanner and a catheter is placed in the rectum to inflate the colon with air or carbon dioxide. Two scans of the abdomen are then performed, one with the patient lying on their back (prone positioning) and one with the patient lying on their stomach (supine positioning). The patient does not require sedation and the entire procedure usually takes less than 30 minutes for set-up and scanning.

The first clinical report of the use of CTC was published in 1996 (Hara et al 1996). The Royal Australian and New Zealand College of Radiologists report that the technique has been performed in Australia since 1997.

Intended purpose of computed tomography colonography

CTC is primarily intended to detect colorectal neoplasia (benign polyps and malignant cancers). It has been proposed for use in the following three patient groups:

1. a diagnostic test in patients with symptoms of colorectal disease;

2. a surveillance test in patients with a past history of colorectal polyps or cancer; and

3. a screening test in asymptomatic patients to detect pre-malignant colorectal polyps and cancers

This report presents an evaluation of CTC for the diagnosis or exclusion of colorectal neoplasia and other colorectal disease in symptomatic patients or in asymptomatic patients with a high risk of colorectal neoplasia. In this role it may be considered as a replacement for double contrast barium enema (DCBE) or colonoscopy.

This report does not assess the value of CTC as a screening test in patients at average risk of colorectal neoplasia.

Clinical need/burden of disease

This section provides an overview of the incidence and mortality of colorectal cancer, the natural history of colorectal cancer, common patient presentations and differential diagnoses. Health service data related to colorectal diagnostic procedures are also presented.

Incidence and mortality rates of colorectal cancer

Colorectal cancer is the most common cancer (excluding non-melanoma skin cancer) and the third most common cause of cancer death reported to Australian cancer registries. In 2001, there were 12,844 new cases of colorectal cancer reported and 4,754 deaths, accounting for 14.5% of all new cases of cancer and 13.1% of cancer deaths (Australian Institute of Health & Welfare (AIHW) & Australasian Association of Cancer Registries (AACR) 2004). In 2001, premature death from colorectal cancer was responsible for an estimated 29,768 person-years of life lost before the age of 75, making it second only to lung cancer (AIHW & AACR 2004).

The incidence rates of colorectal cancer have increased since 1991 by an average of 0.3% for males and 0.1% for females per year; however, mortality rates have fallen steadily by 1.2% per year for males and 1.6% for females between 1991 and 2001 (Figure 1, AIHW & AACR 2004).

Figure 1   Incidence and mortality rates of colorectal cancer in Australia, by sex, 1983-2001
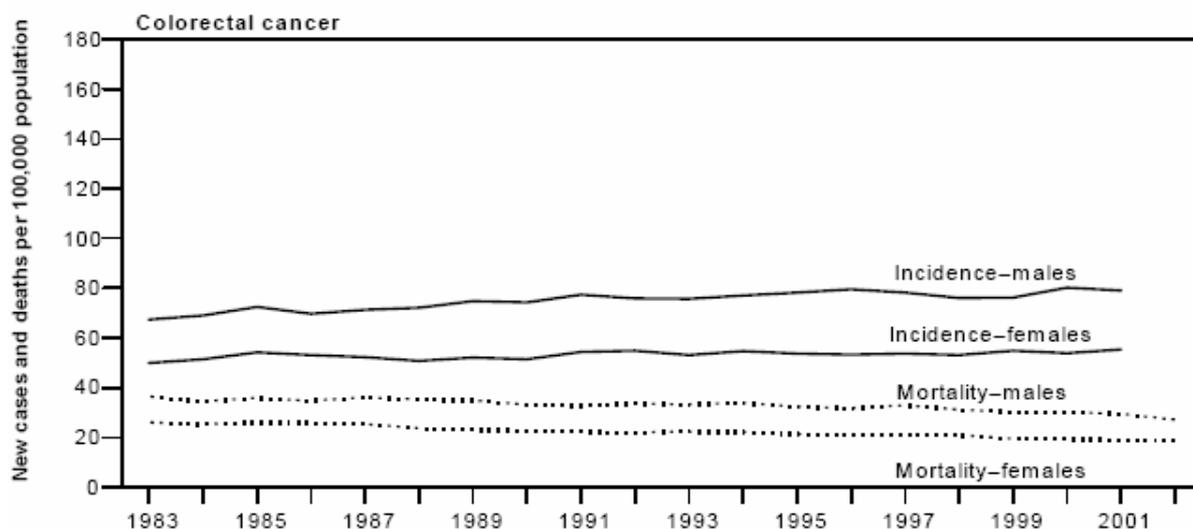
Source: Cancer in Australia 2001 (AIHW & AACR 2004), figure reproduced with permission

The incidence of colorectal cancer is higher in men (annual age standardised incidence 79 per 100,000 based on the Australian population in 2001) than women (55 per 100,000) and increases with age (Figure 2).

Figure 2 Age-specific incidence rates for colorectal cancer in Australia, by sex, 2001
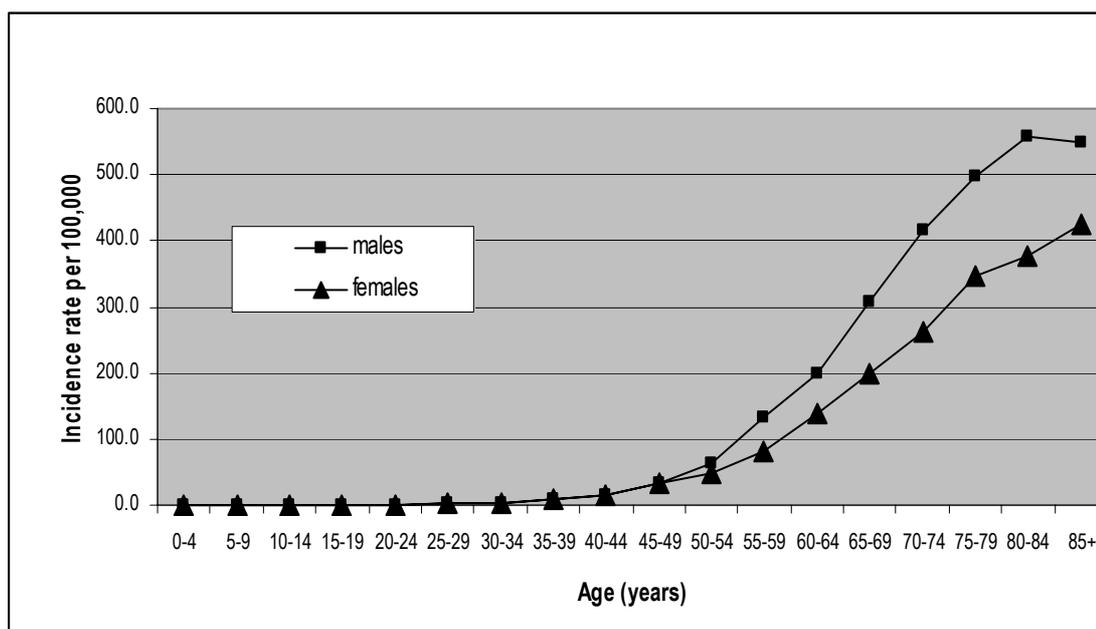
Source: Cancer in Australia 2001 (AIHW & AACR 2004).

The Australian age-standardised incidence rate of colorectal cancer is high compared to other developed countries. Comparisons with standardisation to the Australian population and the World Standard Population shows an annual incidence rate of 50 per 100,000 men and 35 per 100,000 women which is higher than the average for other developed countries (37 and 25 per 100,000 respectively, AIHW & AACR 2004). Australia's age-standardised male and female mortality rates for colorectal cancer are also high by world standards being higher than those of Canada, the United States and the United Kingdom, but not New Zealand (AIHW & AACR 2004).

In addition to age, other known predisposing factors for colorectal cancer include a family history of colorectal cancer and prior colonic disease. An association between colorectal cancer and a diet rich in animal fats, red meat and processed meat has also been observed but this evidence has not been consistent across all studies (Shureiqi 2004). There is also some observational evidence that exercise has a protective effect against colorectal cancer (Shureiqi 2004).

Natural history and staging of colorectal cancer

Colorectal cancers most commonly develop from the mucosal lining of the large bowel. The underlying mechanism is believed to be an accumulation of genetic alterations that progressively alter the normal structure and function of the bowel wall lining. The earliest anatomical change known to be a precursor to colorectal cancer is called an aberrant crypt focus. Later pre-malignant changes include adenomatous polyps (outgrowths of tissue from the bowel wall). These polyps can be detected by direct visualisation of the bowel wall at colonoscopy or sigmoidoscopy. The interval from the development of an adenomatous polyp (benign neoplasm) to transformation into cancer (malignant neoplasm) is estimated to be around 10 years (Winawer et al 2003), although only a minority of all polyps progress to cancer (Stryker et al 1987). The probability of progression to cancer is related to the size of the polyp. Polyps detected at colonoscopy

or sigmoidoscopy can be removed at the time of the procedure and examined histologically. Large observational studies have demonstrated reduced rates of colorectal cancer among patients who have participated in colonoscopy screening programs with excision of adenomatous polyps (Citarda et al 2001, Winawer et al 1993). This evidence supports the theory of an adenoma-carcinoma sequence of tissue changes. Guidelines for colorectal cancer screening programs and the management of colorectal polyps have recommended that patients with polyps greater than or equal to 10 mm or patients with three or more smaller polyps should be referred for polypectomy (Van Dam et al 2004). It has been estimated that 1% of polyps greater than or equal to 10 mm will progress to cancer each year (Van Dam et al 2004). The risk is smaller for polyps less than 5 mm and a decision to proceed to polypectomy versus surveillance with follow-up testing at 3-5 years will depend on other risk factors such as the patient's age, comorbidity, past history and family history of neoplasia (Bond et al 1993). Guidelines for the management of polyps 5-9 mm are less well defined. In polyps in this size range, studies have indicated that 2-7% will contain high grade dysplasia and 0.9% will show invasive cancer (Van Dam et al 2004).

Colorectal cancers can be classified according to their histology and stage. The most common histological type is adenocarcinoma. Staging of disease is essential to determine prognosis and select optimal treatment. The American Joint Committee on Cancer (AJCC) recommends staging using the International Union Against Cancer's TNM classification system of cancer according to the extent of the primary tumour (T0-T4), spread to regional lymph nodes (N0-N2) and presence of distant metastases (M0-M1) as follows:

Table 1   Stages and prognosis for colorectal cancers

Stage[1]	TNM classification	Definition	5-year survival[2]
Stage 0	Tis, N0, M0	Carcinoma in situ	
Stage I	T1, N0, M0	tumour invades submucosa (T1)	93%
	T2, N0, M0	tumour invades muscularis propria (T2)	
Stage IIA	T3, N0, M0	tumour invades through muscularis (T3)	85%
Stage IIB	T4, N0, M0	tumour directly invades other organs (T4)	72%
Stage IIIA	T1-T2, N1, M0	T1-T2 with metastases in 1-3 regional lymph nodes (N1)	83%[3]
Stage IIIB	T3-T4, N1, M0	T3-T4 with metastases in 1-3 regional lymph nodes (N1)	64%
Stage IIIC	Any T, N2, M0	Any T with metastases in ≥ 4 regional lymph nodes (N2)	44%
Stage IV	Any T, any N, MI	Any T, any N with distant metastasis (M1)	8%

1 Source: American Joint Committee on Cancer, 6th edition, 2003.
2 Source: O'Connell et al, 2004
3 No significant difference detected in 5 year survival between Stages IIIA and IIA

This staging system has superseded the Dukes pathological staging system which graded cancers according their spread into submucosa (Dukes A), through muscle (Dukes B), to lymph nodes (Dukes C) or distant metastases (Dukes D), corresponding to AJCC staging I, II, III and IV respectively.

Early detection and surgical excision can be curative; however, prognosis is poorer for more advanced disease, as shown in Table 1. Early, accurate diagnosis of patients presenting with symptoms suggestive of colorectal cancer is therefore critical.

Clinical presentation of colorectal cancer

Most patients with colorectal polyps and early colorectal cancer are asymptomatic. Patients with advanced cancers may present with abdominal symptoms such as pain, persistent changes in bowel habits or bleeding from the rectum. General symptoms and signs can include loss of appetite, weight loss, nausea and vomiting, or unexplained iron deficiency anaemia.

General examination may reveal signs of advanced disease such as an abdominal mass, but in many cases the examination is normal and further investigation including imaging of the bowel is required to diagnose or exclude cancer.

The draft NHMRC guidelines (2005) for the prevention, early detection and management of colorectal cancer recommend a thorough examination of the anus, rectum and colon for all symptomatic patients. The use of sigmoidoscopy at the time of the digital rectal examination is recommended to detect anal abnormalities such as haemorrhoids and fissures at the initial examination (NHMRC 2005). The draft guidelines recommend colonoscopy as the most accurate investigation for assessing the colon and rectum. DCBE plus sigmoidoscopy or CTC is recommended as an alternative test following an incomplete colonoscopy or where there is a problem with local availability or expertise for colonoscopy (NHMRC 2005).

Classification of patient risk

Risk factors for colorectal cancer include patient age over 40 years, personal history of colorectal neoplasia or inflammatory bowel disease (ulcerative colitis and Crohn's disease), and family history of colorectal neoplasia or gynaecological cancer (NHMRC 2005). Certain genetic syndromes such as familial adenomatous polyposis and hereditary non-polyposis colon cancer are also associated with a high risk of colorectal disease. The NHMRC guidelines provide a three-level classification of patient risk for their current recommendations for screening (Table 2). These guidelines also recommend regular colonoscopy for surveillance of patients with a past history of adenomatous polyps.

Table 2   NHMRC classification of colorectal cancer risk and screening recommendations

Risk group	Risk estimation	Screening/surveillance recommendation

1: Average risk/slightly elevated risk
• Asymptomatic, no risk factors
• One 1st or 2nd degree relative with colorectal cancer diagnosed ≥ 55 yrs
	If asymptomatic, no risk factors, age 50 yrs:
	    Absolute risk: at 5 years: 1 in 300
	                at 10 years: 1 in 100
	                at 20 years: 1 in 30
	If one 1st degree relative diagnosed ≥ 55 yrs:
	up to a further 2-fold increase in relative risk
		Individuals aged 50 years of older:
		• Faecal occult blood tests every 1-2 years
		• Consider flexible sigmoidoscopy every 5 years

2: Moderate risk • One 1st degree relative with colorectal cancer diagnosed < 55 yrs • Two 1st or 2nd degree relatives on the same side of the family with colorectal cancer diagnosed at any age	3-6 fold increase in relative risk	• Colonoscopy every 5 years, or from 10 years prior to the age of the earliest diagnosis of colorectal cancer in the family • Flexible sigmoidoscopy and DCBE or CTC if colonoscopy contraindicated

3: High risk
• Three or more 1st or 2nd degree relatives on the same side of the family with colorectal cancer (suspected hereditary nonpolyposis colorectal cancer (HNCC))
• Two or more 1st or 2nd degree relatives on the same side of the family with colorectal cancer plus:
  - multiple bowel cancers in one patient
  - bowel cancer diagnosed < 50 yrs
  - suspected familial syndromes such as HNCC, familial adenomatous polyposis (FAP), or high-risk genetic mutations
	HNCC: Untreated, colorectal cancer incidence is approximately 70% by age 65 years
	
	FAP: Untreated, colorectal cancer incidence approaches 100% by age 50 years
		• High familial risk syndromes
		• Genetic counselling
		• Genetic testing under the supervision of a cancer genetics specialist
		• Surveillance schedule for colonoscopy/flexible sigmoidoscopy based on diagnosis

4: Follow-up for patients with a history of colorectal neoplasia	History of adenomatous polyps: Risk depends on type, size and number of adenomatous polyps removed. Standardised incidence ratio: = 3.6 for prior adenomas > 1 cm = 6.6 for multiple prior adenomas Following treatment of colorectal cancer	• Surveillance of adenomatous polyps • Colonoscopy within a year following incomplete or possible inadequate examination • Colonoscopy at 3 years if polyp removed > 1 cm, high-grade dysplasia, villous, ≥3 polyps, age ≥ 60 yrs with family history of colorectal neoplasia • Colonoscopy every 4-6 years in asymptomatic patients without the above risk factors. • Surveillance following treatment of colorectal cancer • Colonoscopy every 3 to 5 years

Source: draft NHMRC guidelines (2005)

Due to the relatively high prevalence of the disease in the asymptomatic population over 50 years of age (Table 2, average risk population), the Australian Health Technology Advisory Committee on colorectal cancer screening (AHTAC 1997) recommended that Australia develop and evaluate a program for the introduction of population screening for colorectal cancer by annual faecal occult blood testing (FOBT) for the average risk population (asymptomatic individuals aged over 50). The Commonwealth Government funded a two year Bowel Cancer Screening Pilot Study which was successfully completed in 2004. Approximately 57,000 people aged between 55 and 74 years of age from Victoria, South Australia and Queensland participated in the study (DHA 2005).

A National Bowel Cancer Screening Program will be implemented for all Australians over 55 and Indigenous Australians over 45 years of age in mid-2006. This will involve

the provision of annual FOBT with appropriate follow-up of positive results. A positive FOBT rate of approximately 9% was reported in the pilot study (Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee 2005). Most patients with positive tests were followed up with a colonoscopy.

Other common colorectal diseases

A wide range of clinical problems may present with symptoms suggestive of colorectal neoplasia. Common differential diagnoses include diverticular disease and inflammatory bowel disease (see below). Non-colorectal diseases may also present with similar symptoms. If used to detect colorectal neoplasia in symptomatic patients, CTC will therefore also have a role in excluding colorectal disease or distinguishing between colorectal neoplasia and benign colorectal diseases.

Diverticular disease

Diverticulae (outpouchings) of the colon, also called diverticulosis, develop as a normal part of the ageing process. These changes are found in approximately 5% of 50-year olds and more than 50% of 90 year olds (Talley & Martin 1996). They are asymptomatic and may thus present as incidental findings at CTC. No treatment is required in asymptomatic individuals. Complications include infection (diverticulitis), bleeding or stricture. Infection occurs due to the impaction of faeces when the neck of the outpouching becomes narrower than the sac. Management is conservative, with surgery reserved for severe complications, such as abscess, haemorrhage, fistula formation and perforation of the colon (Talley & Martin 1996).

Patients presenting for investigation of colorectal neoplasia may have diverticular disease as a cause of their symptoms or as an incidental finding. As a result, a diagnosis of diverticular disease requires careful exclusion of colorectal neoplasia.

Inflammatory bowel disease

The inflammatory bowel diseases, ulcerative colitis and Crohn's disease, usually begin in young adulthood but may present at any age. Symptoms vary according to the extent and severity of bowel wall involvement and include diarrhoea, abdominal pain, rectal bleeding, mucus and general malaise. Treatment for both these distinct clinical problems is based on general supportive measures, anti-inflammatory medication, immunosuppressants, antibiotics and surgery. Common colorectal complications include infection, stricture and perforation. Patients are at high risk of colorectal cancer and require regular screening.

Existing procedures

As outlined above, the NHMRC guidelines recommend colonoscopy as the investigation of choice for the investigation of symptomatic patients with a differential diagnosis of colorectal neoplasia (NHMRC 2005). These guidelines suggest that appropriate alternatives are: DCBE and flexible sigmoidoscopy if colonoscopy is contraindicated or incomplete (NHMRC 2005). These three techniques are briefly described below.

Colonoscopy

Colonoscopy is performed by a specialist surgeon or gastroenterologist. A long narrow flexible tube (the colonoscope) is inserted into the rectum for an examination of the lining of entire length of the colon. Images are either viewed through an eyepiece at the end of the colonoscope or on an external monitor. As with CTC, patients are required to take a bowel preparation the day before the procedure to empty the bowel. Patients require intravenous sedation and the procedure takes up to 60 minutes with around 1 to 2 hours recovery time. It can be performed in an outpatient clinic setting.

The advantage of colonoscopy over less invasive imaging procedures is that it can be used for diagnosis and treatment. It allows a direct examination of the bowel wall. If any abnormalities are detected, instruments can be passed through the colonoscope to take a biopsy or remove polyps for histopathological examination. Some strictures of the bowel wall can also be treated with dilatation at colonoscopy.

Disadvantages of colonoscopy include test failures and complications. Test failures occur when the entire length of the colon to the caecum cannot be examined (referred to as an incomplete colonoscopy). Two published Australian colonoscopy prospective series have reported incompletion rates for standard colonoscopy of 1% (231 patients invited to a colonoscopy screening program, Corbett et al 2004) and 3.6% (384 patients referred for outpatient colonoscopy with failure defined as nonprogression beyond the sigmoid colon at 10 minutes, Kaffes et al 2003). Comparable rates have been reported in large studies internationally (3196 patients, failure to intubate caecum 2.8%, Nelson et al 2002; 3404 patients, referral to DCBE following incomplete colonoscopy 3%, Brown et al 2001). However, one recent large prospective study from the United Kingdom has suggested that incompletion rates are around 21% in routine practice and higher if a more stringent definition of incompletion is used (9223 colonoscopies, Bowles 2004). The authors reported that completion rates varied between different specialist and trainee groups and also found a wide variation in practice between units. Most colonoscopists reported that they did not receive close supervision in the early learning period (83%) and never attended a formal training course (61%). Members of the Advisory Panel considered whether these findings may also be applicable to colonoscopy success rates outside major Australian centres. It was generally felt that the differences between the United Kingdom and Australia in training and practice precluded any generalisation.

Common reasons for failed colonoscopies include:

- patient discomfort if the sedation is not successful

- bowel preparation unsuccessful

- technical problems in passing the colonoscope, for example due to anatomical variations such as a long redundant bowel segment or colonic strictures

Complications of colonoscopy include mild arm pain and swelling at the site of the intravenous injection of the sedative, abdominal discomfort, flatus and diarrhoea after the procedure, and complications associated with sedation. A small amount of blood loss may occur after a biopsy or polyp removal. Serious adverse events such as perforation and haemorrhage are rare, in particular where colonoscopy is not combined with a therapeutic procedure. Tran et al (2001) reported a perforation rate of 0.06% for

diagnostic colonoscopies and 0.11% for therapeutic colonoscopies in a single-centre retrospective series of 26,162 consecutive colonoscopies. A larger multicentre retrospective series found a lower overall perforation rate (perforation rate 0.03% of 116,000 colonoscopies, includes diagnostic and therapeutic colonoscopies, Korman et al 2003). Other colonoscopy series have reported similar rates of haemorrhage requiring intervention (0.19% of 3196 colonoscopies, Nelson et al 2002; 0.07% of 9223 colonoscopies, Bowles et al 2004).

Another disadvantage of colonoscopy is the potential for false negative results. Even when a complete examination is achieved, colonoscopy may miss clinically significant lesions. One study of consecutive same day colonoscopies in 183 patients reported a 24% miss rate (76% test sensitivity), which was largely due to adenomas less than or equal to 5 mm (27% missed), compared to adenomas 6-9 mm (13% missed) and adenomas 10 mm or larger (6% missed) (Rex et al 2000). False positive results are avoided by the use of biopsy at the time of examination to confirm the diagnosis.

Contra-indications for colonoscopy

Colonoscopy is contra-indicated in patients with suspected perforation of the colon or in patients with complete or high-grade obstruction that will not allow passage of the scope. It also cannot be performed on patients who are unable to tolerate sedation due to co-existent illness or frailty. The Standards Practice Committee of the American Society for Gastrointestinal Endoscopy have also identified the following factors as relative contraindications to colonoscopy: acute inflammation of the colon, pregnancy in the second semester, recent myocardial infarction, pulmonary embolism, large aortic aneurysm and an unco-operative patient (The American Society for Gastrointestinal Endoscopy 2005).

Flexible sigmoidoscopy

Flexible sigmoidoscopy allows a close examination of the lining of the rectum and distal colon where approximately 50% of cancers arise. It is less invasive and less costly than a colonoscopy with reduced risks of adverse events. It is performed by a specialist surgeon or gastroenterologist using a 60-cm flexible sigmoidoscope inserted via the rectum up to the sigmoid colon. The bowel preparation used is less than that required for colonoscopy and barium enemas. Patients may be requested to restrict their diet to clear fluids the day before the procedure and use a mild laxative and are usually given an enema to prepare the bowel around one hour prior to the test. Sedation is not usually required and the procedure takes 15-20 minutes, so it can be performed in a doctor's surgery at the time of the initial physical examination. Biopsy and removal of polyps can be performed at the same time. Possible complications include mild abdominal discomfort and most seriously, perforation of the wall of the rectum or colon.

The major disadvantage of sigmoidoscopy is that it does not allow the examination of the entire colon and will miss cancers that occur above the sigmoid colon. As a result, it is common practice to combine this procedure with a barium enema for patients requiring investigation of colorectal neoplasia who are not eligible for colonoscopy.

Double contrast barium enema

Barium enemas are x-rays of the large bowel that use a barium sulfate enema as a contrast agent. Barium appears opaque on x-rays and thus, when used to coat the bowel wall, it allows images of the bowel wall lining. The standard technique now includes the insufflation of air or carbon dioxide to distend the bowel to improve visualisation of the bowel wall and is referred to as a double contrast barium enema (DCBE). It is performed by a radiologist for the detection of colorectal neoplasia and a range of other condition including diverticulitis, strictures and ulcers. Abnormalities are detected by detection of abnormal mucosal patterns or filling defects caused by space occupying lesions. If perforations or anastomotic leaks (following bowel surgery) are suspected, the procedure is performed using another contrast agent, Gastrografin, because barium can cause inflammation if it leaks outside the colon.

Patients are required to use a bowel preparation the day before the procedure as for CTC and colonoscopy. At the time of the procedure, the patient lies on their side and the radiologist inserts an enema tube into the rectal for delivery of liquid barium. An injection of a muscle relaxant may also be used to enhance imaging. The patient is required to be repositioned during the procedure for additional x-ray views. The procedure takes approximately 30 minutes and an enema is used when the x-rays are complete to expel the barium.

The advantages of DCBE are that they are widely available at x-ray facilities, require no sedation, are less invasive and less costly than colonoscopy. They offer an alternative for patients who are not eligible for colonoscopy and can be combined with a flexible sigmoidoscopy for this purpose.

The disadvantages of DCBE include reduced accuracy compared to colonoscopy, poor-quality images if bowel preparation is inadequate and the inability to combine the test with biopsy of any abnormalities detected. Adverse events include abdominal discomfort, constipation if barium is retained after the procedure, and allergic reaction to barium. Patients are exposed to ionising radiation and the associated slight increased risk of cancer. Serious adverse events are extremely rare but include perforation of the bowel wall (de Zwart et al 2004).

Specialised techniques using computed tomography colonography

Development of CT technology and specialised CTC techniques to improve the diagnostic performance of the procedure is ongoing. Some of the major developments are listed below. The use of these techniques varies among the published studies identified for this review and is likely to vary across different Australian centres.

- Multi-slice versus single-slice CT scanning

  Multi-slice CT scanners allow more rapid data acquisition, greater anatomic coverage and thinner sections than single-slice scanners. This helps to reduce respiratory artefacts that may occur with single-slice imaging protocols due to longer breath holds.

- Dual supine and prone positioning versus supine positioning

   Distension of the colon is required for adequate imaging. Different positions optimise distension at different segments of the colon. The use of dual supine and prone positioning has been introduced to enable optimal imaging of these different segments.

- Image processing

   Standard two-dimensional images can be acquired in axial, coronal, sagittal or oblique planes. Three-dimensional images can now be generated using computer algorithms to reconstruct continuous 'fly-through' views of the colon similar to colonoscopy. These images are used to complement two-dimensional imaging, in particular to distinguish polyps from normal colonic folds. Two-dimensional images allow accurate assessment of areas of interest. Techniques to generate three-dimension images include surface rendering, maximal intensity projection and volume rendering. Compared to the first two techniques, volume rendering has the advantage of using the whole CT dataset.

Other specialised techniques that are sometimes used in Australia include the use of intravenous contrast and spasmolytic agents. Studies have indicated that intravenous contrast may improve the accuracy of CTC (Medical Services Advisory Secretariat, Ontario 2003); however, disadvantages include the potential for adverse events due to patient allergy or poor renal function and cost.

Health service use

Information about the numbers of CTC, DCBE and colonoscopy performed in Australia each year was obtained from data collected from hospital admissions (AIHW National Hospital Morbidity Database 2005) and reimbursements made under the Medicare Benefits Schedule (MBS) (the Health Insurance Commission (HIC) 2005) and the HealthWiz Database (DHA 2005).

These data sources provide overlapping information and do not include the number of procedures performed on public patients treated as day cases or inpatients in public hospitals. Thus, the figures presented below underestimate the total number of procedures performed. Furthermore, because the indications for performing DCBE and colonoscopy are not reported, it is not possible to estimate the proportion of these patients who may be eligible for CTC should it be recommended for MBS funding for symptomatic and high-risk asymptomatic patients requiring investigation for colorectal neoplasia.

The AIHW database provides information about the principal diagnosis and procedures performed on patients admitted to private and public hospitals. These data are collected at all patient separations (defined as discharges, transfers, deaths or changes in care type). These data do not include procedures performed in public and private outpatient settings.

The HIC and HealthWiz databases provide information on the number of processed requests for the Medicare items associated with CTC, DCBE and colonoscopy. Medicare requests are submitted for services that are provided for privately insured patients in

private or public hospitals and for services provided in an outpatient setting; they are not submitted for public patients treated as inpatients or day cases in public hospitals.

Computed tomography colonography

Reimbursement for CTC has been available as an interim item under the MBS since May 2005 for two specific indications: following an incomplete colonoscopy (Medicare item 56549); and in patients with fistulous disease, obstructed colon, or megacolon (Medicare item 56551). Over the six month period, May to October 2005, 665 CTC were billed under these two item numbers (Table 3).

Table 3   Requested Medicare items processed from May to October 2005[1]

Medicare Item and Description		Number of Medicare Items processed						
Item	Description	May	June	July	Aug	Sept	Oct	Total[2]
56549	CT Colonography, following incomplete colonoscopy in the preceding three months	42	75	88	113	96	124	538
56551	CT Colonography, where either (i) fistulous disease, (ii) obstructed colon or (iii) megacolon is present	22	15	12	25	28	25	127
Total		64	90	100	138	124	149	665

Source: HealthWiz database, DHA 2005.
1   These figures do not include procedures performed on public patients treated as in-patients or day cases in public hospitals and thus underestimate the total number of CTC procedures performed.
2   No CTC items were processed from the Northern Territory during this period.

Colonoscopy

According to the AIHW hospital morbidity database, 430,708 fibreoptic colonoscopies were performed in Australian hospitals in 2003-2004. This figure includes 190,546 procedures (44%) performed with biopsy or polypectomy (AIHW 2005).

Medicare reimbursements show the number of colonoscopy services performed in the private sector (Table 4). Although these figures underestimate the total services performed, they reflect the distribution of type of colonoscopy services provided (extent of colonoscopy, polypectomy performed). Approximately 29% of colonoscopies performed beyond the hepatic flexure included a polypectomy.

Colonoscopies up to the hepatic flexure are billed under Medicare items 32084 and 32087, which not only cover colonoscopy but also flexible fibreoptic sigmoidoscopy. Thus, these numbers are likely to be overestimates of the true numbers of fibreoptic colonoscopies up to the hepatic flexure performed.

Table 4   Number of colonoscopies performed under Medicare 2002-2005

Medicare Item and description		Number of Medicare items processed		
		All patients		
Item	Description	2002/2003	2003/2004	2004/2005
32084	flexible fibreoptic sigmoidoscopy or fibreoptic colonoscopy up to the hepatic flexure, with or without biopsy (not sigmoidoscopy ≤ 45 minutes)	15,622	15,345	15,215
32087	flexible fibreoptic sigmoidoscopy or fibreoptic colonoscopy up to the hepatic flexure, with removal of 1 or more polyps (not sigmoidoscopy ≤ 45 minutes)	1,904	1,825	1,939
32090	fibreoptic colonoscopy examination of colon beyond the hepatic flexure with or without biopsy	210,134	214,145	222,428
32093	fibreoptic colonoscopy examination of colon beyond the hepatic flexure with removal of 1 or more polyps	76,900	83,763	92,288
	Total	**304,560**	**315,078**	**331,870**

Source: Health Insurance Commission 2005.

Barium enemas

AIHW data show that 943 DCBEs were performed on Australian hospital inpatients in 2003-2004. DCBEs performed outside public hospitals are generally reimbursed under MBS item 58921, which includes all opaque enemas (including Gastrografin) with or without air contrast studies. These procedures may be used for a variety of indications. In 2002/2003, 33,291 opaque enemas were requested; this number declined to 24,401 in 2004/2005 (Table 5). A subset of these procedures are likely to be DCBEs performed in symptomatic patients requiring investigation to confirm or exclude colorectal neoplasia; however, it is not possible to estimate the size of this proportion.

Table 5   Number of opaque enemas performed under Medicare in 2002/2003, 2003/2004 and 2004/2005

Medicare Item and description		Number of Medicare items processed		
		All patients		
Item		2002/2003	2003/2004	2004/2005
58921	opaque enema, with or without air contrast study and with or without preliminary plain films	33,291	28,138	24,401

Source: Health Insurance Commission 2005.

Comparators

CTC will be compared to DCBE and to colonoscopy as a replacement first-line diagnostic test for the detection or exclusion of colorectal disease, in particular colorectal neoplasia, in symptomatic patients and in asymptomatic patients at high risk of colorectal neoplasia.

This includes a comparison of CTC and DCBE in patients ineligible for colonoscopy due to patient contraindications or inability to perform or complete the test.

Marketing status of the technology

CTC is currently available in public and private radiology facilities across Australia.

Current reimbursement arrangement

CTC was approved for two year interim funding under the Medicare Benefits Schedule in May 2005 for the following two indications:

- MBS Item No. 56549: COMPUTED TOMOGRAPHY OF COLON, following incomplete colonoscopy* in the preceding three months, where the patient is referred by the specialist or consultant physician who performed the incomplete colonoscopy: $385

- MBS Item No. 56551: COMPUTED TOMOGRAPHY OF COLON, where the patient is referred by a specialist or consultant physician and where a) one of the following conditions is present (i) fistulous disease (ii) obstructed colon (iii) megacolon, and where b) the request specifies the condition: $385

*On page 36 of the Medicare Benefits Schedule it is stated that "for audit purposes, an incomplete colonoscopy is defined as one that is not completed for technical or medical reasons …" (MBS Supplement, May 2005)

Previous Medical Services Advisory Committee assessment

MSAC conducted a Horizon Scanning Briefing in 2001 to assess the use and potential application of CTC and the likely impact on the Australian healthcare system (MSAC 2001). A systematic review of the literature and survey of researchers in the field was conducted to inform this report. The main findings of this report were:

- Safety

  CTC appears to be a safe diagnostic test.

- Training

  CTC should ideally be performed within a program of professional accreditation and/or training endorsed by an appropriate professional body.

- Indications

  CTC may be an appropriate test in patients requiring full colonic evaluation if colonoscopy cannot be performed due to: contraindications such as anticoagulation in patients presenting with rectal bleeding, severe comorbidity, unfit for sedation; or in patients with a prior incomplete or technically difficult colonoscopy, obstructed colon, megacolon, or fistulous disease.

  The safety and effectiveness of CTC has not been adequately evaluated as a population-based screening tool.

- Future assessment

  CTC has the potential to replace DCBE in most indications. Its role as a diagnostic test and as a population-based screening test should be reassessed with new evidence about its sensitivity, specificity, cost-effectiveness for these indications.

Practical issues relevant to the interpretation of the evidence

Referral sources for computed tomography colonography

The clinical and cost-effectiveness of a test varies according to the pretest probability of disease. Thus, the referral source (General Practitioner (GP) or Specialist) and the expected position of the test in the clinical pathway need to be clearly defined when assessing the value of the test. Two clinical pathways were developed to describe the two main potential roles for CTC assessed in this review (Appendix E).

In the first scenario, CTC is assessed as a replacement test for DCBE for the detection of colorectal neoplasia in patients in whom colonoscopy has failed or cannot be performed. In this role, it is implied that CTC would generally follow specialist referral and examination, which may be expected to include clinical examination of the rectum with or without sigmoidoscopy and attempted colonoscopy.

In the second scenario, CTC is compared to DBCE and to colonoscopy as a first-line test in patients requiring investigation of colorectal neoplasia with no contra-indications

to colonoscopy. The Advisory Panel debated whether referral to CTC should be available to GPs in this scenario or restricted to specialist gastroenterologists and gastrointestinal surgeons. Reasons not to support direct GP referral to CTC are based on the assumption that all patients requiring investigation for colorectal neoplasia would benefit from a referral to a specialist for a rectal and lower bowel examination with sigmoidoscopy where appropriate prior to the selection of further testing. Reasons to support direct GP referral include: (i) GPs currently undertake assessment and referral to DCBE of patients with suspected colorectal neoplasia with appropriate referral to specialist care. If CTC is superior to DBCE, then it should also be available to GPs; (ii) GPs can currently refer patients to open access colonoscopy in many areas; (iii) GP referral may be more appropriate to exclude colorectal neoplasia in patients with a low pre-test probability of disease to avoid the potential costs (and delay) of specialist referral and harms of colonoscopy; (iv) GP referral to CTC would allow triage of patients in regions where there is limited access to specialist care and colonoscopy (see below).

Lack of access to colonoscopy

Waiting times for colonoscopy are not reported at a national level in hospital waiting list reports; however, members of the Advisory Panel expressed a concern about the lack of access to colonoscopy in some regions of Australia. It has been suggested that a lack of access to colonoscopy may be one of the factors contributing to the poorer cancer outcomes documented in rural areas (Rural Doctors Association of Australia 2005). The Advisory Panel discussed whether CTC may potentially have a role in the triage of patients awaiting colonoscopy. It was proposed that CTC should not be considered as a replacement test for colonoscopy in this scenario unless its safety, effectiveness and cost-effectiveness were found to be comparable to colonoscopy. The Advisory Panel regarded the potential lack of access to colonoscopy as a health service provision and workforce issue that would be addressed outside this review.

Approach to assessment

Research questions

The evaluation team worked with members of the Advisory Panel to develop research questions to assess the value of CTC for the diagnosis or exclusion of colorectal disease, in particular polyps and cancer. These questions were formulated *a priori* from information provided by the Advisory Panel about common clinical presentations of patients requiring investigation for colorectal disease and current Australian practice for the diagnosis or exclusion of colorectal cancer. This report does not assess the value of CTC as a first line screening test for patients at average risk of colorectal neoplasia.

Two primary review questions were developed:

1. What is the safety, effectiveness and cost-effectiveness of CTC versus DCBE and CTC versus colonoscopy for the diagnosis or exclusion of colorectal neoplasia in symptomatic patients or in patients that are asymptomatic but at high risk of colorectal neoplasia due to a personal or family history of colorectal polyps or cancer?

2. What is the safety, effectiveness and cost-effectiveness of CTC versus DCBE for the diagnosis or exclusion of colorectal neoplasia in symptomatic or high-risk patients who are ineligible for colonoscopy due to patient contraindications or the inability to perform or complete the test?

Secondary analyses were planned to assess the safety, effectiveness and cost-effectiveness of CTC versus DCBE and CTC versus colonoscopy to detect other specific colorectal abnormalities; and all colorectal abnormalities.

Two flow charts depicting the clinical pathways for diagnosing and managing colorectal neoplasia were developed to illustrate the potential role of CTC for the two indications addressed in the review questions (Appendix E).

Assessment strategy

The clinical effectiveness of a diagnostic test is determined by how much its use improves health outcomes. Ideally, this could be directly assessed by a randomised controlled trial comparing the test and treatment outcomes following the adoption of the new test with the test and treatment outcomes following the existing testing strategy.

In the absence of direct trial evidence of CTC effectiveness, evidence about the relative accuracy, safety and patient preferences and quality of life outcomes of CTC, DCBE and colonoscopy has been used to infer the relative effectiveness of each test.

This approach is justified by existing evidence from randomised controlled trials of the effectiveness of treatment for colorectal neoplasia, including trials demonstrating the effectiveness of early detection and treatment on improving survival (Hardcastle et al 1996).

Using this approach, conclusions about the relative effectiveness of CTC will be inferred from evidence about:

- the relative safety of CTC compared to DCBE and/or colonoscopy

- the relative accuracy of CTC compared to DCBE and/or colonoscopy

- the impact of CTC on clinical management decisions compared to DCBE, such as avoiding further investigation

- the effectiveness of CTC on patient outcomes (patient preferences, quality of life) compared to DCBE and/or colonoscopy

Where evidence about the relative accuracy of CTC is limited, evidence from studies of CTC accuracy using colonoscopy as a reference standard without comparing the accuracy of CTC and colonoscopy are also considered ("noncomparative" studies).

An economic evaluation has been undertaken to model the relative cost-effectiveness in terms of cost per life years saved of CTC versus DCBE and colonoscopy (see page 90).

Review of literature

Evaluators from the National Health and Medical Research Council (NHMRC) Clinical Trials Centre conducted a systematic review of the medical literature to identify relevant studies published between 1994 and June 2005.

Websites of the international health technology assessment (HTA) agencies were searched for existing HTA reports research (Table 6) and electronic databases of published research (Table 7) were searched for original research papers, including systematic reviews.

Table 6   Electronic databases and HTA websites searched in this review.

Organisation	Database/website
NHS Centre for reviews and Dissemination databases (UK) • Economic evaluation database (EED) • Database of abstracts of reviews of effectiveness (DARE) • Heath Technology Assessment (HTA)	www.york.ac.uk/inst/crd/
Cochrane Database of Systematic Reviews and Cochrane Controlled Trials Register	www.cochrane.org
British Columbia Office of Health Technology Assessment (Canada)	www.chspr.ubc.ca
Swedish Council on Technology Assessment in Healthcare (Sweden)	www.sbu.se
Oregon Health Resources Commission (US)	www.ohppr.state.or.us/index.html
Minnesota Department of Health (US)	www.health.state.mn.us/htac/index.htm
Canadian Coordinating Office for Health Technology Assessment (Canada)	www.ccohta.ca
Alberta Heritage Foundation for Medical Research (Canada)	www.ahfmr.ca
National Library of Medicine Health Service/Technology Assessment text (US)	www.ncbi.nlm.nih.gov
Institute for Clinical Evaluative Science (Canada)	www.ices.on.ca
DIMDI - German Institute for Medical Documentation and Information (Germany)	www.dimdi.de
National Information Centre of Health Services Research and Health Care Technology (US)	www.nlm.nih.gov/nichsr
Finnish Office for Health Technology Assessment (FinOHTA) (Finland)	www.stakes.fi/finohta/linkit/
Institute Medical Technology Assessment (Netherlands)	www.bmg.eur.nl/imta/
Agence Nationale d'Accreditation et d'Evaluation en Sante (France)	www.anaes.fr
Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) (Canada)	www.aetmis.gouv.qc.ca/en/index.php
Health Technology Board for Scotland (UK)	www.htbs.org.uk
National Coordinating Centre for HTA (NCCHTA) (UK)	www.hta.nhsweb.nhs.uk
Centre for Health Program Evaluation (Australia)	Chpe.buseco.monash.edu.au

Table 7   Electronic databases searched

Database	Period covered
Medline	1994 – June 2005
EMBASE	1994 – June 2005
Premedline	As at June 9 2005
Current Contents	June 9 2005 (previous 6 months)
The Cochrane Library Controlled Clinical Trials Registry	Issue 2, 2005

Search strategy

The search strategy was developed using the key elements of the clinical question. The search strategies shown in Tables 8 to 10 were used to identify papers in the databases described in Table 7.

Table 8   Medline search strategy[1]

Number	Search Strategy
1	exp Colonography, Computed Tomographic/
2	exp Tomography, X-Ray Computed/
3	limit 2 to yr = 1994 – 2001
4	exp Colorectal Neoplasms/
5	Colonic Polyps/
6	((colorectal or colon$) adj3 (polyp$ or cancer$ or carcinoma or neoplasm)).mp.
7	or/4-6
8	limit 7 to yr = 1994 – 2001
9	3 and 8
10	exp Pneumoradiography/
11	8 and 10
12	(virtual adj3 colonoscop$).mp.
13	((CT or (computed adj tomography)) adj3 (colography or colonography or pneumocolon)).mp.
14	1 or 9 or 11 or 12 or 13

1 Medline Subject Heading for virtual colonoscopy introduced in 2001, alternative MESH terms applied prior to 2001.

Table 9   EMBASE search strategy[1]

Number	Search History
1	exp Computed Tomographic Colonography/
2	exp Colon Tumor/
3	exp Colon Polyp/
4	((colorectal or colon$) adj3 (polyp$ or cancer$ or carcinoma or neoplasm)).mp.
5	or/2-4
6	limit 5 to yr = 1994-2002
7	exp spiral computer assisted tomography/
8	limit 7 to yr = 1994-2002
9	6 and 8
10	(virtual adj3 colonoscop$).mp.
11	((CT or (computed adj tomography)) adj3 (colography or colonography or pneumocolon)).mp.
12	1 or 9 or 10 or 11

1 Embase Subject Heading for virtual colonoscopy introduced in 2002, alternative terms applied prior to 2002.

Table 10 Premedline, Current Contents & The Cochrane Library controlled Clinical Trials Registry search strategy

Number	Search History
1	((CT or (computed adj tomography)) adj3 (colography or colonography or pneumocolon)).mp.
2	(virtual adj3 colonoscop$).mp.
3	1 or 2

This search strategy may not be sensitive to studies investigating CTC for the detection of non-neoplastic colorectal disease prior to 2001. Reference lists of included publications were also checked for relevant citations that may have been inadvertently missed in the searches of major databases.

Search results – computed tomography colonography

Existing health technology assessment reports

The searches of the HTA agency databases and websites (listed in Table 6) identified 12 HTA reports on CTC. Of these, eight reports were retrieved for appraisal and seven were eligible for inclusion in the present review. Four reports were ineligible for retrieval – two reports were not available in English, one report was a bulletin only, and one report was not publicly available.

Published literature

The search strategy retrieved a total of 1,687 nonduplicate citations. The number of nonduplicate citations retrieved from each database is shown in Table 11.

Table 11 Number of nonduplicate citations retrieved from each database

	Medline	Pre-Medline	Current Contents	Embase	Cochrane Library CCTR	Total
Number of citations	1,317	22	70	276	2	1,687

Eligibility criteria for studies

The 1,687 nonduplicate citations were evaluated by one reviewer who determined whether the retrieved studies met the eligibility criteria outlined in Table 12. All citations were checked by a second reviewer and discrepancies in the results of the screening process were resolved by discussion.

Table 12 Study exclusion criteria

1. Not an appropriate clinical study
Reports excluded were those describing animal, laboratory or scientific studies, technical reports or case reports. Nonsystematic narrative reviews, letters and conference abstracts were also excluded in this category.
Case series where the use or reporting of a reference standard was based on the CTC result (positive/negative) were excluded.
Case-control studies where patients were selected for inclusion in the study based on their known disease status were excluded.
Retrospective case referent studies (reporting on subjects all known to have the condition of interest) were excluded.
2. Wrong patient group
Studies were to include patients being investigated for colorectal disease. Studies with average risk asymptomatic patients and studies with < 10 patients undergoing CTC were excluded.
3. Wrong diagnostic test
Studies were to perform multislice CTC (at least 4-slice CT scanning).
4. Wrong reference standard or comparator
Studies were to use colonoscopy or surgical findings as the reference standard.
Studies which compared two or more different techniques of CTC without performing a reference standard were excluded.
Studies were to use double contrast barium enema and/or colonoscopy as a comparator.
5. Wrong outcomes
Studies had to report on at least one of the following:
• diagnostic accuracy with sufficient data to calculate sensitivity and specificity
• changes in clinical management
• patient outcomes (morbidity, mortality, adverse events, quality of life, patient preferences)
6. Not in English
Due to time constraints, only studies published in English were eligible for inclusion.

Based on these criteria, 1,654 citations were excluded from the review. The QUOROM flowchart (Figure 3) summarises the results of the literature search and the application of the study exclusion criteria. A list of the studies that were retrieved for appraisal but subsequently excluded because they did not meet the eligibility criteria for this review is available in Appendix C.

Figure 3   QUOROM flowchart summarising the results of the literature search and the application of entry criteria

```
┌─────────────────────────┐
│ Potentially relevant    │
│ publications identified │
│ and screened for        │         ┌──────────────────────────────────┐
│ retrieval (n = 1,687)   │────────▶│ Publications excluded (n = 1,589): │
└─────────────────────────┘         │ Not a controlled clinical study    │
            │                       │ (n = 881); wrong patient group     │
            │                       │ (n = 455); wrong diagnostic test   │
            │                       │ (n = 194); wrong reference         │
            │                       │ standard or comparator (n = 9);    │
            │                       │ wrong outcomes (n = 31); not in    │
            │                       │ English (n = 19)                   │
            ▼                       └──────────────────────────────────┘
┌─────────────────────────┐
│ Publications retrieved  │
│ for full-text           │
│ evaluation (n = 98)     │
└─────────────────────────┘
            │            ┌──────────────────────────────────────────┐
            ├───────────▶│ Duplicate publications excluded (n = 6)  │
            │            └──────────────────────────────────────────┘
            │            ┌──────────────────────────────────────────┐
            ├───────────▶│ Publications with overlapping patient    │
            │            │ populations excluded (n = 6)             │
            │            └──────────────────────────────────────────┘
            │            ┌──────────────────────────────────────────┐
            ├───────────▶│ Publications excluded based on           │
            │            │ eligibility criteria (n = 53): Not a     │
            │            │ controlled clinical study (n = 7); wrong │
            │            │ patient group (n = 20); wrong            │
            │            │ diagnostic test (n = 11); wrong          │
            │            │ reference standard or comparator (n = 3);│
            │            │ wrong outcomes (n = 10); not in English  │
            │            │ (n = 2)                                  │
            │            └──────────────────────────────────────────┘
            │            ┌──────────────────────────────────────────┐
            │◀───────────│ Additional studies meeting criteria      │
            │            │ identified through the HTA/websites      │
            │            │ search (n = 6)[1] and one systematic     │
            │            │ review published after the search (n = 1)│
            │            └──────────────────────────────────────────┘
            │
     ┌──────┴──────┐
     ▼             ▼
┌──────────────┐ ┌────────────────────────────────────┐
│ Publications │ │ Publications excluded for systematic │
│ included in  │ │ review, but included for assessment  │
│ the          │ │ of diagnostic yield in patients with │
│ systematic   │ │ incomplete colonoscopy (4) or        │
│ review       │ │ extracolonic findings (1)            │
│ (n = 40)     │ └────────────────────────────────────┘
└──────────────┘
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1 One HTA report was identified in both literature and HTA database search

The 40 publications meeting criteria for inclusion in the review are: HTA reports (7), systematic reviews/meta-analysis (3), studies of diagnostic test accuracy (21) and studies of patient preferences and/or quality of life (9 studies). Five additional studies were included to provide additional information about CTC diagnostic yield in patients with incomplete colonoscopies and frequency (4) and the significance of extracolonic findings

(1). No studies assessing the impact of CTC versus DCBE or colonoscopy on clinical management or treatment outcomes were identified.

As only two of the included publications involve a direct comparison of CTC and DCBE, a further search was conducted to identify studies comparing DCBE and colonoscopy. The full search strategy is outlined in Appendix F, with a summary of results below.

Search results – Double contrast barium enema

Published literature

The search strategy for additional DCBE studies identified a total of 328 nonduplicate citations (Table 13), which resulted in the identification of an additional four eligible studies. These included one systematic review (de Zwart et al 2001) and three studies of test accuracy.

Table 13 Number of nonduplicate citations retrieved from each database

	Medline	Pre-Medline	Current Contents	Embase	Cochrane Library CCTR	Total
Number of citations	102	84	25	107	10	328

The QUOROM flowchart (Figure 4) below summarises the results of the literature search and the application of the study exclusion criteria (see Appendix F).

Figure 4   QUOROM flowchart summarising the results of the additional search for DCBE literature and the application of entry criteria
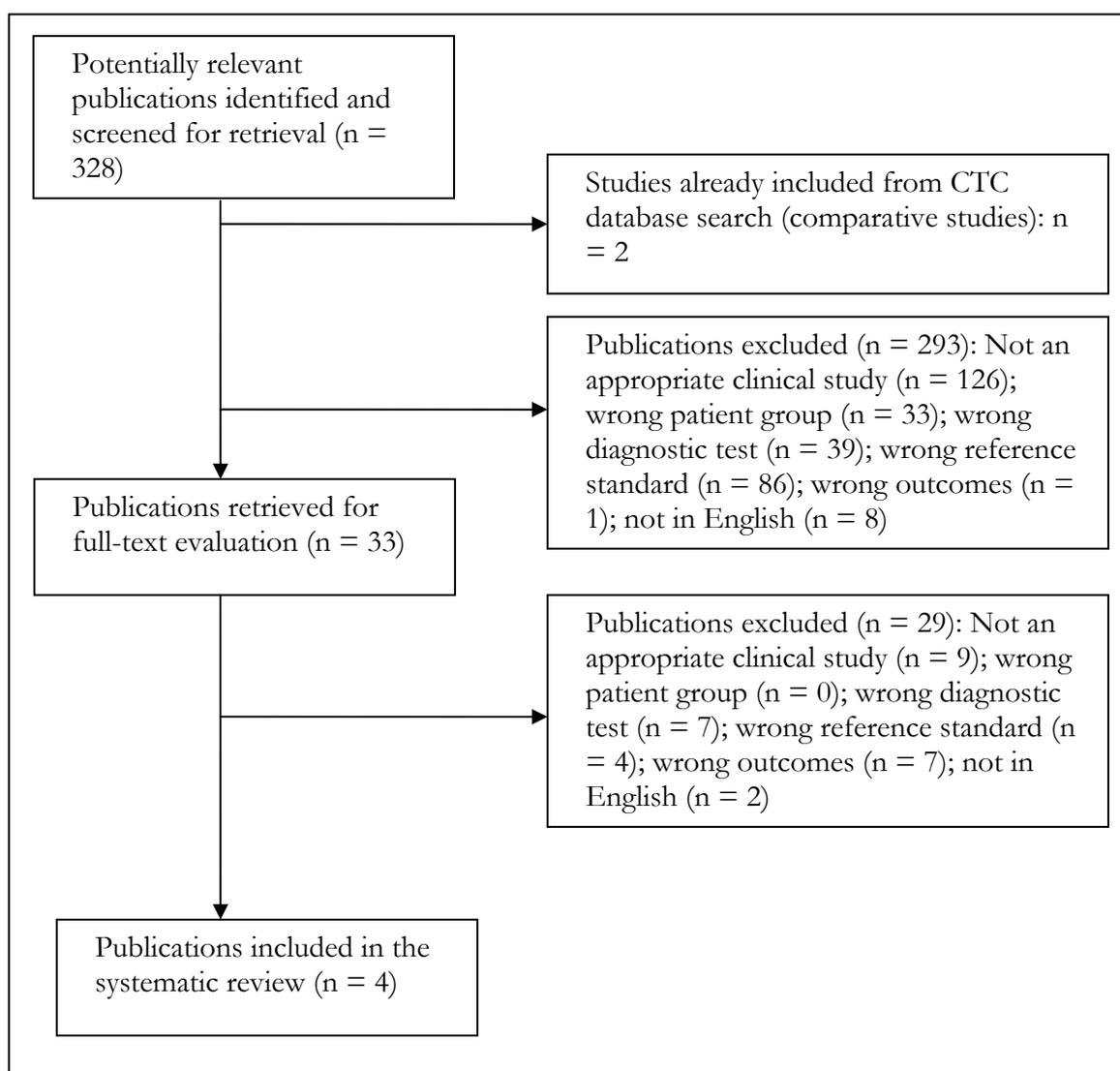
As shown in Figure 4, the main reasons for exclusion of studies identified from the DCBE search were: the study was not an appropriate clinical study (41% of all studies), for example, a case reference study; or an invalid reference standard was used (28% of all studies).

An extended search strategy (described in Appendix F) did not identify any further studies meeting the eligibility criteria for this review.

Study appraisal

Assessment of eligible studies

The evidence presented in the selected studies was appraised and classified using the NHMRC Dimensions of Evidence (NHMRC 1999, 2005) and the MSAC Diagnostic Test Guidelines (MSAC 2005). These dimensions (Table 14) consider important aspects of the evidence supporting a particular diagnostic test and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified for a particular diagnostic test. The last two require expert clinical input as part of their determination.

Table 14 Dimensions of Evidence[1]

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design[2]
Quality	The methods used by investigators to minimise bias within a study design
Statistical precision	The p-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect
Size of effect	The distance of the study estimate from the "null" value and the inclusion of only clinically important effects in the confidence interval
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used

1 Adapted from NHMRC 1999 and MSAC 2005.
2. See Table 16.

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The designations of the levels of evidence are shown in Table 15.

Table 15 Designations of levels of evidence[1]

Level of evidence	Study design
Studies of effectiveness	
I	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudorandomised controlled trial (alternate allocation or some other method)
III-2	A comparative study with concurrent controls: nonrandomised experimental trial, cohort study, case-control study, or interrupted time series with a control group
III-3	A comparative study without concurrent controls: historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes
Studies of test accuracy	
I	A systematic review of level II studies
II	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation
III-1	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among nonconsecutive patients with a defined clinical presentation
III-2	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence
III-3	Diagnostic case-control study
IV	Study of diagnostic yield (no reference standard)

1 Modified from NHMRC 1999 & 2005.

Quality appraisal

The quality of a study refers to the extent to which it is has been designed and conducted to reduce bias in the estimation of the outcome. The potential sources of bias vary according to whether the study is designed to estimate the impact of the test on health outcomes (where the ideal is a randomised trial of alternative tests) or to estimate the diagnostic accuracy of the test (for which the ideal is cross-sectional analytic studies of consecutive patients tested using both the test of interest and a valid reference standard).

A structured appraisal to assess the quality of all included studies was performed. The following sections present the quality criteria used for these appraisals.

Quality of studies of diagnostic test accuracy

The quality of studies of diagnostic test accuracy for this review was assessed using the QUADAS tool (see Table 16). This tool was developed recently by experts in the field following a systematic review of the evidence relating to sources of bias and variation relevant to studies of diagnostic test accuracy (Whiting 2004).

Table 16 Quality assessment of studies of diagnostic test accuracy – the QUADAS tool

Item		Yes	No	Unclear
1	Was the spectrum of patients representative of the patients who will receive the test in practice?	( )	( )	( )
2	Were selection criteria clearly described?	( )	( )	( )
3	Is the reference standard likely to correctly classify the target condition?	( )	( )	( )
4	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	( )	( )	( )
5	Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?	( )	( )	( )
6	Did patients receive the same reference standard regardless of the index test result?	( )	( )	( )
7	Was the reference standard independent of the index test (ie the index test did not form part of the reference standard)?	( )	( )	( )
8	Was the execution of the index test described in sufficient detail to permit replication of the test?	( )	( )	( )
9	Was the execution of the reference standard described in sufficient detail to permit its replication?	( )	( )	( )
10	Were the index test results interpreted without knowledge of the results of the reference standard?	( )	( )	( )
11	Were the reference standard results interpreted without knowledge of the results of the index test?	( )	( )	( )
12	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	( )	( )	( )
13	Were uninterpretable/ intermediate test results reported?	( )	( )	( )
14	Were withdrawals from the study explained?	( )	( )	( )

Source: Whiting *et al* 2003.

For the purposes of this review, four criteria were considered essential for classification as a high-quality study of diagnostic test accuracy. These four criteria are the selection and application of the reference standard, methods and criteria used for the selection of the study population, the execution and interpretation of the index test and presentation of results.

1. Selection and application of the reference standard

When an imperfect reference standard is used, the sensitivity and specificity of the index test are distorted. The direction of the resulting bias depends upon whether the new test and the imperfect reference standard have a tendency to misclassify the same patients. When there is no such tendency, the sensitivity and specificity of the new test will be underestimated when evaluated against the imperfect reference standard. When the new test and the standard tend to misclassify the same patients (that is, the classification errors between the two tests are highly correlated), the sensitivity and specificity of the new test will be overestimated (Valenstein 1990). When different reference standards are used, 'differential verification bias' may occur. This refers to bias due to the different performance of these different tests. 'Partial verification bias' refers to the use of the reference standard according to the result of the index test (positive or negative).

Colonoscopy alone is not a perfect reference standard because it has been associated with both false positive and false negative results (Rockey et al 2005). The perfect reference standard for the assessment of CTC accuracy is the histopathological

examination of a surgically resected specimen. However, it would be unethical to conduct a study where all patients undergoing CTC are followed up by surgery. As a result, studies that use colonoscopy or surgical findings as the reference standard with biopsy and histopathology for positive findings and clinical follow-up for negative findings provide an acceptable reference standard in this review. Still accepted as a valid reference standard in this review are studies using colonoscopy and biopsy for positive results. However, this reference standard is less optimal because although this strategy would avoid false positive results, it is still possible for colonoscopy findings to be negative in a patient who has colorectal pathology (false negative).

The best available reference standard in this review is one that uses a second-look colonoscopy, either after a positive CTC result was not confirmed at colonoscopy or after generally discrepant CTC and colonoscopy results (positive or negative CTC). A second-look colonoscopy is often combined with segmental unblinding, a technique of unblinding the results of CTC after colonoscopic investigation of a specific segment, which facilitates performing a second-look colonoscopy.

The selection and application of the reference standard is addressed by questions 3 and 5 using the QUADAS tool. Answering yes to each of these questions is considered essential to minimise bias and classify a study as high quality. Studies in which the reference standard was considered inappropriate (answering no to question 3) were classified as low quality. For the purposes of this review, a quality criterion was included to distinguish between studies that included a second-look colonoscopy in their reference standard and studies that did not. Only studies with a second-look colonoscopy may be assigned a high quality rating.

QUADAS question 7 refers to the use of an independent reference standard. The inclusion of the index test as part of the reference standard may lead to incorporation bias which inflates the estimate of test accuracy. For the purposes of this review, if a reference standard is reported to be based on a reconciliation of all tests and includes a second-look colonoscopy, it is still considered 'objective' and classified together with independent reference standards.

Not all studies reported how a true match was determined between lesions detected at CTC, DCBE and colonoscopy. Where reported, definitions varied between studies, with some studies using a definition based on size and location and others using a definition based on size only.

2. Methods and criteria used for the selection of the study population

The evaluation of the test in a selected, nonconsecutive sample introduces the potential for bias (for example if the test is only used in those with more severe disease) and compromises the applicability of the results to clinical practice. There is empirical evidence that this problem is greater when data are assessed retrospectively (Lijmer et al 2001). Studies that selected a prospective sample of patients based on the same eligibility criteria for testing that will be used in practice were graded as high quality. Studies that enrolled patients retrospectively were graded as fair quality due to the potential for bias using this method. The selection of the study population is addressed by question 2 in the QUADAS tool.

3. The execution and interpretation of the index test

The accuracy of a test varies according to the additional information available to those interpreting the test (Whiting 2004). This is referred to as review bias. In this review, studies that reported that CTC (and its comparator DCBE) and the reference standard were interpreted independently (blind to the results of the other test) were graded as high quality. This is addressed by questions 10 and 11 in the QUADAS tool. In addition, an appropriate description of the methods used in performing CT colonography, including the definition of a positive result and the type of CT scanner used, was required to define a study as high quality. This is addressed by question 8 in the QUADAS tool. If questions 10 or 11 were not met, the study was identified as low quality.

4. Presentation of results

Studies that do not report on the proportion of eligible patients who were excluded from the analysis (for example, due to test failure) limit the interpretation of the study findings in clinical practice. To be defined as high quality, studies had to report any uninterpretable test results. This is addressed by question 13 in the QUADAS tool. If exclusion included exclusions due to failure of CTC (other than where the patient failed to follow the bowel preparation studies and thus was ineligible for CTC, DCBE or colonoscopy), the study was classified as fair quality. In addition, it was considered essential that studies present data so that 2 × 2 tables can be reconstructed for calculations of sensitivity, specificity, likelihood ratios and their 95% confidence intervals. Studies were not classified as high quality if 2 × 2 tables could not be reconstructed using data available in the publication.

Quality of studies assessing patient preferences and quality of life

Criteria for appraising the quality of studies of patient preferences and quality of life outcomes were adapted from NHS Centre for Reviews and Dissemination guidelines (2001) (see Table 17).

Representativeness of the study population was assessed by considering whether consecutive patients were enrolled. The relevance of the population was assessed by considering whether the characteristics of the study population were applicable to the population specified for this report.

The methods used to assess patient preferences were appraised as high quality if they were adequately described to allow repeatability. The methods used to assess quality of life were only appraised as high quality if validated instruments were used.

Table 17 Quality Assessment of studies of patient outcomes[1]

• Was the study based on a representative sample selected from a relevant population?
• Were the criteria for inclusion and exclusion explicit?
• Were the data collection methods used adequately described?
• Were outcomes assessed using valid and reliable instruments?

1 Modified from NHS Centre for Reviews and Dissemination 2001

Appraisal of applicability of results

The three key criteria assessed for an appraisal of the applicability of the evidence to the review questions were:

- The patients' characteristics and relevance to the intended test population (symptomatic and asymptomatic high-risk patients)

- The type of CTC technique performed and its relevance to Australian practice

- The training and experience of the radiologists performing CTC

Appraisal of comparative evidence

Studies that reported on a head-to-head comparison of CTC, DCBE and/or colonoscopy provide direct evidence about the relative effects of these tests. Studies that report on outcomes for one test without a direct comparison with the comparator tests have been included where direct evidence is not available. However, indirect comparisons of results from different studies can introduce bias as they may overestimate the effect of the intervention (or accuracy of the test) and thus provide weaker evidence than studies reporting on direct comparisons (Bucher et al 1997).

Data analysis

The characteristics of the study population, type of diagnostic test, reference standard, comparator, study quality and relevant endpoints were extracted for each study. Where appropriate, the results of eligible studies were statistically synthesized and pooled results presented.

Data extraction

Data were extracted using a standardised instrument designed for this review. Data extraction was performed by one reviewer and checked by a second reviewer. Any discrepancies were resolved by discussion or a third reviewer if required. The data extraction tables are provided in Appendices C and D. Where the publications presented percentages only, raw numbers have been determined based on the percentages and the number of patients on which each test was performed if possible. Where only raw numbers are available, percentages have been calculated using the number of patients known to have had the test performed. Where possible, 2 × 2 tables were reconstructed from data available to estimate sensitivity, specificity and associated 95% confidence intervals (refer to Figure 5 for a 2 × 2 table).

Measurement of test accuracy

The accuracy of a test is determined by its ability to identify the target condition compared to a reference standard test that is used as a proxy for true disease status. Subjects who test positive using the reference standard are classified as having the disease and those who test negative are classified as disease-free.

Results of the index test and reference standard for a group of tested subjects can be summarised in a 2 × 2 table as shown in Figure 5.

Figure 5 2 × 2 table displaying the data used to determine test accuracy

As shown, subjects who test positive for the disease of interest by both the index test and the reference standard are recorded as true positives (TP). Subjects without the target condition who test negative by both tests are recorded as true negatives (TN). When there is discordance between the results of the index test and reference standard, the index test result is recorded as a false positive (FP) if it detects the target condition and the reference standard does not. A false negative (FN) is recorded if the reference standard detects the target condition and the index test does not.

The primary measure of test accuracy used in this review is the sensitivity and specificity of the test calculated per-patient. Estimates of test sensitivity and specificity calculated per polyp are less relevant to the assessment of clinical and cost-effectiveness. These results have been presented for completeness for studies that do not report per-patient results, but are not discussed.

Sensitivity and specificity

The sensitivity of a test is the probability of a positive test in subjects with the disease of interest. The specificity of a test is the probability of a negative result in subjects without the disease. The sensitivity and specificity of a test are always considered together and vary according to the threshold used to define a positive test. Sensitivity and specificity are known to vary according to the spectrum of disease (for example, variation in disease severity) in the patient group tested.

Calculation:

Sensitivity = $TP/(TP + FN)$

Specificity = $TN/(TN + FP)$

If the sensitivity of a test is sufficiently high, a negative result rules out the disorder. Therefore, high sensitivity is particularly important if the penalty for missing disease is high. If the specificity of a test is sufficiently high, a positive result rules in the disorder. Therefore, high specificity is particularly important if a false positive result can harm the patient.

Assessment of heterogeneity

The true positive rate (sensitivity) and false positive rate (1 − specificity) from studies assessing the same target condition were plotted in receiver operating characteristic (ROC) space for the assessment of nonrandom variation in the study results (study heterogeneity), the presence of a threshold effect for a positive test and to fit a summary

receiver operating characteristic (SROC) curve to provide a summary of test accuracy (Q index) and compare tests. The Meta-Disc program was used in the assessment of heterogeneity (Zamora et al 2004). Study heterogeneity was assessed statistically using the Chi-Square (χ^2) test.

Meta-analysis

Where possible, a meta-analysis was undertaken by pooling results from studies reporting absolute numbers of true positive, true negative, false positive and false negative results for each test, using the MetaDisc program (Zamora et al 2004).

A χ^2 test was used to test for nonrandom variation (heterogeneity) in estimates of sensitivity and specificity between studies. If heterogeneity was not statistically significant (p value > 0.05), the DerSimonian Laird random effects model was used to calculate summary estimates of test sensitivity and specificity.

Data from studies assessing the same target condition were also plotted in receiver operating characteristic space for the assessment of the presence of a threshold effect. A threshold effect occurs when different thresholds are used to define a positive test resulting in different estimates of test sensitivity and specificity. A summary receiver operating characteristic (SROC) curve was fitted using the methods described by Moses et al (1993). A regression coefficient (β) for the fitted curve that is close to zero and not statistically significant indicates that the SROC curve is symmetrical; in this case the pooled diagnostic odds ratio will provide a useful summary measure of test accuracy. The Q* index (the point on the SROC curve where sensitivity = specificity) and the area under the curve can be used to provide a summary of test accuracy. If the regression co-efficient is statistically significant, the diagnostic odds ratio varies with threshold and an asymmetrical SROC can be fitted.

Where heterogeneity between studies was statistically significant and could not be explained by a threshold effect, a meta-analysis was not performed and the median estimates and range of results for test sensitivity and specificity were reported.

Expert advice

An Advisory Panel with expertise in surgery, oncology, gastroenterology, radiology, general practice and consumer issues was established to evaluate the evidence and provide advice to the MSAC from a clinical perspective. In selecting members for Advisory Panels, the MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the panel is listed in Appendix B.

Results of assessment

Characteristics and quality of included studies

Forty-four studies investigating CTC, DCBE and/or colonoscopy were eligible for this review. These included seven HTA reports, four published systematic reviews/meta-analyses and 33 primary studies reporting on test accuracy, patient preferences or quality of life outcomes (Table 18).

Table 18 Summary of eligible evidence

Type of evidence	Number of studies
HTA reports	7 CTC
Systematic reviews/meta-analyses	3 CTC
	1 DCBE
Primary studies	
Test accuracy	24 studies including:
	• CTC versus DCBE versus colonoscopy (1)
	• CTC versus DCBE (1)
	• CTC versus colonoscopy (5)
	• CTC, no comparator (14)
	• DCBE (3)
Patient outcomes	11 (includes 2 accuracy studies)
Total	**44 studies**

The primary studies of CTC accuracy included symptomatic or high-risk asymptomatic patients only. The characteristics and quality of all included studies are described below and summarised in Appendix D.

Systematic reviews

Health technology assessment reports

The seven HTA reports are summarised in Table 19.

Table 19 Summary of existing HTA reports about CTC

Author, Year, Country	Objective	Quality
BlueCross BlueShield Association, 2004 USA	To assess the effectiveness of CTC versus colonoscopy as a screening test for colorectal cancer.	Insufficient reporting of review methods
Canadian Coordinating Office for Health Technology Assessment (CCOHTA), 2004 Canada	To conduct a pre-assessment of CTC versus standard colon imaging tests.	Full systematic review not undertaken
NICE, Interventional Procedures Advisory Committee (IPAC), 2004 UK	To conduct a rapid review of the safety and efficacy of CTC.	Full systematic review not undertaken
Technology Assessment Committee, Institute for Clinical Systems Improvement, 2004 USA	To assess CTC as a screening and diagnostic test for colorectal cancer and polyps.	Insufficient reporting of review methods
Medical Services Advisory Secretariat, Ontario, 2003 Canada	To assess CTC versus colonoscopy as a screening test for colorectal cancer and polyps.	High quality
Health Technology Advisory Committee, Minnesota, 2002 USA	To assess CTC as a screening test for colorectal cancer.	Insufficient reporting of review methods
MSAC Horizon Scanning 001, 2001 Australia	To review the current state of development of CTC, present use and potential application.	Full systematic review not undertaken

One HTA report reported sufficient information for assessment as high quality (Ontario 2003). This report included 18 studies that compared the safety and effectiveness of CTC with conventional colonoscopy in a diagnostic or screening population of greater than 30 patients. Conclusions were largely based on the results of studies comparing the accuracy of CTC versus colonoscopy.

Overall, the HTA reports provide useful background information about the scope of research investigating the value of CT colonography (Appendix D). However, they provide limited data about the relative value of CTC as a diagnostic test in symptomatic patients compared to either DCBE or colonoscopy.

Other published systematic reviews

No systematic reviews were identified that investigated the relative accuracy of CTC versus DCBE. Four eligible meta-analyses assessing the accuracy of CTC (3 studies) or DCBE (1 study) for detecting colorectal neoplasia were identified (Table 20).

Table 20 Summary of characteristics and quality of systematic reviews

Author year	Objective	Number of studies & selection criteria	Quality
Meta-analyses of CTC accuracy			
Halligan et al 2005	To assess CTC accuracy for the detection of: • colorectal cancer • colorectal polyps (large, medium-large, all) To assess the quality of reported data.	24 studies (4,181 patients) published between 1994 and Dec 2003. Inclusion criteria: studies ≥ 30 patients. Exclusion criteria: studies that selected patients with a known high prevalence of abnormality (eg prior positive test), or if ≥ 50% patients underwent CTC because of incomplete colonoscopy. 1 study included only average risk screening patients. Prevalence of colorectal neoplasia 15-72%. Reference standard: endoscopy or surgical findings	High
Mulhall et al 2005	To assess CTC accuracy for the detection of: • colorectal polyps (≥ 10 mm, 6-9 mm, ≤ 5 mm). To identify the variables that may affect test outcomes.	33 studies (6,393 patients) published between 1975 and Feb 2005 Inclusion criteria: Prospective blinded studies in adult patients undergoing CTC followed by complete colonoscopy or surgery 10 studies included average risk screening populations Prevalence of neoplasia not reported Reference standard: complete colonoscopy or surgical findings	High
Sosna et al 2003	To assess CTC accuracy for the detection of: • colorectal polyps (≥ 10 mm, 6-9 mm, ≤ 5 mm).	14 studies (1,324 patients) published between 1994 and July 2002 Inclusion criteria: Prospective blinded studies in patients undergoing CTC followed by complete colonoscopy 2 studies included average risk screening populations. Prevalence of neoplasia not reported Reference standard: complete colonoscopy	Fair
Meta-analysis of DCBE accuracy			
de Zwart et al 2001	To assess DCBE and colonoscopy accuracy for the detection of: • colorectal cancer • colorectal polyps (> 10 mm, < 10 mm, all).	28 studies (25 DCBE, 16 colonoscopy) (number of patients n.r.) published between 1980 and 2000 Inclusion criteria: Studies reporting on DCBE and colonoscopy accuracy and complications Prevalence of neoplasia not reported Reference standard: not specified	Low

Computed tomography colonography

The three meta-analyses applied similar criteria for selecting studies based on the CTC procedure used (full colorectal preparation; dual positioning; at least single-detector CT colonography/helical CT scanner). The meta-analysis by Sosna et al (2002) was appraised as fair quality because details about the characteristics and quality of the individual included studies presented were not reported. The other two meta-analyses were appraised as high quality (Halligan et al 2005, Mulhall et al 2005).

The meta-analysis conducted by Mulhall et al (2005) is the most up to date of the three reviews and searched studies until Feb 2005. It includes all but one of the 14 studies reviewed by Sosna et al (2003) and 18 of the 24 studies reviewed by Halligan et al (2005). However, only Halligan et al (2005) assessed the accuracy of CTC for the detection of

both colorectal polyps and cancer. The authors reported that the number of cancers per study was too small to allow meta-analysis and estimated the sensitivity of CTC by combining the number of cancer cases as if they came from a single study (Halligan et al 2005).

Mulhall et al (2005) investigated potential sources of conflicting results (heterogeneity) between studies using stratified analysis and meta-regression. Halligan et al (2005) reported on deficiencies in the reporting of the studies identified and proposed a minimum dataset for studies reporting comparisons between CTC and colonoscopy.

These reviews did not attempt to directly compare CTC with colonoscopy or DCBE, nor did they assess CTC in patients with a contraindication to colonoscopy or following an incomplete colonoscopy.

Another factor limiting the applicability of the results to the present review is the inclusion of studies with all or a subset of patients that were asymptomatic and at average risk for colorectal neoplasia. There is empirical evidence that test sensitivity increases in populations with a higher prevalence of disease (Whiting et al 2004). Mulhall et al (2005) included three studies conducted in average risk patients and seven studies conducted in a combination of average risk and high-risk patients. The other two meta-analyses did not report on the number of studies that only included symptomatic or high-risk patients; both included at least one study conducted in average risk patients only. Six of the 17 studies included in Halligan's assessment of CTC sensitivity for cancer were excluded from the present review because at least a subset of patients were at average risk for colorectal neoplasia.

Double contrast barium enema

De Zwart et al (2001) conducted a systematic review to compare the safety and accuracy of DCBE and colonoscopy. Twenty five studies reporting on DCBE accuracy in symptomatic or high-risk screening populations, including case referent and retrospective series were reviewed. This review was appraised as low quality because the authors did not present a structured assessment of the characteristics of each study to assist interpretation of the results, although they did classify studies according to the potential for bias. The authors compared the mean sensitivity of DCBE versus colonoscopy for colorectal polyps and cancer in all studies and subsets of studies that were classified as showing less potential for bias.

Eleven of the included studies reported a direct comparison of DCBE and colonoscopy accuracy for detecting cancers (6) and/or colorectal polyps (11). Two of these studies were also eligible for inclusion in the current review and are discussed individually later (Irvine et al 1988, Durdey et al 1987).

Primary studies of test accuracy

The characteristics and quality appraisal of studies comparing the accuracy of CTC with DCBE and/or colonoscopy are described below. Studies that report on CTC accuracy using colonoscopy as a reference standard without comparing the accuracy of CTC and colonoscopy are also described ("noncomparative studies").

Studies comparing CTC, DCBE and/or colonoscopy

Seven studies directly compared the accuracy of CTC, DCBE and/or colonoscopy (Table 21).

Table 21   Characteristics and quality of studies comparing the accuracy of CTC versus DCBE and/or colonoscopy

Author, year, setting	Study design & patient characteristics				CTC technology		Study level & quality
	n	Study design	Patient characteristics	Accuracy endpoints	Scanner & positioning	Radiologist experience	
CTC versus DCBE and versus colonoscopy							
Rockey et al 2005 USA	614	Prospective Multicentre	Symptomatic 88% / high-risk asympt. 32% Mean age 57 yrs Prevalence: all lesions: 89%; Cancer: 1.5%	Cancers Lesions ≥ 10 mm, ≥ 6 mm, 6-9 mm, ≤ 5 mm	Multi-slice Dual positioning	CTC experience > 50 or training[1] DCBE experience 19 yrs (mean)	Level II Fair quality
CTC versus DCBE							
Johnson et al 2004 USA	691	Prospective Single Centre	Symptomatic 3%; high-risk asympt. 97% Mean age 63 yrs Prevalence: lesions ≥ 5 mm: 7.5%; Cancer: 0.87%	Polyps ≥ 10 mm, 5-9 mm	Multi-slice 88%/ Single-slice 12% Dual positioning	CTC experience >150 DCBE experience > 10 yr	Level III-2 Low quality
CTC versus colonoscopy							
Cotton et al 2004 USA	600	Prospective Multicentre	Symptomatic 87%; high-risk asympt. 13% Mean age 61 yrs Prevalence: all lesions: 51%; Cancer: 1.3%	Lesions ≥ 10 mm, ≥ 6 mm, 6-9 mm, ≤ 5 mm	Multi-slice Dual positioning	CTC experience ≥ 10	Level II Fair quality
Hoppe et al 2004 Switzerland	92	Prospective Single Centre	Symptomatic/ high-risk asympt. Mean age 66 yrs Prevalence: all lesions: 53%; Cancer: 9%	Lesions ≥ 10 mm, ≥ 6 mm, ≤ 5 mm	Multi-slice Dual positioning	CTC experience 30-60	Level II Fair quality
Ginnerup Pedersen et al 2003 Denmark	148	Prospective Single Centre	Cancer 5%/ symptomatic 44%; high-risk asympt. 51% Median age 60 yrs Prevalence: lesions ≥ 6 mm: 29.7%; Cancer 7%	Cancers Lesions ≥ 20 mm, 10-19 mm, ≥ 6 mm	Multi-slice Dual positioning	CTC experience ~100	Level II/III-2 Fair quality
Taylor et al 2003 UK	54	Prospective Single Centre	Symptomatic 83%; not specified 17% Median age 69 yrs Prevalence: all lesions: 54%; Cancer: 11%	Cancers Lesions ≥ 10 mm, polyps < 10 mm	Multi-slice Dual positioning	CTC experience not reported	Level II High quality
Van Gelder et al 2004 Netherlands	249	Prospective 2 centres	Symptomatic 8%; high-risk asympt. 92% Mean age 56yrs Prevalence: all polyps: 57%; Cancer: 1.6%	Polyps ≥ 10 mm, 6-9 mm, any size	Multi-slice Dual positioning	CTC experience ≥ 50	Level II/III-2 Fair quality

1 Approximately 50% of CTC readers had experience reading >50 CTC, all others completed a CTC training module.

Evidence about the relative accuracy of CTC versus DCBE and colonoscopy

One large prospective multicentre study conducted in the United States directly compared the accuracy of CTC, DCBE and colonoscopy for the detection of large colorectal polyps and cancers in 614 patients with symptoms (88%) and/or at high-risk for colorectal neoplasia due to family history (32%) (Rockey et al 2005). The mean age of patients was 57 years. The prevalence of colorectal neoplasia was 88.8%, including colorectal cancer in 1.5% of patients.

CTC was performed in supine and prone positions with multi-detector (4- or 8-slice) CT scanners. Radiologists reviewing the CTC images had read more than 50 cases or completed a training module prior to the study.

A second-look colonoscopy with segmental unblinding was performed if the results of the initial colonoscopy were discordant to the CTC findings. The reference standard involved a method of reconciliation of all tests that included repeat review and/or testing for discordant results. A lesion found at one test was identified as a match with a lesion found at colonoscopy based on the location (same segment) and size of the lesion (within 50% of size identified at colonoscopy).

This study was classified as level II evidence and appraised as being of fair quality because 1.8% of patients who did not complete CTC due to inadequate preparation or technical difficulties (test failures) were excluded from the analysis.

Evidence about the relative accuracy of CTC versus DCBE

Another large study from a single centre in the United States directly compared the accuracy of CTC and DCBE for the detection of colorectal polyps in 691 asymptomatic patients with a prior history of colorectal neoplasia (33%), family history of colorectal cancer (64%), or new onset of iron-deficiency anaemia (3%) and aged 50 years or older (mean age 63 years) (Johnson et al 2004). This study also investigated the added value of double reading CTC. The prevalence of polyps of 5 mm or larger and of cancer were 7.5% and 0.87%, respectively.

CTC was performed in supine and prone positions using single-slice CT scanning in 12% of patients and 4-slice CT scanning in 88% of patients. Glucagon was used as muscle relaxant in 89% of patients.

The reference standard was either: colonoscopy (17%), flexible sigmoidoscopy (84%), proctoscopy (13%), or surgery (0.4%). A lesion found at one test was identified as a match with a lesion found at colonoscopy based on the location (same segment) if 'similar' size. Diagnostic review was undertaken by one of three radiologists, who were reported to have more than 10 years experience including experience in reading > 150 CTCs.

This study was classified as level III-2 evidence and appraised as low quality due to the use of an invalid reference standard (proctoscopy or sigmoidoscopy) in patients with a negative finding at CTC or DCBE, which may be expected to introduce verification bias. Unlike colonoscopy, these endoscopic procedures are not able to detect lesions in bowel segments beyond the sigmoid. In addition, different proportions of positive CTC (11%) and DCBE (2%) findings were not followed up by colonoscopy. This may potentially have led to an overestimation of CTC specificity if some of these positive findings were

false-positives. In addition to these methodological flaws, the authors did not report that the investigators interpreting the reference standard were blinded to the results of DCBE and CTC.

Evidence about the relative accuracy of CTC versus colonoscopy

In addition to the study reported by Rockey et al (2005) described above, five other studies compared the accuracy of CTC with colonoscopy. These studies included a total of 1,143 patients. The largest study was a multicentre study conducted in the United States (Cotton et al 2004, 600 patients). Two studies were designed to compare the accuracy of CTC and colonoscopy and used additional diagnostic testing to establish the true diagnosis (Cotton et al 2004, Ginnerup Pedersen et al 2003). In the other three studies, colonoscopy was not assessed as a comparator; the accuracy of colonoscopy was only assessed in those patients undergoing further diagnostic testing due to discordant findings at CTC and initial colonoscopy (Hoppe et al 2004, Taylor et al 2003, van Gelder et al 2004).

Van Gelder et al (2004) only investigated asymptomatic patients with a personal or a family history of colorectal polyps or cancer. The other four studies included symptomatic as well as asymptomatic patients at high risk for colorectal neoplasia. Of these studies, the proportion of symptomatic patients ranged from 44% (Ginnerup Pedersen et al (2004) to 87% (Cotton et al 2004). The per-patient prevalence of lesions ranged from 30% (Ginnerup Pedersen et al 2003, for lesions greater or equal to 6 mm) to 57% (van Gelder et al 2004). The prevalence of cancer varied between 1.3% (Cotton et al 2004) and 11% (Taylor et al 2003).

All studies used colonoscopy and histopathology as the reference standard with a second-look colonoscopy for discordant results. Cotton et al (2004) performed a second-look colonoscopy if the initial colonoscopy result was discordant with the CTC result. The other studies used a second-look colonoscopy only if there was a negative initial colonoscopy after any positive CTC finding (Hoppe et al 2004, Ginnerup Pedersen et al 2003, Taylor et al 2003), or after a positive CTC finding of a polyp ≥ 10 mm (van Gelder et al 2004, median time to follow-up 13 months). Three studies used a technique of segmental unblinding of the initial colonoscopy results to guide investigators as to whether a second-look colonoscopy was indicated (Cotton et al 2004, Hoppe et al 2004, Ginnerup Pedersen et al 2003). Further methods to establish the reference standard were the use of additional diagnostic tests if results were still discordant after second-look colonoscopy (Cotton et al 2004), a repeat colonoscopy or DCBE if colonoscopy was incomplete (Ginnerup Pedersen et al 2003) and follow-up diagnostic procedures (Taylor et al 2003).

The studies differed in the way they determined whether a lesion found at CTC matched a lesion found at colonoscopy for classification as a true positive finding. All studies used a method based on the location and size of the lesion, but the definitions used differed slightly between the studies.

All five studies used multi-slice CT scanning and dual positioning (prone and supine). Three studies used a muscle relaxant (buscopan or glucagon) and one study injected IV contrast medium in 74% of patients (Hoppe et al 2004).

CTC reading experienced varied in the four studies reporting on this issue. Reader experience was lowest in the study reported by Cotton et al (2004). Only one of the nine

centres had substantial involvement in CTC prior to the study, but radiologists were required to have completed 10 CTC readings and had five recorded procedures checked for quality.

Three of these five studies of CTC compared to colonoscopy were classified as level II evidence (Cotton et al 2004, Hoppe et al 2004, Taylor et al 2003). Two studies reported insufficient information to distinguish between a classification of evidence level II and level III-1 (Ginnerup Pedersen et al 2003, consecutive patient enrolment not reported) or between level II and III-2 (van Gelder et al 2004, blinding to CTC results at colonoscopy not reported).

The quality appraisal resulted in one study being appraised as high quality (Taylor et al 2003) and four studies as fair quality (Cotton et al 2004, Hoppe et al 2004, Ginnerup Pedersen et al 2003 and van Gelder et al 2004).

Reasons why studies were rated as fair quality rather than high quality were that blinding of the reference standard to the results of the index tests CTC was not reported (van Gelder et al 2004) and that patients with CTC tests that were not completed due to test failure such as inadequate preparation or technical difficulties were excluded (Cotton et al 2004, Hoppe et al 2004, Ginnerup Pedersen et al 2003). Other potential methodological flaws in the study reported by Ginnerup Pedersen et al (2003) were that not all patients received the reference standard and that it could not be determined whether all consecutive eligible patients were enrolled in the study.

Additional evidence about CTC accuracy (no comparator tests)

Fourteen studies investigated CTC accuracy in a total of 1129 patients with study size ranging from 27 patients (Iannaccone et al 2002) to 160 patients (Hara et al 2001).

The characteristics and quality of these studies are summarised in Table 22. Eight studies included a mixed population of symptomatic patients and asymptomatic patients at high risk of colorectal neoplasia. Two studies included symptomatic patients only (Munikrishnan et al 2003, Vogt et al 2004), whereas three studies included only high-risk asymptomatic patients (Bruzzi et al 2004, Laghi et al 2003, Van Gelder et al 2002).

The per-patient prevalence of all lesions and of cancer varied widely across the studies (all lesions: 8.6-82% for all lesions; cancer 2.8%-36%).

Thirteen studies used multi-slice CT scanning and 11 studies performed scans using dual positioning on all patients. In one study, it was unclear whether multi- or single-slice scanning was used (Johnson et al 2003). Three studies investigated CTC accuracy using an ultra-low radiation dose (Cohnen et al 2004, Iannaccone et al 2002 and Vogt et al 2004). One other study compared different radiation dosage regimens (van Gelder et al 2002).

Table 22   Characteristics of noncomparative studies of CTC accuracy

Author, year, setting	Study design & patient characteristics				CTC technology		Study level & quality
	n	Study design	Patient characteristics	Accuracy endpoints	Scanner & positioning	Radiologist experience	
Bruzzi et al 2004, Ireland	82	Prospective single centre	High-risk asymptomatic Mean age: 57 yrs Prevalence: all polyps: 41%, Cancer: n.r.	Polyps ≥ 10, 6-9, ≤ 5 mm	Multi-slice dual positioning Interpreted axial images only	Read > 50 CTC	II/III-2, Insufficient information
Cohnen et al 2004, Germany	137	Prospective single centre	Symptomatic 73%, high-risk asympt. 27% Mean age: 57 yrs Prevalence: all lesions: 43%	Overall lesions	Multi-slice supine positioning Ultra-low dose technique	Level of experience n.r.	II/III-2, fair
Gluecker et al 2002, Switzerland	50	Prospective single centre	Symptomatic/ high-risk asympt. Age range: 50-75 yrs Prevalence: all polyps: n.r., Cancer: n.r.	Sensitivity reported per polyp only	Multi-slice CT scanner dual positioning	Read ~ 60 CTC	II/III-1, fair
Hara et al 2001, USA	160	Prospective single centre	Symptomatic, high-risk asympt. Mean age: 64 yrs Prevalence: polyps >10 mm: 5.6%, Cancer: n.r.	Polyps > 10 mm	Multi-slice dual positioning	Level of experience n.r.	II/III-2, Insufficient information
Iannaccone et al 2002, Italy	27	Prospective single centre	Symptomatic 52%, high-risk asympt. 48% Mean age: 62 yrs Prevalence: all lesions: 56%, Cancer: 33%	Cancer Lesions ≥ 10, 6-9, 5 mm	Multi-slice dual positioning Ultra-low dose technique	Read > 200 CTC	II/III-1, fair
Johnson et al 2003, USA	93	Retrospective multi-centre	Symptomatic 40%, high-risk asympt. 74% Mean age: 62 yrs Prevalence: all lesions: 82%, Cancer: 7.5%	Lesions ≥ 10, ≥ 5 mm	Multi-slice? dual positioning	Varied: read ≤ 10 CTC + instruction, up to 500 CTC	III-1, fair
Laghi et al 2003, Italy	35	Prospective single centre	High-risk asymptomatic Mean age: 62 yrs Prevalence: all lesions: 8.6%, Cancer: 2.8%	Cancer Overall lesions	Multi-slice dual positioning	"Experienced"/ level of experience n.r.	II/III-1, fair
Laghi et al 2002, Italy	66	Prospective single centre	Symptomatic 39%, high-risk asympt. 61% Mean age: 61 yrs Prevalence: all lesions: 48%, Cancer: 23%	Cancer all lesions	Multi-slice Supine +/- prone positioning	Level of experience n.r.	II/III-1, fair
Macari et al 2002, USA	105	Prospective single centre	Symptomatic, high-risk asympt. Mean age: 58 yrs Prevalence: all polyps: 56%, Cancer: 5.7%	All polyps	Multi-slice dual positioning	4 yrs CTC experience	II, fair

Author, year, setting	Study design & patient characteristics				CTC technology		Study level & quality
	n	Study design	Patient characteristics	Accuracy endpoints	Scanner & positioning	Radiologist experience	
Morrin et al 2000, USA	81	Prospective single centre	Symptomatic 93%, high-risk asympt. 7% Mean age: 62 yrs Prevalence: all polyps/masses: 57%, Cancer: n.r.	Masses ≥ 20 mm, Polyps 10-19, 5-9, < 5 mm	90% Multi-slice dual positioning	> 18 mths CTC experience	II/III-2, fair
Munikrishnan et 2003, UK	80	Prospective single centre	Symptomatic patients Median age: 68 yrs Prevalence: all polyps: n.r., Cancer: 36%	Cancer All polyps, polyps ≥ 10, 6-9, ≤ 5 mm Overall colorectal disease	Multi-slice dual positioning	Level of experience n.r.	II/II-2, Insufficient info
Roettgen et 2005, Germany	48	Prospective single centre	Symptomatic/ high-risk asympt. Mean age: 57 yrs Prevalence: all polyps: 31%, Cancer: n.r.	All polyps	Multi-slice CT scanner dual positioning	"Experienced"/level of experience n.r.	Insufficient info
Van Gelder et al 2002, Netherlands	50	Prospective single centre	High-risk asymptomatic Mean age: 59 yrs Prevalence: all polyps: 54%, Cancer: n.r.	Polyps ≥ 5, < 5 mm	Multi-slice CT scanner dual positioning	Read > 50 CTC	II, fair
Vogt 2004	115	Prospective single centre	Symptomatic patients Mean age: 58 yrs Prevalence: all polyps: n.r., Cancer: 3.5%	Sensitivity reported per polyp only	Multi-slice CT scanner supine positioning Ultra-low dose technique	Level of experience n.r.	II, fair

Table 23   Characteristics of studies of DCBE accuracy

Author, year, setting	n	Study design	Patient characteristics	Accuracy endpoints	Index test characteristics	Radiologist experience	Study level & quality
Durdey et al 1987, UK	66	Prospective, single centre	Symptomatic patients Mean age: 62 yrs Prevalence: all polyps: 17%/ Cancer: 3%	Cancer adenomatous polyp other	Standard DCBE and colonoscopy	Level of experience n.r.	II, fair
Irvine et al 1988, Canada	71	Prospective, single centre	Symptomatic patients Mean age: 54 yrs Prevalence: all polyps: 37%/ Cancer: 7%	Cancer lesions ≥ 5 mm	Prepation: Rapid colonic lavage	Level of experience n.r.	II, fair
Rockey et al 2004, USA	89	Prospective, 2 centres	Symptomatic patients Mean age: 60 yrs Prevalence: all polyps: 34%/ Cancer: 6%	Overall polyps, polyps >10, ≥ 6 mm	Standard DCBE and colonoscopy Preliminary x-ray to ensure adequate colon cleansing	Trainee specialist under supervision	II/III-1, fair

Studies of CTC accuracy differed in their use of a muscle relaxant (buscopan or glucagon). Five studies also used an intravenous contrast medium for CT scanning in some patients.

All studies used colonoscopy as the reference standard and histopathology for any lesions detected. In addition, Laghi et al (2003) included clinical follow-up and Morrin et al (2000) included a second colonoscopy for discordant results as part of the reference standard; both studies also accepted surgical findings to establish the true disease status. One study also reported on patient tolerance of CTC versus colonoscopy (Laghi et al 2003)

Three of the 14 studies of CTC accuracy reported CTC readers were 'experienced', without reporting the level of experience (Cohnen et al 2004, Laghi et al 2003, Roettgen et al 2005). Reader experience varied widely in the seven studies that provided further information and within the study reported by Johnson et al (2003), where some radiologists had previously read less than 10 CTC images and received additional instruction, while other radiologists had read up to 500 images.

Nine studies clearly described how they determined whether a lesion found at CTC matched a lesion found at colonoscopy for classification as a true positive finding. Criteria were based on location and size of lesion, but the definitions used differed between the studies.

Generally, assigning a level of evidence and appraising the quality of the included studies of CTC was hindered by a lack of reporting of important aspects of study design, a problem that has also been identified in the recent systematic review by Halligan et al (2005).

Three of the 14 studies of CTC accuracy using colonoscopy as a reference standard were classified as level II evidence (Macari et al 2002, van Gelder et al 2002, Vogt et al 2004). It was not possible to determine whether the remaining 11 studies could be classified as level II or III evidence because information on blinding (7 studies) and (non)consecutive sampling (4 studies) was not reported.

Ten of the fourteen studies were of fair quality. In the remaining four studies, information on blinding of CTC to colonoscopy was not provided so that a quality rating could not be assigned; however, studies would be of either fair or low quality (Table 22).

Thirteen studies (all except Morrin et al (2000)) did not perform a second-look colonoscopy for CTC findings that were not confirmed at the initial colonoscopy. Other quality criteria that were not met were: data to allow reconstruction of 2 × 2 tables were not provided (5 studies; Gluecker et al 2002, Iannaccone et al 2002, Johnson et al 2003, Roettgen et al 2005, Vogt et al 2004); an inadequate description of how a true positive CTC result (true match with reference standard) was determined (7 studies; Bruzzi et al 2004, Gluecker et al 2002, Iannaccone et al 2002, Laghi et al 2003, Morrin et al 2000, Munikrishnan et al 2003, Roettgen et al 2005); and where not all patients received the reference standard (Laghi et al 2003). A lack of clarity about whether the patients selected were a representative sample was a quality issue in six studies (Bruzzi et al 2004, Gluecker et al 2002, Iannaccone et al 2002, Roettgen et al 2005, Laghi et al 2001, Laghi et al 2003, Johnson et al 2003). Exclusion of test failures where bowel preparation instructions were not followed as reported by Gluecker et al (2002) was not assessed as a deficiency in study quality because it would lead to exclusions for both CTC and colonoscopy and

thus is not likely to bias estimates of the relative accuracy of the tests. In seven studies, blinding of colonoscopy to CTC and/or CTC to colonoscopy was not reported (Bruzzi et al 2004, Cohnen et al 2004, Hara et al 2001, Johnson et al 2003, Morrin et al 2000 fair, Munikrishnan et al 2003, Roettgen et al 2005).

Additional evidence about DCBE accuracy (no comparator tests)

Three single-centre studies reported on DCBE accuracy in a total of 226 symptomatic patients (Table 23). Two of these studies were conducted over 15 years ago (Irvine et al 1988, Durdey et al 1987). The mean age of patients was between 54 and 60 years.

The prevalence of patients with polyps was between 17% (Durdey et al 1987) and 37% (Irvine et al 1988). The prevalence of cancer in these studies ranged between 3% and 7% respectively.

All three studies defined colonoscopy with or without histopathology as the reference standard. In two studies a second colonoscopy was conducted if results were discordant (Irvine et al 1988, Rockey et al 2004). Two studies used the 'maximum diagnostic information available' as the reference standard to establish the final diagnosis (Durdey et al 1987, Irvine et al 1988). Only one of the studies (Rockey et al 2004) reported how the DCBE and colonoscopy findings were compared to determine a true match for classification as a true positive.

Two of the three studies of DCBE were classified as level II evidence (Durdey et al 1987, Irvine et al 1988). Rockey et al (2004) did not report whether patients were consecutively enrolled to determine classification as level II or level III-1 evidence.

All of the studies of DCBE accuracy using colonoscopy as the reference standard were appraised as fair quality. Reasons why these studies did not receive a high quality rating were that the descriptions of how a true positive DCBE result (true match) was determined (Durdey et al 1987, Irvine et al 1988) and how DCBE was performed (Irvine et al 1988) were not adequate. In the study by Rockey et al (2004), the method of patient enrolment was not reported which precluded an appraisal of high quality.

Primary studies of patient preferences and quality of life

Eleven studies (total patients = 2,709) reported on patient preferences and tolerance of CTC or other quality of life measures. These studies compared CTC to DCBE and colonoscopy (2 studies); DCBE (1 studies); or colonoscopy (6 studies). Two of these studies reported on different outcomes for the same patient group and two studies also investigated CTC accuracy (Table 24).

Table 24 **Characteristics of studies of patient preference and quality of life**

Author, year, setting	n (n evaluated)	Objective	Study design and patient characteristics	Quality
Akerkar et al 2001, USA	300 (295) response rate 98%	To compare CTC versus colonoscopy for: • patient preference • Quality of Life (QoL)/patient tolerance	Prospective single-centre study, consecutive enrolment Patients referred for colonoscopy due to symptoms (35%) or screening (65%) Males 97%; mean age 62 yrs 3 post-test questionnaires with 7-point Likert scale adapted from validated instrument Modified time-trade-off technique to assess waiting time accepted for preferred test	Fair
Cotton et al, 2004, USA and UK	600 (518) response rate 86%	To compare CTC versus colonoscopy for: • patient preference	Prospective multicentre study, consecutive enrolment Patients referred for colonoscopy due to symptoms (87%) or post-polypectomy surveillance (14%) Males 45%; mean age 61 yrs 1 post-test questionnaire, instrument validation not reported	Fair
Gluecker et al 2003, USA	1. 696 (515) response rate 74% 2. 617 (538) response rate 87%	To compare CTC versus colonoscopy and DCBE for: • patient preference • QoL/patient tolerance	Prospective single-centre study, consecutive enrolment Patients referred for colonoscopy (group 1); or DCBE (group 2) with recent onset iron-deficiency anaemia or asymptomatic but increased risk of colorectal neoplasia Group 1: males 63%, mean age 65 yrs Group 2 = males 49%; mean age 64 yrs 1 post-test questionnaire, instrument validation not reported	Fair
Laghi et al, 2003	35 (31) response rate 89%	To compare CTC versus colonoscopy for: patient preference • QoL/patient tolerance	Prospective single-centre study, consecutive enrolment not reported Asymptomatic patients referred for colonoscopy for surveillance of colorectal cancer Males 51%; mean age 62 yrs 1 post-test questionnaire, instrument validation not reported	Fair
Ristvedt et al, 2003, USA	120 response rate not reported	To compare CTC versus colonoscopy for: • patient preference • QoL/patient tolerance	Prospective single-centre study, consecutive enrolment not reported Symptomatic patients/ asymptomatic patients at higher risk of colorectal neoplasia/ screening patients Males 44%; mean age 58 yrs Pre-test and 2 post-test questionnaires, instrument validation not reported	Fair
Svensson et al 2002, Sweden	111 (104) response rate 94-95%	To compare CTC versus colonoscopy for: • patient preference • QoL/patient tolerance	Prospective single-centre study, consecutive enrolment Symptomatic patients and asymptomatic patients at higher risk of colorectal neoplasia Males 59%; median age 66 yrs 3 post-test questionnaires, instrument validation not reported	Fair

Author, year, setting	n (n evaluated)	Objective	Study design and patient characteristics	Quality
Taylor et al, 2005, UK	77 (71) response rate 93%	To compare CTC versus DCBE for: • patient preference • QoL/patient tolerance • patient satisfaction	Prospective single-centre study, consecutive enrolment Symptomatic patients Males 44%; median age 70 yrs Handheld device for pain assessment and 3 post-test questionnaires using validated instruments	High
Taylor et al, 2003b, UK Additional outcomes for group 1 reported in Taylor et al 2003c	1. 168 (144) response rate 86% 2. 140 (126) response rate 90%	To compare CTC versus colonoscopy or flexible sigmoidoscopy; and DCBE for: • patient preference • patient satisfaction • QoL/patient tolerance	Prospective multicentre study, consecutive enrolment Symptomatic patients and asymptomatic patients at higher risk of colorectal neoplasia Group 1: male 50%, median age 65yrs Group 2: male 45%, median age 62yrs 3 post-test questionnaires using validated instrument	High
Taylor et al, 2003c, UK Additional outcomes reported in group 1 of Taylor et al 2003b	144 response rate for original cohort 86%	To compare CTC versus colonoscopy or flexible sigmoidoscopy for: • cardiovascular effects • perceived pain	Prospective multicentre study, consecutive enrolment Symptomatic patients and asymptomatic patients at higher risk of colorectal neoplasia Males 49%; mean age 64 yrs Handheld device for pain assessment. Pre and post-test physical observations, oxygen saturation. Holter ECG for cardiovascular assessment (40 patients)	High
Thomeer et al, 2002, Belgium	124 response rate not reported	To compare CTC versus colonoscopy for: • Patient preference • QoL/Patient tolerance	Prospective single-centre study, consecutive enrolment Symptomatic and asymptomatic patients (at average or high risk of colorectal neoplasia) Males 55%; mean age 64 yrs 1 post-test questionnaire, instrument validation not reported	Fair
Van Gelder et al 2004, The Netherlands	249 response rate not reported	To compare CTC versus colonoscopy for: • patient preferences (short- and midterm) • QoL/Patient tolerance	Prospective two centre study, consecutive enrolment Asymptomatic patients at high risk of colorectal neoplasia Males 59%; mean age 56 yrs 1 pre-test and 4 post-test questionnaires, instrument validation not reported	Fair

In nine studies, all patients received all tests assessed in the study (CTC before colonoscopy/DCBE). In the study reported by Gluecker et al (2003), two patient groups received CTC before colonoscopy or before DCBE. In the study reported by Taylor et al (2003b) DCBE was performed in a different patient cohort than CTC and colonoscopy.

The methods used to assess patient preference and quality of life were inconsistent between the studies and no study assessed an overall measure of quality of life. All studies assessed abdominal pain/discomfort and patient preferences (Taylor et al 2003b and Taylor et al 2003c assessed these outcomes for the same patient group). Pain was measured as perceived pain by means of a handheld device in two studies (Taylor et al 2003c, Taylor et al 2005) or self-administered questionnaires. Quality of life outcomes also included patient satisfaction, worry, tolerance, sense of disrespect, embarrassment, difficulty and overall unpleasantness for CTC versus the comparator tests. Quality of life and patient preference outcomes were assessed through self-administered questionnaires (Akerkar et al 2001, Gluecker et al 2003, Taylor et al 2003b, Taylor et al 2005, Thomeer et al 2002, Svensson et al 2002, van Gelder et al 2004) and/or patient interview (Akerkar et al 2001, Ristvedt et al 2003).

The mean or median age of patients ranged from 56 years (van Gelder et al 2004) to 70 years (Taylor et al 2005). One study included 97% males (Akerkar et al 2001), all other studies between 44 and 60% males. Nine studies included mixed populations of symptomatic patients and asymptomatic patients; three of these studies included screening patients at average risk of colorectal cancer (Akerkar et al 2001, Ristvedt et al 2003, Thomeer et al 2002). One study only included symptomatic patients (Taylor et al 2005), whereas one study only included patients with a personal or family history of colorectal cancer or polyps (van Gelder et al 2004).

CTC techniques varied in terms of multi-slice or single- and multi-slice CT scanning, single/dual positioning and the use of muscle relaxants. Colonoscopy techniques and the use of sedation and/or analgesia also varied between studies.

Three studies were appraised as high quality (Taylor et al 2003b, 2003c & 2005). The remaining seven studies were appraised as fair quality, because they did not report to use a validated instrument for quality of life assessment.

Applicability

The main factors that may limit the applicability of the results of this review to Australian clinical practice are the comparability of the study populations to the intended Australian test population, and the comparability of the type of CTC techniques performed and level of prior radiologist training and experience in these studies to Australian practice.

Accordingly, only studies conducted in symptomatic patients or asymptomatic patients at high risk due to a family or a personal history of colorectal cancer (the intended test population) were considered eligible for this review of CTC accuracy. Studies that enrolled average-risk screening patients were excluded, although two studies included some patients who were not representative of the intended test population. In the study reported by Ginnerup Pedersen et al (2003), 5% of patients were undergoing preoperative colonoscopy with a known diagnosis of colorectal cancer. In the study reported by Taylor et al (2003), the reason for referral to colonoscopy was not available for 17% of patients. All other studies only included symptomatic or high-risk

asymptomatic patients; however, prevalence of colorectal neoplasia varied widely between studies (lesions ≥ 10 mm prevalence 2-23%). As there is empirical evidence that sensitivity increases in populations with a higher prevalence of disease (Whiting et al 2004), the applicability of these results to Australian practice may depend on the range of disease prevalence in the intended test population.

The assessment of patient preferences and quality of life measures associated with testing included two studies conducted in screening populations. The applicability of these results to the intended test population may be limited if patient perceptions about CTC and comparator tests vary between symptomatic and screening populations.

According to the Advisory Panel, CTC is currently performed using multi-slice scanners and thus, only studies using this technique were included in this review. Other CTC techniques differed between the studies, for example, dual/single positioning, use of contrast-agents and muscle relaxants. The differences in these techniques may affect the applicability of results to Australian practice.

The level of experience of the radiologist reading the CTC scans was specified in twelve of 21 studies assessing CTC accuracy. The reviewing radiologists' level of experience in these studies varied, with three studies accepting relatively low levels of prior experience. In these studies, radiologists were involved who had completed 10 CTC readings (Cotton et al 2004), who had attended a training module if they had previously read less than 50 cases (Rockey et al 2005) or less than 10 cases (Johnson et al 2003). In contrast, two of these studies also assessed DCBE accuracy and reported a mean experience in this technique of 19 years (Rockey et al 2005) or at least 10 years (Johnson et al 2004). As the accuracy of CTC has been reported to differ depending on the level of experience of the CTC reviewing radiologist (Ontario 2003), the applicability of the results of these three studies to the Australian setting may be limited if CTC training and experience is routinely available at a high standard in Australia. Similarly, radiologist experience in performing and interpreting DCBE studies may also vary between study settings and Australian practice.

Is it safe?

Background information

General information about the risks associated with CTC is presented below, followed by a summary of the evidence from included studies.

Ionising radiation exposure

Patients undergoing CT scans are exposed to ionizing radiation. Large doses and/or repeated exposure to ionizing radiation are associated with a small increase in cancer risk after a latency period of around 20 years. The effective dose from CTC varies widely in the literature according to the type of scanner and scanning protocol. Multi-slice scanning and dual positioning result in higher doses than single-slice scanning and single positioning. The median dose for CTC used for research purposes has been reported at 8.8 mSv when dual positioning is used (Van Gelder et al 2002). Three studies included in the present review that used standard scanning protocols reported radiation doses. These doses ranged from 4 to 7.8 mSv (Ginnerup Pedersen et al 2003, Hara et al 2001, Macari et al 2002). Three other included studies investigated the use of ultralow dose multidetector CTC (effective dose range of 0.7 mSv to 2.3 mSv) (Cohnen et al 2004; Iannaccone et al 2002; Vogt et al 2004). A fourth study investigated CTC performance at different doses (range 2 to 6 mSv, van Gelder et al 2002). These doses can be compared to 0.02 mSv for a plain chest x-ray and approximately 3 mSv per year from natural background radiation (CDRH 2005). An effective dose of 8.8 mSv is associated with a 0.02% risk of cancer in a 50 year old individual and a lower risk for older individuals (Van Gelder 2002). This represents a very small increased risk compared to the baseline risk of fatal cancer which has been estimated to be one in 5 in the United States (CDRH 2005).

The effective dose is higher in women than men (Mascari M 2002, Wise 2003). CTC may also lead to greater biological damage to women than men due to ionizing radiation exposure to the ovary, uterus and breast.

Children and foetuses are more sensitive to the effects of radiation than adults (Wise 2003), therefore CTC is not recommended for use in children and pregnant women.

The effective dose of ionizing radiation for DCBE is lower than for CT scanning using standard protocols (Ontario 2003). However, there is a trend to reduce CTC radiation exposure eg by using low-dose CTC protocols or tailoring image acquisition according to clinical context (Advisory Panel, 25 November 2005). Studies have indicated that lower dose scanning protocols reduce ionising radiation to a level equivalent to or below DCBE without impairing the performance of the test (Iannaccone et al 2003, Van Gelder et al 2002). Colonoscopy does not involve ionizing radiation.

Bowel preparation

Patients undergoing CTC require the same bowel preparation as patients undergoing DCBE or colonoscopy. In addition to the inconvenience of the 24 hour clear liquid diet, potential adverse events of the diarrhoeal agents used include: nausea, faecal incontinence, abdominal pain and loss of sleep (Ginnerup Pedersen et al 2004).

Bowel perforation

CTC involves insufflation of air or carbon dioxide to distend the colon for visualisation of the bowel wall. This procedure has been associated with abdominal cramping, bloating and pain. Case reports of perforation of the bowel wall following CTC due to over inflation of air have also been reported in the literature (Kamar et al 2004, Coady-Fariborzian et al 2004). The incidence of perforation due to CTC is not known, but is likely to be lower than that reported for colonoscopy, which is a more invasive test. One large retrospective series from a single centre in the United States has estimated the risk of perforation requiring surgical intervention following diagnostic colonoscopy at 0.06% (based on 16,948 consecutive diagnostic colonoscopies, Tran et al 2001). This study also reported one death following diagnostic colonoscopy (mortality 0.006%, Tran et al 2001). DCBE also involves insufflation of air and a very small risk of perforation.

Evidence from included studies

Most HTA reports concluded that CTC is a relatively safe procedure compared to colonoscopy, although noting the small risks associated with exposure to ionizing radiation. The Ontario report (2004) recommended that these risks required further assessment and may preclude the repeated use of CTC for colorectal cancer screening.

One HTA report stated that no deaths have been attributed to CTC (ICSI 2004). None of the studies included in the present review reported any deaths following CTC, DCBE or colonoscopy. The results of the seven studies that reported on complication rates for CTC are summarised below.

CTC versus DCBE

Neither of the two studies investigating the relative accuracy of CTC and DCBE reported on complications. Three other studies compared patient discomfort following both tests (see results page 87).

CTC versus colonoscopy

Seven studies reported on test complications for CTC and colonoscopy (n = 1,152: Ginnerup Pedersen et al 2003, Cotton et al 2004, Gluecker et al 2002; Johnson et al 2003, Laghi et al 2002, Vogt et al 2004; Munikrishnan et al 2003). Six of these studies reported no complications for CTC or colonoscopy (552 patients: Gluecker et al 2002, Ginnerup Pedersen et al 2003; Johnson et al 2003, Laghi et al 2002, Vogt et al 2004; Munikrishnan et al 2003). One large study reported an overall rate for minor adverse events of 2.3% (14 of 600 patients). This figure included events other than test complications including minor bleeding following polypectomy (1 patient) and identification of extracolonic lesions of possible clinical significance (8 patients). The reasons for the adverse events experienced by the other 6 patients (1%) were not reported (Cotton et al 2004). No serious complications were reported.

DCBE versus colonoscopy

A systematic review of DCBE accuracy estimated the risk of bowel perforation at 0.0001-0.004% of patients tested with DCBE but did not report the complication rate for colonoscopy (de Zwart et al 2001).

Interpretation

CTC is a relatively safe procedure compared to DCBE and at least as safe as, or safer than, colonoscopy. The most common adverse event reported in the literature is abdominal discomfort (refer to page 70). Colonic perforation following CTC is a serious but very rare complication. No perforations or deaths from CTC, DCBE or colonoscopy were reported in the studies reviewed (1,152 patients undergoing CTC). The true incidence of perforation following CTC is unknown.

Exposure to ionising radiation occurs with both CTC and DCBE. This risk increases with repeated exposures and is higher for younger individuals. CTC is contraindicated in children and pregnant women due to these harms.

Is it effective?

No randomised controlled trials were identified that compared health outcomes in patients following testing with CTC, DCBE or colonoscopy for the detection or exclusion of colorectal disease and subsequent treatment. Evidence from studies comparing the accuracy, patient preferences and quality of life outcomes for CTC, DCBE and colonoscopy are summarised below for conclusions about the relative effectiveness of these tests.

Health technology assessment reports

Overall findings

The seven existing HTA reports all noted variation in estimates of the accuracy of CTC among published studies. In general, they found that test accuracy varied according to the size of the lesion, test methods and type of technology used. The high-quality Ontario (2003) report included the largest number of primary accuracy studies (18 studies) and reported that estimates of CTC sensitivity using multislice scanning ranged from 86 to 100% for the detection of cancer, 80 to 100% for the detection of polyps $\geq$ 10 mm, falling to 33-86% for polyps between 6 and 9 mm in size and 3-70% for polyps $\leq$ 5 mm. CTC specificity ranged from 75-100% and was not reported by lesion type in any study. The findings of other reports were largely based on the same set of studies and were consistent with these findings.

Based on their review of the literature, the authors of the Ontario report (2003) suggested that in addition to increasing lesion size, factors that improved the accuracy of CTC included: multi-slice versus single-slice scanning, dual positioning, adequate bowel cleansing, adequate bowel distension and radiologists' experience (Ontario 2003).

Relative accuracy of CTC versus DCBE and versus colonoscopy in symptomatic patients

Two HTA reports summarised evidence about the relative safety, effectiveness, cost-effectiveness and patient preferences for CTC versus DCBE or colonoscopy as a diagnostic test (ICSI 2004, Ontario 2003).

Conclusions about the relative value of CTC versus DCBE were drawn from different sources of evidence. The ICSI report cited evidence about the accuracy of DBCE compared to colonoscopy to conclude that CTC was superior to DBCE (ICSI 2004). The Ontario report cited two small studies that compared CTC versus DCBE in patients following incomplete colonoscopy and concluded that both tests were equivalent for polyps > 5 mm. However, the authors noted that CTC may have an advantage over DCBE because it can offer images of the proximal colon and any extra-colonic involvement when there is an obstructive lesion.

Both reports concluded that CTC was not superior to colonoscopy for the detection of colorectal cancers and polyps (ICSI 2004, Ontario 2003).

Other published systematic reviews

No other systematic reviews directly compared CTC with DCBE or colonoscopy for the detection of colorectal disease.

Systematic reviews of CTC accuracy

Two recent high-quality systematic reviews provide estimates of accuracy of CTC in detecting colorectal cancer (Halligan et al 2005) and polyps (Halligan et al 2005, Mulhall et al 2005).

Halligan et al (2005) reported that CTC sensitivity for the detection of cancer ranged from 67% to 100% in 17 studies. Overall, CTC detected 144 of 150 cancers found, resulting in an overall sensitivity of 96% (95% CI: 91-99%) if these cancers were treated as if they were from one study. The authors did not estimate CTC specificity for detecting cancer.

Mulhall et al (2005) conducted the most up-to-date and largest meta-analysis of CTC accuracy for the detection of colorectal polyps. Overall, pooled per-patient sensitivity was 70% (95% CI 53-87%) and pooled per-patient specificity was 86% (84-88%). For polyps ≥ 10 mm, pooled per-patient sensitivity was 85% (79-91%) and specificity was 97% (96-97%). Sensitivity was reduced for smaller polyps: polyps 6-9 mm: pooled per-patient sensitivity 70% (55-84%), specificity 93% (91-95%); polyps ≤ 5 mm: pooled per-patient sensitivity 48% (25-70%), specificity 91% (89-95%).

The authors found a statistically significant difference (heterogeneity) in the estimates of sensitivity (p < 0.001) between the included studies, but not in the estimates of specificity. Differences in collimation, CT scanners and image processing were identified as potential sources for this heterogeneity with studies using thinner slices, multi-detector scanners and fly-through imaging technology showing higher CTC sensitivity. Patient factors such as age, sex or risk classification were not found to be a source of heterogeneity in this meta-analysis. The prevalence of cancer in the study population was not investigated as a potential source of heterogeneity.

Systematic review of DCBE accuracy

De Zwart et al (2001) reviewed a total of 28 studies and reported a wide variation in estimates of DCBE sensitivity (62-96% for cancers, 48-100% for polyps > 10 mm, 53-96% for polyps < 10 mm) and specificity (67-85% for all lesions). Based on the results of 16 studies, colonoscopy sensitivity was reported as 79-100% for colorectal cancer, 79-100% for polyps > 10 mm and 75-85% for polyps < 10 mm. Colonoscopy specificity was estimated by three studies (specificity for lesions of all sizes ranged from 78% to 99%).

The authors concluded that overall the sensitivity of DCBE for the detection of colorectal polyps was lower than colonoscopy but resulted in fewer complications. This difference was statistically significant when 10 studies that were appraised as vulnerable to reference standard bias were excluded (p = 0.04). However, the authors noted that DCBE sensitivity was similar to colonoscopy for the detection of cancer and polyps ≥ 10 mm.

Primary studies

The following sections report the results of included primary studies of CTC accuracy followed by studies of quality of life and patient preference and a section discussing additional considerations (incomplete colonoscopy, extracolonic findings, test failures).
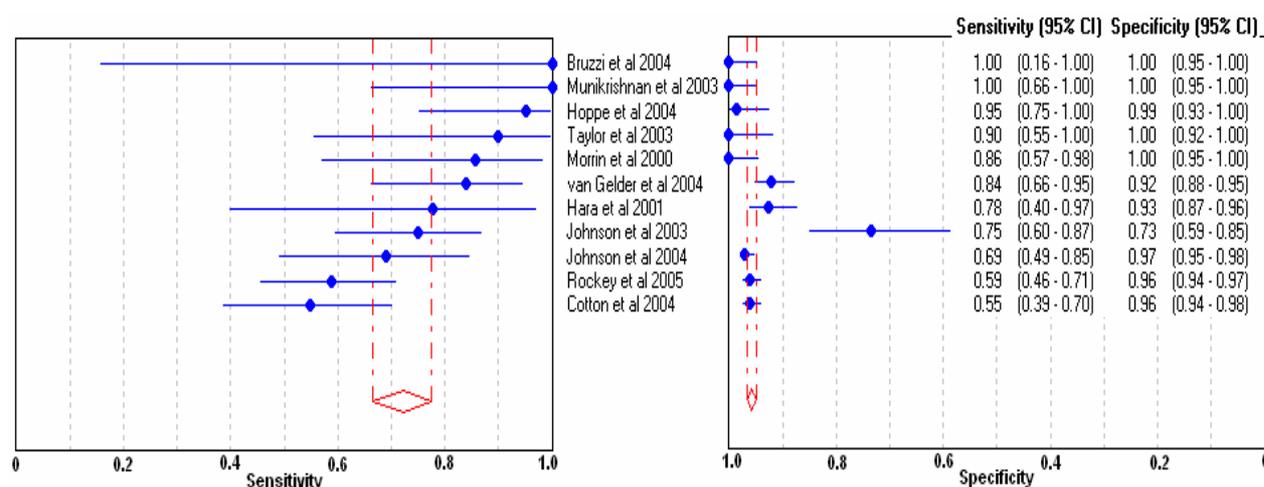
CTC accuracy results are presented as test sensitivity and specificity per patient. Four eligible studies of CTC accuracy did not report sensitivity per patient (Gluecker et al 2002, Roettgen et al 2005, Vogt et al 2004) or the relevant categories of polyp size (van Gelder et al 2002) and are thus not cited in the following results section (however, results of these studies are presented in the tables in Appendix D (Table 62).

Evidence about CTC sensitivity and specificity for the detection of cancer and polyps ≥ 10 mm are presented first, followed by results for the detection of cancers, lesions 6-9 mm, ≤ 5 mm and overall colorectal disease. A summary of all evidence from studies of CTC accuracy is presented followed by evidence from studies that report on a direct comparison of CTC and DCBE and/or colonoscopy.

Detection of cancers and polyps ≥ 10 mm

Eleven studies reported on CTC sensitivity and specificity for the detection of lesions ≥ 10mm in the population of interest. As shown in Figure 6, findings varied widely between studies.

Figure 6   Estimates of CTC sensitivity and specificity for detection of lesions ≥ 10 mm[1, 2]

	Sensitivity (95% CI)	Specificity (95% CI)
Bruzzi et al 2004	1.00 (0.16 - 1.00)	1.00 (0.95 - 1.00)
Munikrishnan et al 2003	1.00 (0.66 - 1.00)	1.00 (0.95 - 1.00)
Hoppe et al 2004	0.95 (0.75 - 1.00)	0.99 (0.93 - 1.00)
Taylor et al 2003	0.90 (0.55 - 1.00)	1.00 (0.92 - 1.00)
Morrin et al 2000	0.86 (0.57 - 0.98)	1.00 (0.95 - 1.00)
van Gelder et al 2004	0.84 (0.66 - 0.95)	0.92 (0.88 - 0.95)
Hara et al 2001	0.78 (0.40 - 0.97)	0.93 (0.87 - 0.96)
Johnson et al 2003	0.75 (0.60 - 0.87)	0.73 (0.59 - 0.85)
Johnson et al 2004	0.69 (0.49 - 0.85)	0.97 (0.95 - 0.98)
Rockey et al 2005	0.59 (0.46 - 0.71)	0.96 (0.94 - 0.97)
Cotton et al 2004	0.55 (0.39 - 0.70)	0.96 (0.94 - 0.98)

1 Estimates and confidence intervals presented were calculated from reconstruction of 2 × 2 tables using reported data and may vary slightly from figures reported in the studies.
2 Patients in Johnson et al (2003) might also be included in Johnson et al (2004), data in Morrin et al (2000) are for lesions 10-19 mm.

Plotting these data in the ROC plane showed that this heterogeneity was not explained by a threshold effect and a meta-analysis was not performed (SROC regression coefficient ß = –0.63, p = 0.26).

The median findings may provide the most reasonable summary estimate of CTC sensitivity and specificity (median CTC sensitivity 84%, median CTC specificity 97%). However, the wide range of findings from individual studies indicates the broad range of

uncertainty, in particular about the true sensitivity of CTC to detect lesions ≥ 10 mm (sensitivity 55-100%, specificity 73-100%). Differences in study quality (low to high), prevalence of lesions ≥ 10 mm (2-47%), the type of techniques used and radiologist experience may explain some of the variation observed.

Meta-analysis of five studies that included a second-look colonoscopy in the reference standard provided a pooled estimate of CTC sensitivity of 69% (95% CI 61-76%, heterogeneity χ^2 = 21.31, df = 4, p < 0.0001), and CTC specificity of 96% (95% CI 95-97%, heterogeneity χ^2 = 11.62, df = 4, p = 0.02) (Cotton et al 2003, Hoppe et al 2004, Rockey et al 2005, Taylor et al 2003, van Gelder et al 2004, all appraised at least as fair quality). Again, heterogeneity between studies was not explained by a threshold effect (SROC regression coefficient ß = 0.61, p = 0.56) or other factors and thus these pooled estimates may not provide a valid summary of CTC accuracy.

Seven of these 11 studies reported on CTC accuracy for cancers and polyps ≥ 10 mm without providing a comparison to DCBE and/or colonoscopy and are not discussed further (Bruzzi et al 2004, Hara et al 2001, Hoppe et al 2004, Johnson et al 2003, Morrin et al 2000, Munikrishnan et al 2003, Taylor et al 2003).

Relative accuracy of CTC versus DCBE

Two studies compared the accuracy of CTC versus DCBE. Both studies indicated that CTC may be more sensitive than DCBE for the detection of cancers and polyps ≥ 10 mm, but the differences observed did not reach statistical significance (Table 25). Findings about the relative specificity of CTC versus DCBE were not consistent between studies, nor between radiologists in the study by Johnson et al (2004).

Table 25   Accuracy studies comparing CTC versus DCBE for detecting lesions ≥ 10mm[1]

Study author, year	n	Prevalence lesions ≥ 10 mm	CTC		DCBE		Test comparison CTC versus DCBE	Study level & quality
			Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)		
Rockey et al 2005	614	10.3%	59% (45-71%)	96% (94-98%)	48% (35-61%)	90% (87-92%)	Sensitivity p = 0.11 Specificity p < 0.0001	level II fair quality
Johnson et al 2004[2]	691	4.2%	69% (49-85%)	97% (95-98%)	48% (29-68%)	99% (98-100%)	Sensitivity p ≥ 0.06 for 3 reviewers Specificity (p < 0.05 for 2 of 3 reviewers)	level III-2 low quality

1 Results are figures reported in the studies, estimates and confidence intervals calculated from reconstruction of the 2 × 2 table using reported data may differ slightly.
2 Estimated from average results of three radiologists (range: CTC sensitivity 56-77%, CTC specificity 96-99%; DCBE sensitivity 44- 56%, DCBE specificity 99-100%).

The study reported by Rockey et al (2005) indicated that CTC was more specific than DCBE (p < 0.0001, Table 25). In contrast, Johnson et al (2004) reported that CTC specificity was statistically significantly lower than DCBE for 2 of 3 reviewers (p < 0.05, Table 25).

Johnson et al (2004) also reported that double reading of CTC images resulted in a statistically significantly higher sensitivity than DCBE with a corresponding decrease in specificity (double read CTC sensitivity 79% versus DCBE sensitivity 48%, p = 0.04;

double read CTC specificity 95%, DCBE specificity 99%, p < 0.001). However, this study included an invalid reference standard and verified a higher proportion of DCBE findings, which may have inflated the estimates of DCBE specificity according to the investigators. Thus the results of this study are difficult to interpret and a meta-analysis was not undertaken.

Relative accuracy of CTC versus colonoscopy

In addition to the study reported by Rockey et al (2005), two other studies compared the sensitivity and specificity of CTC versus colonoscopy to detect cancers and polyps ≥ 10 mm (Cotton et al 2004, van Gelder et al 2004). All three studies were appraised as fair quality and used a reference standard that included a second-look colonoscopy if the initial test findings were discordant. The results are presented in Table 26.

Table 26 **Accuracy studies comparing CTC versus colonoscopy for detecting lesions ≥ 10mm[1]**

Study author, year	n	Prevalence lesions ≥ 10 mm	CTC		Colonoscopy		Test comparison	Study level & quality
			Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)		
Rockey et al 2005	614	10.3%	59% (45-71%)	96% (94-98%)	98% (91-100%)	100% (99-100%)	sensitivity p < 0.0001 specificity p < 0.0001	level II fair quality
Cotton et al 2004	600	7.0%	55% (40-70%)	96% (94-98%)	100% (92-100%)	100% (99-100%)	test comparison n.r. difference in sensitivity & specificity[2]	level II fair quality
Van Gelder et al 2004	249	12%	84% (67-93%)	92% (87-95%)	81% (63-93%)	100% (98-100%)	test comparison n.r difference in specificity[2]	level II/III-2 fair quality
Pooled results	1,463		63% (55-71%) (χ^2 = 8.25, df = 2, p = 0.016)	95% (94-97%) (χ^2 = 5.30, df = 2, p = 0.071)	95% (90-98%) (χ^2 = 14.4, df = 2, p = 0.001)	100% (99.5-100%) (χ^2 = 3.52, df = 2, p = 0.17)	difference in sensitivity & specificity[2]	

1 Where confidence intervals were not reported, confidence intervals were calculated from reconstruction of the 2 × 2 table using reported data.
2 Confidence intervals do not overlap, indicating that CTC and colonoscopy sensitivity/specificity are statistically significantly different.

Two of these studies indicated that CTC is less sensitive and specific than colonoscopy for the detection of lesions ≥ 10 mm (Table 26). Rockey et al (2005) reported that these differences were highly statistically significant (p < 0.0001). Cotton et al (2004) and Van Gelder et al (2004) showed that the 95% confidence interval surrounding estimates of colonoscopy specificity excluded the 95% confidence interval surrounding estimates of CTC specificity, indicating a statistically significant difference between the specificities of these tests. One of these studies also reported that the 95% confidence interval surrounding the estimate of colonoscopy sensitivity excluded the 95% confidence interval surrounding the estimate of CTC sensitivity (Cotton et al 2004).

The meta-analysis also indicated that colonoscopy is a more sensitive and specific test than CTC (Table 26). However, estimates of test sensitivity were statistically significantly

different across studies, thus the pooled results may not provide a valid summary of CTC and colonoscopy sensitivity for the detection of lesions ≥10mm.

Other evidence about DCBE accuracy

The systematic review by De Zwart et al (2001) reported that DCBE sensitivity for the detection of polyps ≥ 10 mm in high-risk, symptomatic populations ranged from 48 to 100%. DCBE specificity for polyps of all sizes ranged from 67-85%. No additional studies of DCBE accuracy using colonoscopy with or without other tests as the reference standard reported per-patient sensitivity for lesions ≥ 10 mm. The studies by Rockey et al (2005) and Johnson et al (2004) estimated DCBE sensitivity at the lower end of the range reported by the earlier systematic review, but reported higher estimates of DCBE specificity.

Interpretation of results

Evidence from 11 studies reporting on CTC accuracy for the detection of lesions ≥ 10 mm with or without comparing its accuracy with DCBE or colonoscopy accuracy demonstrate the wide range of uncertainty about CTC sensitivity (median CTC sensitivity 84%, range 55-100%; median CTC specificity 97%, range 73-100%). This evidence is consistent with results from another recent systematic review and meta-analysis with broader inclusion criteria (Mullhall et al 2005, polyps ≥ 10 mm, pooled CTC sensitivity 85% (95% CI 79-91%), CTC specificity 97% (95% CI 96-97).

These findings suggest that CTC may be highly sensitive in some but not all population subgroups or settings in which it may be indicated for the diagnosis or exclusion of lesions ≥ 10 mm. Parameters such as prevalence of disease, CTC techniques and the experience of those interpreting the tests that may contribute to this variation in CTC performance have not yet been clearly defined.

One study of fair quality provides direct evidence about the relative accuracy of CTC versus DCBE and versus colonoscopy for the detection of cancers and polyps ≥ 10 mm (Rockey et al 2005). The results of this study indicates that CTC is more specific than DCBE (CTC specificity 96% [95% CI 94-98], DCBE specificity 90% [95% CI 87-92], p < 0.0001) and may be more sensitive than DCBE (CTC sensitivity 59% [95% CI 45-71%], DCBE sensitivity 48% [95% CI 35-61%, p = 0.11]. Colonoscopy was found to be statistically significantly more sensitive and specific than CTC (colonoscopy sensitivity 98.3% [95% CI 92-100%], colonoscopy specificity 99.6% [95% CI 99-100%], p < 0.0001 for comparisons with CTC)

Consistent with the findings of Rockey et al (2005), two additional studies of fair quality indicated that CTC specificity was significantly lower than colonoscopy specificity for the detection of lesions ≥ 10 mm (Cotton et al 2004, Van Gelder et al 2004), and one of these studies also indicated a statistically significant difference between CTC and colonoscopy sensitivity favouring colonoscopy (Cotton et al 2004). Meta-analysis of these three studies indicate that colonoscopy is a highly accurate test for the detection of lesions ≥ 10 mm with a sensitivity of 95% (95% CI: 90-98%) and specificity of 100% (95% CI: 99.5-100%), whereas CTC was moderately sensitive and highly specific (pooled CTC sensitivity 63% (95% CI: 55-71%), pooled CTC specificity 95% (94-97%).

This review did not identify any studies that directly compared the relative accuracy of CTC versus DCBE in study populations where CTC was observed to be highly sensitive.

Expert opinion from the Advisory Panel suggested that additional studies comparing CTC and DCBE accuracy may not be expected due to the large sample size that would be needed to demonstrate a statistical significant difference between these tests and current clinician perceptions about the superiority of CTC over DCBE.

Detection of colorectal cancer

Six studies reported on CTC sensitivity and specificity for the detection of cancers in the population of interest with or without comparing CTC to DCBE or colonoscopy (Table 27).

Table 27 Estimates of CTC sensitivity and specificity for detection of cancer[1]

Study author, year	n	Prevalence of cancer	Sensitivity (95% CI)	Specificity (95% CI)	Study level & quality
Reference standard: includes a second-look colonoscopy (+/- histopathology)					
Ginnerup Pedersen et al 2003	148	7.4%	100% (72-100%)	97% (92-99%)[2]	II/III-1, fair
Rockey et al 2005	614	1.5%	78% (40-97%)	96% (95-98%)[3]	II, fair
Taylor et al 2003	54	13%	83% (36-100%)	100% (93-100%)	II, high
Reference standard: colonoscopy (+/- histopathology)					
Iannaccone et al 2002	27	33%	100 (66-100%)	100% (82-100%)	II/III-1, fair
Morrin et al 2000[4]	81	n.r.	100% (78-100%)	96% (87-99%)	II/III-2, fair
Munikrishnan et al 2003	80	36%	97% (82-100%)	98% (90-100%)	II/III-2, fair-low
Median results	1004		98.5%	97.5%	
Pooled results[5]	242		97% (88-100%) $\chi^2 = 3.10$, df = 3, p = 0.38	98% (95-99%) $\chi^2 = 4.20$, df = 3, p = 0.24	

1 Where confidence intervals were not reported they were calculated from reconstruction of the 2×2 table using reported data.
2 CTC specificity for detection of lesions ≥ 6 mm.
3 CTC specificity for detection of lesions ≥ 10 mm.
4 Refers to colorectal masses ≥ 20 mm.
5 Based on studies reporting CTC sensitivity and specificity for cancer (excludes Ginnerup Pedersen et al 2003 and Rockey et al 2005).

As shown in Table 27, meta-analysis from the four studies that reported on both CTC sensitivity and specificity provides a summary estimate of CTC sensitivity of 97% (95% CI: 88-100%, χ^2 test for heterogeneity: $\chi^2 = 3.4$, df = 3, p = 0.34) and specificity of 98% (95% CI: 95- 99%, χ^2 test for heterogeneity 4.25, df = 3, p = 0.24). The median results of all six studies provided similar summary estimates (median sensitivity 98.5%; median specificity 97.5%).

Relative accuracy of CTC versus DCBE

Rockey et al (2005) reported on the relative sensitivity of CTC versus DCBE and versus colonoscopy to detect colorectal cancer; the test specificity for detecting cancer was not reported.

A final diagnosis of colorectal cancer was made in nine patients (cancer prevalence 1.5%). DCBE detected one more case of colorectal cancer than CTC. However, the estimate of CTC sensitivity falls well within the bounds of uncertainty surrounding the estimate of DCBE sensitivity. Assuming that the specificity of each test for detecting cancer is at least as high as their specificity for detecting lesions ≥ 10 mm, CTC specificity appears to be higher than DCBE specificity (see results under 'Detection of cancer and polyps ≥ 10 mm' and Table 25). (CTC sensitivity 78% [95% CI: 40-97%], assumed CTC specificity 96% [95% CI: 94-98%]; DCBE sensitivity 89% [95% CI: 52-100%], assumed DCBE specificity 90% [95% CI: 87-92%]).

Relative accuracy of CTC versus colonoscopy

In addition to the study reported by Rockey et al (2005), two other studies reported on a direct comparison of the sensitivity and specificity of CTC versus colonoscopy to detect cancers (Taylor et al 2003, Ginnerup Pedersen et al 2003). These studies were appraised as fair to high quality and the results are presented in Table 28.

Table 28 Accuracy studies comparing CTC versus colonoscopy for detecting colorectal cancer[1]

Study author, year	n	Prevalence cancer	CTC		Colonoscopy		Study level & quality
			Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	
Ginnerup Pedersen et al 2003	148	7.4%	100% (72-100%)	97% (92-99%)[2]	100% (72-100%)	n.r.	level II-III-1 fair quality
Rockey et al 2005	614	1.5%	78% (40-97%)	96% (95-98%)[3]	100% (66-100%)	100% (99-100%)[3]	level II fair quality
Taylor et al 2003	54	13%	83% (36-100%)	100% (93-100%)	86% (42-100%)	n.r.	level II high quality

1 Where confidence intervals were not reported they were calculated from reconstruction of the 2 × 2 table using reported data.
2 CTC specificity for detection of lesions ≥ 6 mm. The relative specificity of CTC and colonoscopy for the detection of cancer was not reported.
3 CTC specificity for detection of lesions ≥ 10 mm. The relative specificity of CTC and colonoscopy for the detection of cancer was not reported.

The results reported by Rockey et al (2005) indicate that CTC may have a lower sensitivity for the detection of cancer than colonoscopy; however, a statistical test for this comparison was not reported and the 95% confidence interval surrounding the estimate of CTC sensitivity is wide due to the low prevalence of cancer in this large study and overlaps with the confidence interval surrounding the estimate of colonoscopy sensitivity. The authors did not report on a comparison of test specificity for the detection of cancer but did demonstrate that CTC specificity for the detection of lesions ≥ 10 mm was statistically significantly lower than colonoscopy (p < 0.0001).

The two other studies suggest that CTC sensitivity may be similar to the sensitivity of colonoscopy for the detection of cancer. CTC was found to be highly specific for the detection of cancer in both studies (Table 27). The specificity of colonoscopy was not reported, but the combination of colonoscopy with biopsy in routine clinical practice avoids the problem of false positive colonoscopy results.

Other evidence about DCBE accuracy

Estimates of DCBE sensitivity for the detection of colorectal cancer reported in the systematic review by de Zwart et al (2001) ranged from 62% to 100% (15 studies) with a median sensitivity of 91%. Two of these studies that met the eligibility criteria for this review reported 100% DCBE sensitivity for cancer, neither study reported on DCBE specificity for cancer (Durdey et al 1987, DCBE sensitivity 100%, specificity 78% for all lesions; Irvine et al 1988, DCBE sensitivity 100%, specificity 67% for lesions ≥ 5 mm).

Interpretation

Six eligible studies reported on CTC sensitivity and specificity for the detection of cancer with or without comparing CTC to DCBE or colonoscopy. The median estimates from these studies (CTC sensitivity 98.5%; CTC specificity 97.5%) and the pooled estimates from the subset of four studies (pooled CTC sensitivity 97% (95% CI 89-100%); pooled CTC specificity 98% (95% CI 95-99%)) are consistent with the findings from the one other systematic review that estimated CTC sensitivity for detecting cancer (Halligan et al 2005, CTC sensitivity 96% (95% CI 91-99%). These results indicate that CTC is highly sensitive and specific for the detection of cancer in at least some populations or settings.

One fair-quality study provided evidence about the relative sensitivity of CTC versus DCBE and versus colonoscopy for the detection of cancer (Rockey et al 2005). This study suggested that colonoscopy was more sensitive than CTC and DCBE, but did not demonstrate a statistically significant difference in the sensitivity of the three tests (CTC sensitivity 78% [95% CI: 40-97%]; DCBE sensitivity 89% [95% CI: 52-100%]; colonoscopy sensitivity 100% [95% CI: 66-100%]). Test specificity for cancer was not reported; however, estimates of test specificity for the detection of lesions ≥ 10 mm demonstrated that the specificity of CTC was superior to DCBE (p < 0.0001) but inferior to colonoscopy (p < 0.0001). The prevalence of cancer in this study population was low (9 cancers, 1.5%) which limited the power of this study to detect a true difference between tests.

Two other studies of fair quality have indicated that CTC sensitivity for cancer is similar to colonoscopy, but did not compare CTC with DCBE (Taylor et al 2003, Ginnerup Pedersen et al 2003).

Detection of cancers and polyps 6-9 mm

Six eligible studies reported on CTC accuracy per-patient for detecting lesions 6-9 mm. Estimates of CTC sensitivity ranged from 30% to 80% (6 studies: Bruzzi et al 2004, Cotton et al 2004, Johnson et al 2004, Morrin et al 2000, Munikrishnan et al 2003, Rockey et al 2005) and estimates of CTC specificity ranged from 93% to 99% (5 studies: Bruzzi et al 2004, Cotton et al 2004, Johnson et al 2004, Morrin et al 2000, Munikrishnan et al 2003) (median CTC sensitivity 61%, median CTC specificity 96%).

Relative accuracy of CTC versus DCBE

Two studies compared the accuracy of CTC versus DCBE for the detection of lesions 6-9 mm (Rockey et al 2005, Johnson et al 2004). As discussed in the previous section, the methods used by Johnson et al (2004), in particular the use of an invalid reference

standard in the majority of patients, limit the interpretation of the study results and they are not discussed any further.

Rockey et al (2005) found that CTC was statistically significantly more sensitive than DCBE for the detection of lesions 6-9mm (CTC sensitivity 51% [95% CI: 41-60%]; DCBE sensitivity 35% [95% CI: 27-45%]; p = 0.008; Table 29). The authors did not report on the relative specificity of each test for detecting lesions of 6-9 mm; however, they showed that CTC specificity for detecting all lesions ≥ 6 mm was statistically significantly higher than DCBE (CTC specificity 89% [95% CI 86-92%]; DCBE specificity 82% [95% CI 78-85%]; p = 0.0007).

Relative accuracy of CTC versus colonoscopy

Two studies compared the accuracy of CTC versus colonoscopy to detect lesions 6-9mm (Rockey et al 2005, Cotton et al 2004).

Both studies showed that colonoscopy was a near perfect test for the detection of lesions 6-9mm with a superior sensitivity and specificity to CTC (Table 29).

Table 29   Studies comparing CTC versus DCBE and versus colonoscopy for the detection of lesions 6-9 mm

Study author, year level & quality	n	Preval-ence	CTC		DCBE		Colonoscopy		Test comparisons
			Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	
Rockey et al 2005 Level II fair quality	614	18.9%	51% (41-60%)	89% (86-92%)[1]	35% (27-45%)	82% (78-85%)[1]	99% (95-100%)	100 (98-100%)[1]	CTC vs DCBE: • Sensitivity p = 0.008 • Specificity p = 0.0007 CTC vs colonoscopy: • Sensitivity p < 0.0001 • Specificity p < 0.0001
Cotton et al 2004 Level II fair quality	600	9.8%	30% (20-40%)	93% (91-95%)			99% (96-100%)	100%	CTC vs colonoscopy: difference in sensitivity & specificity[2]

1 Test specificity estimated for all polyps and cancers ≥ 6 mm.
2 Confidence intervals do not overlap indicating that CTC and colonoscopy sensitivity/specificity are statistically significantly different.

Other evidence about DCBE accuracy

The systematic review by de Zwart et al (2001) identified two studies that estimated DCBE sensitivity to be 53% (95% CI 50-56%) and 84% (95% CI 75-93%) for the detection of polyps 6-10 mm (DCBE specificity not reported).

Detection of cancers and polyps ≤ 5 mm

Four studies reported on CTC per-patient sensitivity and specificity for detecting lesions ≤ 5 mm (Bruzzi et al 2004, Cotton et al 2004, Morrin et al 2000, Munikrishnan et al 2003). Estimates of CTC sensitivity ranged from 14% to 57% and estimates of CTC

specificity ranged from 83% to 97% (median CTC sensitivity 34%, median CTC specificity 92%).

Relative accuracy of CTC versus DCBE and versus colonoscopy

No study compared CTC accuracy with DCBE for detection of lesions ≤ 5 mm. One large study compared CTC accuracy with colonoscopy for lesions of this size (Cotton et al 2004, prevalence of lesions ≤ 5 mm 11.3%). The authors showed that the sensitivity of CTC for the detection of lesions ≤ 5 mm was poor, although CTC specificity was moderately high (CTC sensitivity 14% (95% CI 10-18%), CTC specificity 91% (95% CI 87-94%). These estimates were statistically significantly lower than those for colonoscopy (colonoscopy sensitivity 97% (95% CI 95-99%); colonoscopy specificity 100%).

Other evidence about DCBE accuracy

The systematic review by de Zwart et al (2001) presented the results of one study that estimated DCBE sensitivity to be 32% (95% CI 29-35%) for the detection of polyps ≤ 5 mm. No other estimates of DCBE accuracy for lesions of this size were identified.

Interpretation of results for lesions < 10 mm

The detection of polyps < 10 mm in symptomatic patients is less clinically relevant than detection of larger lesions because only a small minority of these lesions will slowly progress to cancer (as described on page 4), and small lesions are unlikely to be the cause of the patients' symptoms. However, cancers may also occur as small or flat lesions rather than masses and thus the accuracy of CTC to detect small lesions is also relevant to this review.

Six studies reporting on CTC accuracy and one systematic review reporting on DCBE accuracy found that both CTC and DCBE showed limited sensitivity for detecting lesions 6-9 mm (CTC sensitivity: range 30-80%, median 61%; DCBE sensitivity: range 53-84%, median not reported), although CTC specificity was found to be moderately high (CTC specificity: range 93-99%, median 96%, DCBE specificity not reported). Four of these studies reported lower estimates of CTC sensitivity for the detection of lesions ≤ 5 mm although specificity remained moderately high (CTC sensitivity: range 14-57%, median 34%; CTC specificity: range 83-97%, median 92%). One study identified in the systematic review of DCBE accuracy also showed DCBE sensitivity was low for detecting lesions ≤ 5 mm.

The systematic review reported by Mulhall et al (2005) reported that CTC accuracy was limited for lesions < 10 mm. This review included a broader patient population and reported slightly higher pooled estimates for CTC sensitivity than the present review (lesions 6-9 mm: CTC sensitivity 70% [95% CI 55-84%], CTC specificity 93% [95% CI 91-95%]; polyps ≤ 5 mm: CTC sensitivity 48% [95% CI 25-70%], CTC specificity 91% [95% CI 89-95%]).

Only one study compared CTC sensitivity and specificity versus DCBE for the detection of lesions 6-9 mm (Rockey et al 2005). This study found that CTC sensitivity was superior to DCBE (CTC sensitivity 51% [95% CI: 41-60%]; DCBE sensitivity 35% [95% CI: 27-45%]; p = 0.008). Specificity of CTC for all lesions ≥ 6 mm was also superior to

specificity of DCBE (CTC specificity 89% [95% CI 86-92%]; DCBE specificity 82% [95% CI 78-85%]; p = 0.0007).

No eligible studies assessed the relative accuracy of these two tests for detecting lesions ≤ 5 mm.

Two studies comparing CTC accuracy versus colonoscopy for lesions < 10 mm demonstrated that colonoscopy was statistically significantly superior to CTC. (Rockey et al 2005, Cotton et al 2004). Cotton et al (2004) reported the lowest estimates of CTC accuracy for detecting small lesions (lesions 6-9 mm: CTC sensitivity 30%; CTC specificity 93%; lesions 1-5 mm: CTC sensitivity 14%; CTC specificity 91%). However, some of the CTCs in this study were reviewed by radiologists with limited experience (at least 10 prior CTCs), which may have contributed to low performance of CTC for detecting small lesions. The relevance of these results to Australian practice may depend on the level of experience of Australian radiologists who are/will be performing CTC.

Overall colorectal disease

One study investigating CTC accuracy reported overall sensitivity and specificity for all colorectal disease (Munikrishnan et al 2003); three other studies reported overall sensitivity and specificity of CTC for 'all lesions' – polyps and cancers (Cohnen et al 2004, Laghi et al 2002, Macari et al 2002).

The study by Munikrishnan et al (2003) included symptomatic patients and was appraised as fair quality. The authors included diagnoses of cancer, polyps, diverticulosis and colitis in their definition of 'overall colorectal disease'. CTC sensitivity was estimated at 82% and specificity 93% (data for estimation of 95% confidence interval not available).

The results from the three studies reporting on overall sensitivity and specificity for colorectal polyps and cancers showed a wide variation: CTC sensitivity ranged between 58% (95% CI: 44-70%) and 94% (79%-99%) and specificity ranged between 76% (95% CI: 65-85%) and 94% (95% CI: 80-99%) (Cohnen et al 2004, Laghi et al 2002, Macari et al 2002). Level and quality do not vary widely between these three studies. However, although all the studies include a mix of symptomatic/high-risk asymptomatic patients, the prevalence of cancer varied between 23% (Laghi et al 2002) and 6% (Macari et al 2002). This variation may explain the observed variability in results; Laghi et al (2002) reported the highest prevalence of cancer and the highest sensitivity and specificity of lesions.

Relative accuracy of CTC versus DCBE or colonoscopy

The eligible studies that compared the accuracy of CTC with DCBE and/or colonoscopy did not report estimates of the overall sensitivity and specificity of these tests to detect colorectal disease. Similarly, existing eligible systematic reviews of CTC or DCBE accuracy have not reported on test accuracy for overall colorectal disease.

Without any evidence to directly compare the performance of CTC and DCBE for the detection of overall colorectal disease, we can indirectly compare the above results with evidence from studies of DBCE accuracy.

One fair-quality study investigating DCBE accuracy in symptomatic patients reported overall sensitivity and specificity for all colorectal disease (Durdey et al 1987). This study included a diagnosis of cancer, polyps, diverticular disease and inflammatory bowel disease in their definition of 'overall colorectal disease'. In this study, DCBE sensitivity was estimated at 56% (95% CI: 40-71%) and specificity at 78% (95% CI: 56 -93%). Irvine et al (1988) report on lesions ≥ 5 mm and it is assumed that the authors included diverticular disease and IBD in their definition of lesions, although this is not explicitly stated in the paper. This study was also appraised as fair quality. DCBE sensitivity for lesions > 5 mm was estimated at 50% and specificity 67% (data for estimation of 95% confidence interval not available) (Irvine et al 1988).

The study of DCBE accuracy reported by Durdey et al (1987) also reported the sensitivity and specificity of colonoscopy for detecting 'overall colorectal disease' (cancer, polyps, diverticular disease and inflammatory bowel disease) was 91% (95% CI: 78-97%) and specificity 91% (95% CI: 72-99%). This evidence can be used for an indirect comparison with the evidence of CTC accuracy reported by Munikrishnan et al (2003) described above (CTC sensitivity 82%; specificity of 93%, 95% CI: could not be calculated).

The accuracy of CTC compared to colonoscopy for the detection of overall lesions – polyps and cancer – could not be determined. Cotton et al (2004) did report on accuracy of overall lesions for CTC and colonoscopy, but reported per-polyp sensitivity only.

Interpretation

One fair-quality study of CTC accuracy (Munikrishnan et al 2003) and one fair-quality study of DCBE and colonoscopy accuracy (Durdey et al 1987) provide indirect evidence to suggest that CTC may be more accurate than DCBE for the detection of overall colorectal disease but less sensitive than colonoscopy (CTC sensitivity 82%, CTC specificity: 93%; DCBE sensitivity 56% [95% CI: 40-71%], DCBE specificity 78% [95% CI: 56 -93%], colonoscopy sensitivity 91% [95% CI: 78-97%], colonoscopy specificity 91% [95% CI: 72-99%]. These studies were conducted on different patient groups at different time periods (2003 versus 1987 respectively).

Patient preferences and quality of life outcomes associated with testing

Two HTA reports noted that evidence about patient tolerance showed inconsistent results, with some studies concluding that patients favoured colonoscopy or DCBE over CTC and others concluding that patients favoured CTC (NICE 2004, MSAC 2001).

Eleven studies that assessed patient preferences and/or quality of life outcomes of CTC are described in the following section and are summarised in Appendix D. These studies include two studies that assessed patient outcomes for CTC compared to DCBE and colonoscopy (Gluecker et al 2003, Taylor et al 2003b), one study of CTC compared to DCBE (Taylor et al 2005) and eight studies of CTC compared to colonoscopy (Akerkar et al 2001, Cotton et al 2004, Laghi et al 2003, Ristvedt et al 2003, Svensson et al 2002, Taylor et al 2003c, Thomeer et al 2002, van Gelder et al 2004).

An Australian study has been undertaken in conjunction with the bowel screening pilot study to assess patient preferences of CTC compared to colonoscopy using discrete

choice methodology. Preliminary results of this study have been presented as a conference abstract (Howard & Salkeld 2005), but a full report of the study has not yet been published.

Patient preferences

Eleven studies assessed whether patients preferred CTC over the alternative tests colonoscopy or DCBE using self-administered questionnaires. The following results of patient preferences include outcomes of patient satisfaction with CTC versus DCBE from two studies and results from the assessment of patient satisfaction and acceptance with CTC versus colonoscopy from one study.

CTC versus DCBE

Patient preferences for CTC compared to DCBE were assessed in two studies (Taylor et al 2005, Gluecker et al 2003). These studies were appraised as fair (Gluecker et al (2003) or high quality (Taylor et al 2005) and included a mixed population of symptomatic and asymptomatic high-risk patients.

Both studies indicated that patients prefer CTC over DCBE. Results showed that a higher proportion of patients would have CTC again than would have DCBE again (Taylor et al 2005, 83% vs 36%; p < 0.001) and that a larger proportion preferred CTC over DCBE in general (Gluecker et al 2003, 97% vs 0.4%, p < 0.001) and as a future test (100% of n = 52 [88%], p < 0.001) or a more acceptable test (Taylor et al 2005, 98% of n = 45 [76%], p < 0.001).

Patient satisfaction was reported in the two studies by Taylor et al (2003b & 2005). Both studies reported higher satisfaction scores for CTC than DCBE (Taylor et al 2003b, p < 0.001; Taylor et al 2005, p = 0.03)

CTC versus colonoscopy

Patient preference for CTC versus colonoscopy was reported in nine studies, two of which were studies of test accuracy. All studies were of fair quality (Akerkar et al 2001; Cotton et al 2004, Gluecker et al 2003, Laghi et al 2003, Ristvedt et al 2003, Svensson et al 2002, Taylor et al 2003b, Thomeer et al 2002, van Gelder et al 2004). Two studies included average risk screening patients in their study population (35%, Akerkar et al 2001; 16%, Thomeer et al 2002); two only included high-risk asymptomatic patients (van Gelder et al 2004, Laghi et al 2003), the other seven studies included a mix of symptomatic patients and asymptomatic patients at high risk.

The results of these studies indicate that CTC may be preferred over colonoscopy by patients who have had both procedures. Five studies reported that a significantly larger proportion of patients preferred CTC over colonoscopy (Laghi et al 2003: 71% versus 29%, p < 0.0001; Gluecker et al 2003: 72% versus 5%, p < 0.001; Svensson et al 2002: 82% versus 18%, p < 0.0001; Taylor et al 2003b: 73% versus 27%, p = 0.001; van Gelder et al 2004: 71% versus 19%, p < 0.001 (directly after examination), 61% versus 31%, p < 0.001 (after 5-week follow-up)). The reported percentages refer to patients expressing a preference for either one of the procedures; proportions of up to 23% (Svensson et al 2002) and 39% (Taylor et al 2003b) did not express a preference. Two studies found a higher proportion of patients preferred CTC than preferred colonoscopy, but statistical significance was not reported (Ristvedt et al 2003, Thomeer et al 2002).

Two studies did not find that patients prefer CTC over colonoscopy. Little difference in preferences were found in Cotton et al (2004) with 46% of patients expressing a preference for CTC and 41% for colonoscopy, and 13% expressing no preference. One study found a higher proportion of patients (64%) preferred colonoscopy over CTC (Akerkar et al 2001) (no test of statistical significance reported).

Patient satisfaction and acceptance was reported in Taylor et al (2003b), who found that although patients appear less satisfied with CTC than with colonoscopy, significantly more patients found CTC acceptable than found colonoscopy acceptable (70% versus 30%, p = 0.003).

Interpretation

All studies investigating patient preferences were of fair quality and suggest that patients prefer CTC over DCBE and over colonoscopy. However, the studies used different methods to assess patient preferences, limiting comparisons between studies. The study populations differed with two studies including patients at average risk of colorectal cancer undergoing screening CTC and colonoscopy. One of these two studies is the study by Akerkar et al (2001), which was the only study that found a higher proportion of patients preferred colonoscopy over CTC. This study may not be applicable to the patient groups under study in this review because individuals at average risk of colorectal cancer may perceive CTC and colonoscopy differently and may thus express different preferences for these tests than symptomatic patients or patients at high risk for colorectal cancer. Preliminary results from a recent Australian study suggest patients with a positive FOBT prefer colonoscopy over CTC (Howard & Salkeld 2005).

Quality of life

Besides patient preference, studies also included an assessment of patient outcomes that can be broadly termed as 'quality of life outcomes' related to the test procedure. The outcome definitions and/or measurement instruments used in these assessments differed between the studies. The following section describes the results of studies that assessed pain and discomfort associated with CTC. Other outcomes assessed are described under the heading 'Other quality of life outcomes'; these outcomes differed between studies and thus comparison across studies was not possible.

Pain and discomfort – CTC versus DCBE

Three studies included a comparison of the pain and/or discomfort experienced with CTC and DCBE procedures (Gluecker et al 2003 (group 2), Taylor et al (2003b & 2005); the earlier study by Taylor et al (2003b) only included an indirect comparison of CTC with DCBE. All three studies were in symptomatic or symptomatic/high-risk asymptomatic patients and appraised as fair quality.

The results indicate that patients experience more physical discomfort with DCBE than with CTC. Patients reported higher ratings of discomfort for DCBE when asked the relevant question in Gluecker et al (2003, p < 0.001). Two studies by Taylor et al (2003b & 2005) assessed discomfort through several questions with overall higher discomfort scores for DCBE than for CTC (Taylor et al 2003b: p < 0.001; Taylor et al 2005: p = 0.003). In addition, during the measurement of perceived pain during CTC and DCBE by means of a handheld device, significantly less pain was registered during CTC than

during DCBE (Taylor et al 2005: proportion clicking at least once during CTC versus DCBE: 38% versus 19%, p = 0.007).

Pain and discomfort – CTC versus colonoscopy

Eight studies of CTC versus colonoscopy reported on the pain and discomfort associated with the procedures. All studies were appraised as fair quality except the two studies by Taylor et al (2003b & 2005), which were appraised as high quality. Seven studies included a mix of symptomatic patients and asymptomatic patients at high risk (Taylor et al 2003b, Ristvedt et al 2003, Svensson et al 2002, Taylor et al 2003c, Thomeer et al 2002) or were in high-risk asymptomatic patients only (van Gelder et al 2004, Laghi et al 2003), whereas one study included a proportion of 35% average risk screening patients in their study population (Akerkar et al 2001).

The results varied between studies with five studies indicating less pain and discomfort associated with CTC than with colonoscopy, and three studies reporting less favourable pain and discomfort outcomes for CTC (one study reported outcomes in both directions). Two studies reported patients experienced a higher degree of discomfort (van Gelder et al 2004) or physical discomfort (Taylor et al 2003b) with colonoscopy than with CTC (Taylor et al 2003b: p = 0.002; van Gelder et al 2004: p < 0.001) when the degree of discomfort was assessed through two questions on a 5-point scale (van Gelder et al 2004) or several 7-point questions that were part of a validated questionnaire (Taylor et al 2003b). Three studies found more patients that experienced 'severe pain' or 'extreme pain' during colonoscopy than during CTC (van Gelder et al 2004: 34% versus 3%, p < 0.001) or found colonoscopy 'painful' (Laghi et al 2003: 58% versus 16%, p < 0.0001) or 'fairly' or 'very painful' (Svensson et al 2002: 29% versus 6%, p < 0.00001 (for overall differences in pain rating)). In Taylor et al (2003c), patients registered pain or discomfort statistically significantly more often during conventional colonoscopy than during CTC, when pain and discomfort was measured using a handheld counting device (RR: 1.89 to register pain for colonoscopy versus CTC, p = 0.03). One study showed that CTC was slightly better tolerated than colonoscopy (3.5 vs 3.0 on a 5 point scale); however, no statistical significance was reported.

In contrast, two studies reported patients experienced more pain and/or discomfort with CTC than with colonoscopy when pain was assessed on a 5 or 7-point scale (Akerkar et al 2001, p < 0.01; Ristvedt et al 2003, p < 0.001). More specifically, Svensson et al (2002) reported more patients experienced a higher degree of discomfort with airfilling at CTC than with instrumentation at colonoscopy (40% versus 21%, p = 0.02).

Other quality of life outcomes – CTC versus DCBE

Taylor et al (2003b & 2005) also compared patient 'tolerance' and 'worry' associated with CTC and DCBE. In Taylor et al (2005), all patients reporting at follow-up tolerated CTC 'well' or 'fairly well', whereas only 83% reported so on DCBE (p = 0.002). Taylor et al (2003) also showed that patients were less worried with CTC than with DCBE (p < 0.001); however, Taylor et al (2005) did not show any statistically significant differences in 'worry' between the two tests.

These results may indicate more favourable quality of life outcomes with CTC than with DCBE; however, outcomes and measurement tools differed in the two studies and these results are not conclusive.

Other quality of life outcomes – CTC versus colonoscopy

Three studies of fair quality (Akerkar et al 2001, Ristvedt et al 2003, Svensson et al 2002) and one study of high quality (Taylor et al 2003b) examining CTC and colonoscopy did not assess quality of life overall, but reported different quality of life outcomes such as 'tolerance', 'unpleasantness', 'difficult', 'disrespect' and 'embarrassment'.

Results varied, with better outcomes shown for CTC than for colonoscopy in three studies and less favourable CTC outcomes in two studies. Findings included: more patients tolerated CTC well than colonoscopy (p = 0.005, Taylor et al 2003b); and more patients found colonoscopy more unpleasant (71% of n = 76 (68%), p = 0.0008) and more difficult than CTC (69% of n = 71 (64%), p = 0.002) (Svensson et al 2002). In contrast, one study found favourable outcomes for colonoscopy for patient perceptions of difficulty (p < 0.001) and embarrassment (p < 0.001) (Ristvedt et al 2003). One further study showed that patients appeared to have a higher 'sense of disrespect' after CTC than after colonoscopy (p < 0.01, Akerkar et al 2001).

Additional considerations

Incomplete colonoscopy

Studies investigating the accuracy of CTC generally used colonoscopy as the reference standard and excluded patients in whom colonoscopy could not be performed. As a result, there is little evidence about the accuracy of CTC in detecting colorectal neoplasia in this patient group. Colonoscopy incompletion rates of 0 to 52% (median 8%) were reported in 15 CTC studies included in this review (Appendix D). Three of these studies reported on the diagnostic yield from CTC following an incomplete colonoscopy. One study reported no additional lesions detected in 5 (8%) of patients with an incomplete colonoscopy (Laghi et al 2002). Two studies reported that CTC led to the detection of proximal lesions that were not viewed at colonoscopy. Hoppe et al (2004) reported that additional lesions were detected in two of six patients with incomplete colonoscopy. Neither patient completed colonoscopy due to a distal obstructive tumour. Taylor et al (2003) reported detection of a large proximal cancer in one of the five patients who had an incomplete colonoscopy.

Four other studies that were not eligible for the review of CTC accuracy investigated CTC performance following incomplete colonoscopy (Neri et al 2002, Mingyue et al 2002, Macari et al 1999, Morrin et al 1999). Three of these studies were also included in the Ontario report (Neri et al 2002, Macari et al 1999, Morrin et al 1999). These studies are summarised in Table 30 and represent the best available evidence about the relative value of CTC and DCBE in patients with an incomplete colonoscopy.

The findings indicate that CTC is successful in visualising the entire colon in at least 92% of patients who have had an incomplete colonoscopy. All four studies demonstrated that the addition of CTC following incomplete colonoscopy yielded additional clinically relevant cases of colorectal neoplasia. The largest study (60 patients) detected additional lesions in 27% of patients (Mingyue et al 2002).

None of the studies were designed to estimate the comparative accuracy of CTC versus DCBE using an independent reference standard. In a small study of 10 patients, Macari et al (1999) reported that CTC and DCBE both detected two polyps. However, Morrin et al (1999) demonstrated that DCBE was less useful than CTC for the visualisation of the proximal colon in patients with a distal obstruction and did not detect seven 5 mm polyps detected by CTC. Two studies also reported on clinically relevant extracolonic abnormalities detected by CTC as a potential additional advantage of this test (Morrin et al 1999, Neri et al 2002). CTC also has a technical advantage over DCBE because it is difficult to coat the bowel wall with barium following an incomplete colonoscopy, whereas CTC can be performed immediately with additional air insufflation.

Table 30 Summary of studies assessing CTC performance after an incomplete colonoscopy

Author year & setting	N	Study objective and design	Patient and test characteristics	Quality
Neri et al 2002 Italy	34	To assess the value of CTC following incomplete colonoscopy Case control study Comparator: nil Reference standard: surgery for positive results, colonoscopy and CTC for negative results	**Patient characteristics:** Males 18/34 (53%). Mean age 63 years Presenting symptoms suggestive of colorectal cancer Causes of incomplete colonoscopy: • Group A: Distal obstruction 19/34 (56%) • Group B: Patient intolerance or stricture 15/34 (44%) Prevalence of cancer 29/34 patients (85%) Control group 20 asymptomatic (screening patients) **CTC technique:** Single detector CT, dual positioning, iv contrast	Level III-3 Limited quality Specificity based on results from selected patients known to be disease free (controls)
Results: **Colonic visualisation:** CTC total distension 34/34 (100%) **CTC yield:** 10 cases of colon cancer missed at incomplete colonoscopy. 3 cases of liver metastases			Group A: distal obstruction (n = 19) • Prevalence of cancer = 19/19 (100%) • CTC: sensitivity100%, specificity 100% • Identified all distal lesions and 3 synchronous cancers • Colonoscopy: sensitivity 90%, specificity 90% • Difference between tests p = 0.42 Group B: intolerance or stricture • Prevalence of cancer = 10/15 (67%) • CTC: sensitivity100%, specificity 96% • Colonoscopy: sensitivity 0%, specificity 92% • difference between tests p < 0.01	**Test accuracy:** For cancer detection: • CTC: sensitivity 100%, specificity 96% • Colonoscopy: sensitivity 56%, specificity 92% • Difference between tests p < 0.01 CTC accuracy for polyp detection: • > 10 mm: sensitivity 100%, specificity 100% • 5-10 mm: sensitivity 100%, specificity 80% • ≤ 5 mm: sensitivity 86%,specificity 70% **CTC extracolonic findings:** 4/34 (12%) patients with liver metastases.
Minyue et al 2002 China	60	To assess the value of CTC following incomplete colonoscopy Comparator: nil Reference standard: repeat colonoscopy (CTC neg), surgery +/- biopsy (CTC pos)	**Patient characteristics:** Males 35/60 (58%). Mean age 58 years Presenting symptoms: not reported Causes of incomplete colonoscopy: Obstructive mass 58%, redundant colon loops 23%, colon spasm 12%, other 7% Prevalence of cancer: not reported, 1/55 case detected by CTC (2%) **CTC technique:** Multi-slice scanner? Supine positioning	Level III-2 Insufficient information about patient selection and investigator blinding to allow quality assessment
Results: **Colonic visualisation:** 55/60 (92%) with adequate visualisation of each colon segment. CTC failure 5/60 (8%) due to severe obstruction and poor distension of proximal segments. **CTC yield:** in proximal colon segments 15/55 (27%): cancer 1/55 (2%), polyps 13/55 (24%), inflammatory bowel disease 1/55 (2%).				

Author year & setting	N	Study objective and design	Patient and test characteristics	Quality
Morrin et al 1999 USA	40	To assess the value of CTC following incomplete colonoscopy Comparator: DCBE 26/40 (65%), others refused Reference standard: Repeat colonoscopy following positive CTC	**Patient characteristics:** Males 12/40 (30%). Mean age 62 years Presenting symptoms: symptomatic, personal or family history Causes of incomplete colonoscopy: • redundant tortuous colon loops 17/40 (43%) • excessive colonic spasm 10/40 (25%) • severe diverticular disease 4/40 (10%) • obstructing sigmoid masses 3/40 (8%) • other 6/40 (15%) Prevalence of cancer: not reported, one case mentioned. **CTC technique:** Multi-slice scanner, dual positioning	Level IV Insufficient information about patient selection and investigator blinding to allow quality assessment DCBE may have been performed in select subpopulation
Results: **Colonic visualisation:** CTC adequately visualized 192/200 (96%) of colonic segments DCBE adequately visualized 118/130 (91%) segments; due to inability to pass barium in 3 patients with sigmoid cancers Incomplete colonoscopy showed 82/200 (41%) segments			**CTC yield:** Revealed cause of incomplete colonoscopy in 73% patients 7/40 (18%) patients with polyps detected in segments not visualised at incomplete colonoscopy. Polyp sizes: 8 mm (1), 6 mm (1), 5 mm (7). However, 8 mm polyp not detected at 2nd colonoscopy and 5 mm polyps not detected at DCBE **DCBE yield**: revealed cause of incomplete colonoscopy in 65% of patients tested with DCBE	**CTC extracolonic findings:** 5/40 (13%) patients with clinically significant findings. **Patient tolerance:** CTC better tolerated than incomplete colonoscopy or DCBE (p < 0.001) in 26 patients who underwent all three tests. Validation of assessment instrument not reported.
Macari et al 1999 USA	20	To assess the value of CTC following incomplete colonoscopy Comparator: DCBE 10/20 (50%) Reference standard: Nil (repeat colonoscopy following positive CTC).	**Patient characteristics:** (reported for 10 patients with CTC and DCBE) Males 4/10 (40%). Mean age 65 years Presenting symptoms: bleeding (2), screening (8) prevalence of cancer: 0% **CTC technique:** Multi-slice scanner, 2D and 3D images, dual positioning, iv glucagon	Level IV Low quality Selected population Unblinded test comparison
Results: **Colonic visualisation:** CTC fully visualized proximal colon in 10/10 (100%) patients. Sigmoid colon partially collapsed in one patient, 5 mm polyp removed from sigmoid colon at colonoscopy in second patient **CTC yield:** 2/10 (20%) patients with polyps detected, one of which was missed at colonoscopy **DCBE yield:** 2/10 (20%) patients with polyps detected to confirm CTC results				

Colonoscopy, although incomplete, may allow biopsy diagnosis of the obstructive lesion but CTC may yield additional information relevant to patient management. Neri et al (2002) classified reasons for incomplete colonoscopy as due to distal obstruction or other. CTC provided additional clinically relevant information about the proximal colon in both patient groups, including a synchronous finding of cancer in 3 patients who had a distal obstruction and 3 cases of metastatic liver disease.

The Ontario report also reported on four studies that investigated the value of CTC versus colonoscopy in patients presenting with possible colonic obstruction (Laghi et al 2002, Morrin et al 2000, Fenlon et al 1999, Frager et al 1998). In three studies, colonoscopy was performed for diagnosis and the addition of CTC yielded synchronous cancers, proximal polyps and/or metastatic disease (Laghi et al 2002, Fenlon et al 1999; Morrin et al 2000). Based on final surgical staging, Morrin et al (2000) reported on CTC sensitivity as an additional test for detection of synchronous cancers (16/17 (93%) detected) and staging (13/16 (81% correctly staged) in 34 patients with known colorectal masses, benign obstructive stricture or prior colorectal resection. Frager et al (1998) compared abdominal CT (2/75 patients received rectal insufflation) with colonoscopy for the detection and diagnosis of colonic obstruction and is less relevant to this review.

Extracolonic findings

Six of the 24 accuracy studies reported on clinically significant extracolonic findings at CTC. These are defined as clinical findings outside the colon and rectum that require further investigation and/or treatment. Rates of clinically significant findings ranged from 1% (Cohnen et al 2004) to 13% (Munikrishnan et al 2003). The most common diagnoses were metastatic cancer (to lymph nodes or liver), primary non-colorectal cancer, and abdominal aortic aneurysm.

Three studies also reported rates of incidental (nonsignificant) extra-colonic findings with rates of 19% (Munikrishnan et al 2003) to 63% (Laghi et al 2003). These findings included: renal cysts, hepatic cysts, hiatus herniae and gallbladder stones. None of these studies reported on the rate of further investigation for extracolonic findings that were subsequently diagnosed as inconsequential (false positive rate).

The literature search identified one high-quality systematic review that investigated the incidence of extracolonic findings (Xiong et al 2005). The authors identified 17 studies involving 3,488 patients tested with CTC. The average frequency of extracolonic findings per patient was 40% (total 2,015 incidental findings). Overall approximately 14% of patients underwent further investigation due to extracolonic findings (data available from 6 studies). Common diagnoses were extracolonic cancer (2.7%) and aortic aneurysm (0.9%). Only 0.9% of patients required immediate treatment as a result of such findings.

The impact of investigating extracolonic findings that are subsequently found to be nonsignificant or do not change management has not been investigated in this review.

Test failures

Twenty-one of the 24 studies of test accuracy reported on test failure rates for CTC (11 studies), DBCE (3 studies) and/or colonoscopy (18 studies). Test failure refers to the failure of the test to provide adequate or complete visualisation of the colon. This definition does not include test images reported as adequate but mildly to moderately

suboptimal. Patients who did not undergo CTC because they did not comply with bowel preparation instructions were not classified as test failures for the purposes of comparing test failure rates because they were also assumed to be ineligible for colonoscopy and DCBE.

CTC failure rates ranged from 0% to 24% (11 studies median 5%, mean 5%). Reasons for CTC failure included: inadequate visualisation due to retained stool, poor distension or collapsed colon. DCBE failure rates ranged from 1% to 11% (3 studies: Rockey et al 2004: 9%; Durdey et al 1987: 11%; Irvine et al 1988: 1%, median 9%). Reasons for DCBE failures included: incomplete to caecum or terminal or inadequate visualisation of colon. Incomplete colonoscopy failure rates ranged from 0% to 52% (18 studies median 8%, mean 8%).

No studies were designed to determine whether there was a difference in failure rates between tests and so the information available should be interpreted with caution due to the possibility of selective reporting. None of the studies reported on failure rates for all three tests. Eight studies reported on failure rates for both CTC and colonoscopy. Of these, two studies showed similar small (< 2%) failure rates for both tests (Rockey et al 2005, Macari et al 2002); four studies showed lower failure rates for CTC than colonoscopy (Hoppe et al 2004 2% versus 7%, Morrin et al 2000 13% versus 52%, Munikrishnan et al 2003 5% versus 23%, Vogt et al 2004, 0% versus 4%); and two studies showed lower failure rates for colonoscopy (Ginnerup Pedersen et al 2003, 24% versus 9%, van Gelder et al 2004, 7% versus 2%).

One of the three studies reporting on failure rates for DCBE and colonoscopy showed higher rates for DCBE (Rockey et al 2004, 9% versus 2%), two other studies showed higher rates for colonoscopy (Durdey et al 1987 11% versus 24%; Irvine et al 1988, 1% versus 17%).

What are the economic considerations?

Economic evaluation of new health care technologies is particularly important where the new technology offers health benefits at additional cost. It is clear there will always be a limit to the additional cost which would be paid for a given health gain. Economic evaluation is generally aimed at determining whether such incremental costs represent value for money.

The usual process for an economic evaluation is first to consider the additional benefits accrued with the new device/procedure relative to the comparator (ie the incremental effectiveness), and to then proceed with determining cost differences between the new procedure and the comparator (ie incremental costs). Effectiveness is measured in clinically appropriate natural units or a multidimensional measure such as quality adjusted life years (QALYs). When both costs and effects are known, then an incremental cost-effectiveness ratio (ICER) can be determined. The calculation of an incremental cost-effectiveness ratio is shown below:

$$ICER = \frac{Cost_{NEW} - Cost_{COMPARATOR}}{Effectiveness_{NEW} - Effectiveness_{COMPARATOR}}$$

In cases where a new technology offers inferior or equal health benefits at a higher cost it clearly does not provide value for money. This technology is "dominated" by the comparison technology. In cases where the new technology offers superior health benefits at a lower cost to the comparator it is said to be "dominant".

Existing Literature

A broad literature search was conducted to identify papers that describe economic evaluations of CTC for the diagnosis of colorectal neoplasia in symptomatic patients. The databases examined were Medline, EMBASE, Pre-medline and Current Contents. Clinical search terms used in the literature search for the systematic review of the evidence of effectiveness (see Tables 8-10) were combined with the economic search terms (cost$ or econ$).mp.

This search identified 125 studies, of which three were economic evaluations that compared both costs and effectiveness of CTC with existing procedures (Ladabaum 2004, Sonnenberg 1999, McGrath 2002). One (nonsystematic) review of economic evaluations of screening strategies for colorectal cancer, including CTC, was identified; however, no additional study was retrieved (Provenzale 2002).

A search of the HTA databases retrieved three reports that included reviews of cost-effectiveness studies of various strategies to detect colorectal neoplasia (Canadian Coordinating Office for Health Technology Assessment (CCOHTA; 2004), Institute for Clinical Systems Improvement (ICSI; 2004), Minnesota Department of Health (2002)). These reviews included economic evaluations of CTC in screening populations, but no additional study from the search described above could be identified. The Harvard CEA registry did not offer any additional articles.

Of the three economic evaluations identified, two studies used Markov models to estimate the cost-effectiveness of screening an average-risk population over 50 years

every 10 years with CTC compared with colonoscopy (Sonnenberg et al 1999; Ladabaum et al 2004). Both studies showed colonoscopy to be more cost-effective than CTC for various scenarios.

McGrath (2002) reported on the cost-effectiveness of four strategies for evaluating patients with a positive FOBT, all compared to no evaluation. The four strategies investigated were CT colonography, colonoscopy, sigmoidoscopy with DCBE and flexible sigmoidoscopy to the splenic flexure. Cost-effectiveness was determined in terms of cost per advanced adenoma detected. The decision-tree-based analysis found that to clear a patient of adenomas, CTC was the most costly of the four strategies over a range of probabilities of an adenoma.

For an assumed probability of an advanced adenoma of 16.9%, the cost to find an advanced adenoma of CTC compared to sigmoidoscopy with DCBE was CAN$8,280. Compared to colonoscopy, CTC was less effective in detecting advanced adenoma and more costly and thus, CTC was dominated by colonoscopy.

Economic evaluation of computed tomography colonography

This economic evaluation used a simple decision-analytic model to determine the costs and effects associated with CTC and its comparators DCBE and colonoscopy in patients with symptoms of colorectal neoplasia. The analysis takes the perspective of the Australian Health Care System and effectiveness is measured in terms of life years saved (LYS). The decision-tree structure of the model is displayed in Figure 7.

The systematic review of the evidence presented in the previous section of this report has indicated that CTC may be more accurate than DCBE, but that CTC is less accurate than colonoscopy. Investigating the cost-effectiveness of CTC compared to DCBE and colonoscopy is still useful to explore:

- how the tests compare, assuming different scenarios of the relative accuracy of the three tests,

- how the tests compare in terms of health outcomes by linking evidence of test accuracy to evidence about the effects of treatments to determine years of life until death; and

- how the tests compare at different levels of prevalence of colorectal neoplasia in the tested population.

The model is designed for patients presenting with symptoms of colorectal neoplasia. The model captures both patients that are eligible and patients that are not eligible for colonoscopy, eg due to a previous incomplete colonoscopy. It is assumed that patients only undergo a diagnostic test if they are fit to undergo potential further treatment. Thus, therapeutic colonoscopy may be used in patients classified as 'ineligible' for diagnostic colonoscopy for the treatment of detected lesions and the course of diagnosis and treatment is assumed to be the same in both patient groups.

Figure 7   Simplified decision-tree structure of cost-effectiveness model of CTC, DCBE and colonoscopy[1]
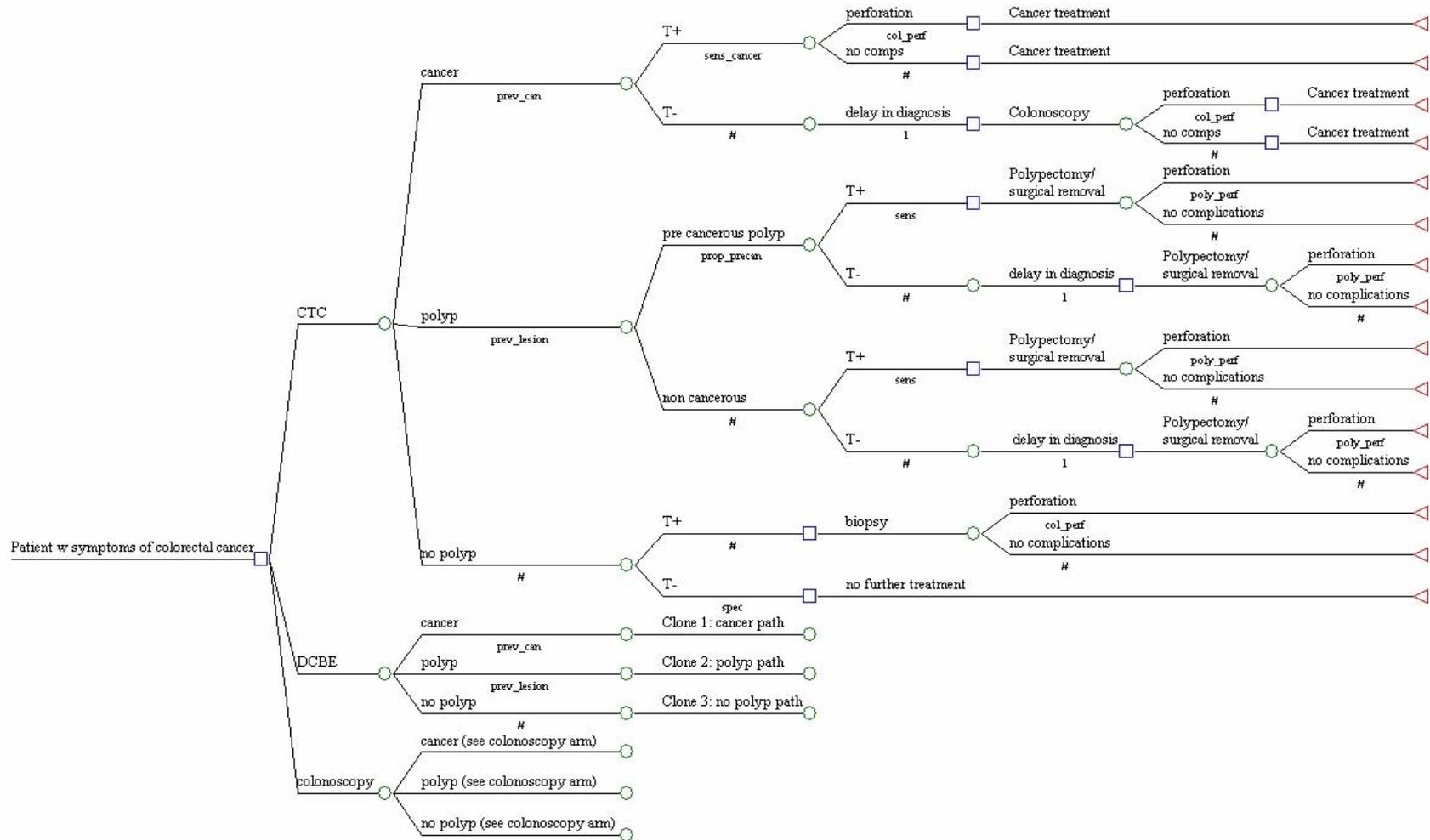
1 All arms of the model (CTC, DCBE and colonoscopy) have essentially the same structure. The colonoscopy arm differs in terms of follow-up of positive test result. This difference is reflected in the costs that are not displayed in this simplified decision-tree.

Assumptions

The main assumptions underlying the modelled economic evaluation are:

- At the start of the model evaluation, the patient has an age of 61 years, which was derived as the weighted average age of patients in the studies of patients with a previously incomplete colonoscopy and also reflects the mean of the age range of all included studies. Using Australian life-tables and assuming that 50% of the model population is male, 'normal' life-expectancy of patients at this age is 22.8 years.

- Patients are assumed to present with symptoms associated with colorectal neoplasia.

- The model only includes the consequences of significant colorectal neoplasia, which are defined as colorectal polyps (> 5 mm) and cancer. The consequences of other colorectal disease and extracolonic disease are not considered.

- Colorectal neoplasia detected by CTC, DCBE and colonoscopy are modelled as cancer, precancerous polyp (will develop into cancer given time) and noncancerous polyp (will not develop into cancer).

- All patients with colorectal neoplasia are assumed to be diagnosed and treated eventually, but a false negative result from the initial diagnostic test delays diagnosis and treatment for a period that depends on the type and stage of colorectal neoplasia (see Table 31).

- Cancer and precancerous lesions progress during treatment delay which affects patient survival (5-year survival and life expectancy) and costs.

- It is assumed that all test results are followed by a histopathological confirmation (colonoscopy/polypectomy) before treatment can proceed.

- For patients without colorectal neoplasia, no further treatment is assumed. If these patients have a false positive test result, a colonoscopy follows.

Epidemiological parameters

Epidemiological parameters that are used as input data for the model are displayed in Table 31.

The calculation of 'normal' 5-year survival and life expectancy of patients is based on the average life-expectancy of patients at age 61, which is 22.8 years. To calculate life expectancy in patients with colorectal neoplasia, it is assumed that if an individual with a diagnosed precancerous polyp or cancer survives the five years after diagnosis, he/she continues with a 'normal' life-expectancy (assumption made in MSAC FOBT report 2004, based on Loeve et al 2000; Australian Bureau of Statistics 2005).

Colorectal polyps and cancer progress during treatment delay after a false-negative initial test result, so that patients with a delay in diagnosis of polyps and cancer have a lower survival overall than patients that are diagnosed and treated immediately.

Test characteristics

Although this review provided good estimates of the comparative specificity of the three tests, uncertainties exist around the comparative sensitivity of the tests, especially of CTC and DCBE in the detection of cancers. Different scenarios for the sensitivity of these tests in cancer were assumed to explore how CTC compares to DCBE and colonoscopy in terms of cost-effectiveness and to define a range of plausible incremental cost-effectiveness ratios. The scenarios are summarised in Table 32 and are described as follows:

Base case scenario – best available evidence about test sensitivity for cancer

The base case model used the best available evidence for the relative sensitivity of the three tests, which is the relative sensitivity for detecting cancers and polyps ≥ 10 mm reported by Rockey et al (2005) (CTC sensitivity = 59%, DCBE sensitivity = 48%, colonoscopy sensitivity: 98.4%). These sensitivities were used in the model for both cancers and polyps ≥ 10 mm.

The robustness of cost-effectiveness results of this base case were explored in sensitivity analyses that tested how results change when the prevalence of lesions (cancer and polyps ≥ 6 mm) and the delay in diagnosis of cancer (in terms of effects on survival and costs associated with delayed diagnosis of cancer) are varied.

Scenario 2 – all evidence available about test sensitivity for cancer

For scenario 2, all the evidence available on the sensitivity of the three tests in the detection of cancer was used. For CTC, this is the sensitivity of 97% estimated in the pooled analysis of all CTC studies included in this review; for DCBE, the median sensitivity for cancer of 91% for DCBE reported in the de Zwart (2001) review was used and for colonoscopy, the median sensitivity of 100% from the three included studies of CTC compared to colonoscopy was used.

This scenario represents the 'best case' in terms of the sensitivity of CTC for cancer, when compared to colonoscopy. Thus, sensitivity analyses of this scenario around the prevalence of lesions (cancer and polyps ≥ 6 mm) explore the range of plausible incremental cost-effectiveness ratios in different patient populations, in particular of CTC versus colonoscopy.

Scenario 3 – evidence from the Rockey et al (2005) study

Scenario 3 used the only evidence available about the comparative sensitivity of the three tests for the detection of cancer from Rockey et al (2005), which was 78% for CTC, 89% for DCBE and 100% for colonoscopy. These estimates are surrounded by wide confidence intervals due to the low prevalence of cancer in this study.

Table 31   Key epidemiological parameters used in the economic model (values for base case and low/high values for sensitivity analyses)

Variable	Base case	Low	High	Source/ Comment
Epidemiology/Natural history of colorectal neoplasia				
Prevalence of cancer	0.015	0.008	0.11	Rockey et al (2005)/ range: included studies w high-quality reference standard (low: Hoppe et al 2004, high: Taylor et al 2003)
Prevalence of polyp ≥ 6 mm	0.24	0.17	0.37	Rockey et al (2005); range: included studies w high-quality reference standard (low: Cotton et al 2004/Hoppe et al 2004)
Proportion of large lesion given polyp	0.3			Rockey et al 2005 (derived from Table 2)
Proportion of small lesion given polyp	0.7			Rockey et al 2005 (derived from Table 2)
Risk of cancer if polyp ≥ 10 mm	0.1			Stryker et al 1987 (natural history study, retrospective, 3,572 subjects)
Risk of cancer if polyp < 10 mm	0.05			Stryker et al 1987 (natural history study, retrospective, 3,572 subjects)
Proportion of polyps that develop into cancer (precancerous lesions)	0.065			Calculated: (Risk of cancer if large polyp*proportion of large polyps)+ (Risk of cancer if small polyp*proportion of small polyps) range: assumption
Proportion of Dukes A stage cancer given cancer	0.091			MSAC (2004) FOBT report (from Bell et al (1996)/Mapp et al (1999) (Cancer NSW data) (symptomatic patients)
Proportion of Dukes B stage cancer given cancer	0.268			MSAC (2004) FOBT report (from Bell et al (1996)/Mapp et al (1999) (Cancer NSW data) (symptomatic patients)
Proportion of Dukes C stage cancer given cancer	0.488			MSAC (2004) FOBT report (from Bell et al (1996)/Mapp et al (1999) (Cancer NSW data) (symptomatic patients)
Proportion of Dukes D stage cancer given cancer	0.154			MSAC (2004) FOBT report (from Bell et al (1996)/Mapp et al (1999) (Cancer NSW data) (symptomatic patients)
				Calculated: 0.39*10 + 0.61*5
Duration in precancerous adenoma state (in years)	7			Based on Bond et al (1993): 5 year duration if lesion>10 mm, 10 yr duration if lesion <10 mm
Duration in Dukes A (in years)	2			MSAC (2004) FOBT report (from Loeve et al 2000)
Duration in Dukes B (in years)	1			MSAC (2004) FOBT report (from Loeve et al 2000)
Duration in Dukes C (in years)	1.5			MSAC (2004) FOBT report (from Loeve et al 2000)
Delay in diagnosis				
Delay in diagnosis if false negative CTC or DCBE for precancerous polyp (in months)	18	12	24	Assumption Advisory Panel
Delay in diagnosis if false negative CTC or DCBE for stage I (in months)	12	8	16	Assumption Advisory Panel
Delay in diagnosis if false negative CTC or DCBE for stage II (in months)	12	8	16	Assumption Advisory Panel
Delay in diagnosis if false negative CTC or DCBE for stage III (in months)	6	2	10	Assumption Advisory Panel
Delay in diagnosis if false negative CTC or DCBE for stage IV (in months)	3	0	6	Assumption Advisory Panel

Variable	Base case	Low	High	Source/ Comment
Survival				
Average age of patients when taking test	61			Weighted mean from 4 studies of incomplete CC
General 5 year survival rate for patient group	0.95			Australian life tables
5 year survival for immediately treated precancerous lesion	0.95			Australian life tables
5 year survival with immediate treatment of cancer Dukes A	0.91			McLeish et al 2002
5 year survival with immediate treatment of cancer Dukes B	0.85			McLeish et al 2002
5 year survival with immediate treatment of cancer Dukes C	0.58			McLeish et al 2002
5 year survival with immediate treatment of cancer Dukes D	0			McLeish et al 2002
Life years with normal life expectancy	22.8			Australian life tables (50% men/50% women)
Life years if precancerous lesion treated immediately	22.8			Extrapolation from 5-year survival rates based on assumption that patients who survive 5 years have normal life expectancy for that age
Life years if precancerous lesion treated with delay	21.62			Extrapolation from 5-year survival rates based on assumption that patients who survive 5 years have normal life expectancy for that age
Life years if cancer treated immediately	14.53			Extrapolation from 5-year survival rates based on assumption that patients who survive 5 years have normal life expectancy for that age
Life years if cancer treated with delay	11.11	13.08	7.29	Extrapolation from 5-year survival rates based on assumption that patients who survive 5 years have normal life expectancy for that age; low and high values: calculated for low and high values of delay of diagnosis (and associated proportions in each stage of Dukes)

Table 32   Test characteristics for CTC and DCBE used in the economic model (value for base case scenario and scenarios 2 and 3 tested in sensitivity analyses)

Variable	Base case scenario	Scenario 2	Scenario 3	Source/ Comment
Accuracy of CTC, DCBE and colonoscopy				
Sensitivity of CTC cancer	0.59	0.97	0.78	Base case: Rockey et al (2005) sens for lesions $\geq$ 10 mm; Scenario 2: pooled sens (table 29); Scenario 3: Rockey et al (2005) sens for cancer
Sensitivity of CTC polyps $\geq$ 10 mm	0.59			Rockey et al (2005) sens for lesions $\geq$ 10 mm
Sensitivity of CTC polyps 6-9 mm	0.51			Rockey et al (2005)
Sensitivity of DCBE cancer	0.48	0.91	0.89	Base case: Rockey et al (2005) sens for lesions $\geq$ 10mm; Scenario 2: median sensitivity de Zwart et al (2001) review; Scenario 3: Rockey et al (2005) sens for cancer
Sensitivity of DCBE polyps $\geq$ 10 mm	0.48			Rockey et al (2005) sens for lesions $\geq$ 10 mm
Sensitivity of DCBE polyps 6-9 mm	0.35			Rockey et al (2005)
Sensitivity of colonoscopy cancer	0.984	1.00	1.00	Base case: Rockey et al (2005) sens for lesions $\geq$ 10 mm; Scenario 2: Median sensitivity from 3 studies (table 28); Scenario 3: Rockey et al (2005) sens for cancer
Sensitivity of colonoscopy polyps $\geq$ 10 mm	0.984			Rockey et al (2005)
Sensitivity of colonoscopy polyps 6-9 mm	0.99			Rockey et al (2005)
Specificity of CTC lesions > 5 mm	0.89			Rockey et al (2005)
Specificity of DCBE lesions > 5 mm	0.82			Rockey et al (2005)
Specificity of colonoscopy lesions > 5 mm	0.996			Rockey et al (2005)
Complications associated with tests				
Probability of serious complication associated with colonoscopy	0.06			Tran et al (2001)
Probability of serious complication resulting from polypectomy	0.11			Tran et al (2001)

Costs

The resource use associated with performing the three diagnostic tests under study – CTC, colonoscopy and DCBE – as well as the costs for treatment of colorectal neoplasia (polyps and cancer) were considered and associated costs were calculated (Table 33 to Table 36). Costs have been calculated based on MBS, PBS and DRG costs and were not discounted.

Costs of treatment of colorectal neoplasia

For the resource use associated with management of colorectal neoplasia, it was assumed, based on estimates from the Advisory Panel, that 1% of polyps larger than or equal to 10 mm would be treated by bowel resection; all others are treated by polypectomy. It was further assumed that 1% of cancers would be treated by polypectomy, all others by bowel resection and adjuvant therapies.

If a patient is diagnosed with colorectal cancer (through CTC, DCBE, colonoscopy, or delayed if the initial test is false negative), treatment costs are accrued. Lifetime treatment costs for each Dukes stage of colorectal cancer include costs of initial investigation, surgical, chemotherapy and radiotherapy and follow-up investigations for these treatments.

The calculation of lifetime treatment costs was based on an Australian cost-effectiveness study by Bolin et al (1999) who undertook a survey of oncology units in two public teaching hospitals and one private hospital in Sydney. The costs derived in this study were updated as follows:

- MBS/PBS/DRG prices from 2005 were used to cost resource use items

- One per cent of cancer patients (Dukes A) are treated with a polypectomy and associated costs are accrued (see Table 3), 99% undergo surgical management.

- All patients with cancer Dukes B and C undergo surgical management and, according to the NSW patterns of colorectal cancer care survey (2004), 95% of Dukes D patients.

- After surgical management, a proportion of colorectal cancer patients receive chemotherapy and/or radiotherapy (according to NSW patterns of colorectal cancer care survey (Armstrong et al 2004)):

  - 20% of Dukes B and 45% of Dukes C cancer patients receive chemotherapy

  - 10% of Dukes B and 11% of Dukes C cancer patients receive radiotherapy

  - As estimated by Bolin et al (1998), 100% of Dukes D patients receive palliative chemotherapy.

- The chemotherapy regimen used was updated (from 5-FU and levamisole) and a 5-FU, low-dose leucovorin regimen was costed (most commonly used according to NSW patterns of colorectal cancer care survey (2004)) (see Table 5).

Based on the estimated lifetime treatment costs per cancer stage and the proportion of cancer patients in each stage of Dukes cancer, the average overall lifetime cancer treatment costs that were derived are $16,228 for patients that are immediately treated and $16,146 for patients treated after a delay of diagnosis (varying from $16,299 to $15,346 for the high and low values of delay of diagnosis).

As the proportions of cancer patients in the Dukes stages are different for patients that are immediately treated and those that are treated after a delay of diagnosis, the lifetime cancer treatment costs are different in these two groups. As cancer progresses during treatment delay, a higher proportion of patients with a delayed diagnosis will present with Dukes D than those who are diagnosed immediately. As Dukes D accrues lower treatment costs than the earlier cancer stages, lower overall cancer treatment costs are accrued for patients with a delayed diagnosis.

Sensitivity analysis

The robustness of the results of the cost-effectiveness analysis was tested in sensitivity analyses around the sensitivity of the tests, the prevalence of cancer and polyps and around the delay of diagnosis. The uncertainty around the comparative sensitivity of the tests was explored in the three different scenarios of test sensitivity for the detection of cancer described above (see page 96). For the base case scenario, the impact of varying prevalence and delay of diagnosis on the results was separately tested in a sensitivity analysis; for scenario 2, only prevalence was tested. If appropriate, threshold analyses were conducted to elicit at which level of sensitivity the ICER changes its direction (conducted for scenario 3).

Table 33 Costs associated with diagnosis (CTC, barium enema and colonoscopy) and treatment (polypectomy, bowel resection) of lesions

	MBS/DRG Item	Costs	No.	Total costs/item	Source
CTC					
Bowel preparation (50% Prep Kit C; 50% Ticoprep)		$11.20	1	$11.20	Hospital pharmacy information
Procedure – CTC	MBS 56549/56551	$385.00	1	$385.00	
Total medical costs of CTC				*$396.20*	
DCBE					
Bowel preparation (50% Prep Kit C; 50% Ticoprep)		$11.20	1	$11.20	Hospital pharmacy information
Procedure – Barium enema of lower gastrointestinal tract with air contrast study	MBS 58921	$135.25	1	$135.25	
Total medical costs of DCBE				*$146.45*	
Colonoscopy					
Bowel preparation (50% Prep Kit C; 50% Ticoprep)		$11.20	1	$11.20	Hospital pharmacy information
Procedure – fibreoptic colonoscopy beyond the hepatic flexure without removal of polyps	MBS 32090	$283.65	1	$283.65	
Cost of sedation					
Sedation (50%: 4 mg Midazolam/100 microgram Fentanyl; 50%: 80 mg Propofol)		$1.73	1	$1.73	Resource use: Advisory Panel; unit cost: hospital pharmacy information
Anaesthesist (in 50% of patients receiving propofol)					
Anaesthetist (basic units)	MBS 20810*	$67.00	0.5	$33.50	
Anaesthetist (time)	MBS 23023**	$33.70	0.5	$16.85	
Bed day charge		$664.00	0.5	$332.00	Estimated from DRGs G43Z, G44A, G44B, G44C, from average component cost for Ward Medical/Nursing, Pathology, Imaging, Emerg Depts, Supplies, Hotel
Total medical costs of diagnostic colonoscopy				*$678.93*	
Colonoscopy and Biopsy					
Cost of colonoscopy (see above)				$678.93	
Pathology					
Examination of complexity level 4 biopsy material with 1 or more tissue blocks	MBS 72823	$97.95	1	$97.95	MSAC FOBT 2004
Initiation of a patient episode associated with MBS 72823	MBS 73903	$14.75	1	$14.75	MSAC FOBT 2004
Total medical costs of colonoscopy and biopsy				*$791.63*	

	MBS/DRG Item	Costs	No.	Total costs/item	Source
Colonoscopy with side effect (perforation)					
Colonoscopy with moderate to severe complications	DRG G44B	3,006	1	$3,006	
Total medical costs of colonoscopy with perforation				*$3,006*	
Therapeutic colonoscopy (polypectomy)					
Bowel preparation (50% Prep Kit C; 50% Ticoprep)		$11.20	1	$11.20	Hospital pharmacy information
Procedure – fibreoptic colonoscopy beyond the hepatic flexure with removal of 1 or more polyps	MBS 32093	398.10			
Cost of sedation					
Sedation (50%: 4 mg Midazolam/100 microgram Fentanyl; 50%: 80 mg Propofol)		$1.73	1	$1.73	Resource use: Advisory Panel; unit cost: hospital pharmacy information
Anaesthesist (in 50% of patients receiving propofol)					
Initiation of management of anaesthesia	MBS 20810	$67.00	0.5	$33.50	MSAC FOBT 2004
Administration of anaesthesia	MBS 23023	$33.70	0.5	$16.85	MSAC FOBT 2004
Bed day charge		$664.00	0.5	$332.00	Estimated from DRGs G43Z, G44A, G44B, G44C, average of average component cost for Ward Medical/Nursing, Pathology, Imaging, Emerg Depts, Supplies, Hotel
Pathology					
Examination of complexity level 4 biopsy material with 1 or more tissue blocks	MBS 72823	$97.95	1	$97.95	MSAC FOBT 2004
Initiation of a patient episode associated with MBS 72823	MBS 73903	$14.75	1	$14.75	MSAC FOBT 2004
Total medical costs of therapeutic colonoscopy (polypectomy)				*$906.08*	
Surgical removal of polyp					
Major small and large bowel procedures (DRG G02B (65%)/anal and stomal procedures without complications (G11B (35%))	DRG G02B/ G11B	$7,133.85	1	$7,133.85	O'Leary et al (2004)
Total medical costs of surgical removal of polyp				*$7,133.85*	

Table 34 Cost items for estimation of lifetime treatment costs for colorectal cancer (adapted from Bolin et al 1998)

	MBS/DRG/PBS item	Unit costs	No. of units	Cost/item	Source/ comments
Initial assessment					Initial assessment according to Bolin et al (1998) (colonoscopy not costed as considered separately in this model)
Specialist consultation	MBS 104	$72.60	1	$72.60	
Total initial assessment costs				*$72.60*	
Surgical management					
Inpatient costs	DRG G02B (60%) DRG G01B (40%)	$11,061.80	1	$11,061.80	DRG G02B: Major small and large bowel procedures w/o catastrophic consequences (60% (colon cancers)); G01B:Rectal resection w/o catastrophic CC (40% (rectal cancers)) (DRG includes imaging/staging costs)
Total surgical management costs				*$11,061.80*	
Therapeutic chemotherapy					
Chemotherapy (5-FU + Leucovorin) (6 cycles)	see Table 35	$197.3078	6.0	$1,183.85	
Administration of chemotherapy (5 d per cycle, 6 cycles)	MBS 13915	$55.2000	30.0	$1,656.00	
Attendance with consultant physican	MBS 110	$128.05	6.0	$768.30	Medical consultation costed according to Bolin et al (1998), number of consultations assumed at 1 per month
Additional costs (anti-emetic (metoclopramide)) 1 month/25 d supply	PBS 1207M	$6.36	1.0	$6.36	According to Bolin et al (1998)
Total cost for chemotherapy treatment				*$3,614.51*	
Radiotherapy					MBS items for 3 field standard radiation for rectal cancer
Radiation dosimetry (CT interfacing planning computer)	MBS 15521	$288.40	1.0	$288.40	
Radiation field setting (for treatment by multiple fields)	MBS 15503	$264.40	1.0	$264.40	
Radiation oncology treatment (1 field)	MBS 15254	$50.65	25.0	$1,266.25	
Radiation oncology treatment (subsequent 2 fields (@ $32.15)	MBS 15269	$64.30	25.0	$1,607.50	
Total cost for radiotherapy treatment				*$3,426.55*	
Palliative Chemotherapy					Palliative chemotherapy resource use items according to Bolin et al (1998)
Chemotherapy (5-FU + Leucovorin) (6 cycles)	see Table 35	$197.3078	6.0	$1,183.85	

	MBS/DRG/PBS item	Unit costs	No. of units	Cost/item	Source/ comments
Administration of chemotherapy (5 d per cycle, 6 cycles)	MBS 13915	$55.2000	30.0	$1,656.00	
Attendance with consultant physican	MBS 110	$128.05	6.0	$768.30	Medical consultation costed according to Bolin et al (1998), number of consultations assumed at 1 per month
Full blood count weekly (26 weeks)	MBS 65070	$17.20	26	$447.20	
Liver function tests monthly (6 month)	MBS 66515	$19.80	6	$118.80	
Prednisone (30 tablets @ 25 mg)	PBS 1936	$9.90	1.0	$9.90	
Morphine (2 × 20 tablets @ 10 g)	PBS 8669 G	$11.49	2.0	$22.98	
Total cost for palliative chemotherapy treatment				*$3,023.18*	
F/u assessments and tests					Follow-up assessment and tests according to Bolin et al (1998)
Follow-up specialist consultation (4 × per year, first 3 y)	MBS 104	$72.60	12	$871.20	
Follow-up specialist consultation (3 × per year, 4th year)	MBS 104	$72.60	3	$217.80	
Liver function tests monthly (12 mo)	MBS 66515	$19.80	12	$237.60	
CT scan (lung, abdomen, pelvis and neck) annually (3 y)	MBS 56801/ 56841	$349.95	3	$1,049.85	50% with equipment newer than 10 years (MBS 56801)/50% with equipment older than 10years (MBS 56841)
CEA every 6 mo (3 y)	MBS 66650	$24.75	6	$148.50	
Chest x-ray annually for 3 y	MBS 58503	$47.15	3	$141.45	
Colonoscopy every 2 y (2)	See Table 33	$678.93	2	$1,375.86	
Total cost per treatment f/u				*$4,024.26*	

Table 35   Cost per cycle of chemotherapy

Therapeutic chemotherapy (5-FU + Leucovorin)[1]	Unit cost	Source	Dose mg/m^2	BSA (70kg; 1.75m)[2]	Average mg/cycle	Total \$/cycle
Bolus 5-FU (450 mg/m^2 daily for 5 days)	\$0.0133	dispensed price / mg (PBS 2528C)	2250	1.91	4297.5	\$57.11
Leucovorin (20mg/m^2 daily for 5 days)	\$0.7340	dispensed price / mg (PBS 8740B)	100	1.91	191	\$140.19
Total cost per cycle of chemotherapy						*\$197.31*

1 These costs are based on NCCTG regimen described by National Cancer Institute), most commonly used chemotherapy regimen and duration according to NSW patterns of care report.
2 Regimens are costed on basis of 75kg, height 1.75 m – BSA 1.91 m^2 (Mosteller formula).

Table 36   Lifetime treatment costs for colorectal cancer by stage[1]

Dukes A	Costs
Total initial assessment costs	\$73
Total surgical management costs	\$11,062
Total cost for treatment f/u	\$4,024
Total costs for cancer treatment Dukes A	*\$15,159*
Dukes B	
Total initial assessment costs	\$73
Total surgical management costs	\$11,062
Total cost for treatment f/u	\$4,024
Total cost for chemotherapy treatment (20% of patients) (\$3,614.51x 0.2)	\$723
Total cost for radiotherapy treatment (10% of patients) (\$3,426.55x 0.1)	\$342
Total costs for cancer treatment Dukes B	*\$16,224*
Dukes C	
Total initial assessment costs	\$73
Total surgical management costs	\$11,062
Total cost for treatment f/u	\$4,024
Total cost for chemotherapy treatment (45% of patients) (\$3,614.51x 0.45)	\$1,626
Total cost for radiotherapy treatment (11% of patients) (\$3,426.55x 0.11)	\$377
Total costs for cancer treatment Dukes C	**\$17,162**
Dukes D	
Total initial assessment costs	\$73
Total surgical management costs (95% of patients) (\$11,061.80x 0.95)	\$10,508
Total cost for palliative chemotherapy treatment	\$4,207
Total costs for cancer treatment Dukes D	*\$14,788*

1 Costs were rounded to nearest dollar.

Results of the modelled evaluation

Base case scenario – best available comparative evidence on sensitivity of cancer

In the base case scenario, which used the sensitivity estimates for detecting lesions ≥ 10 mm reported by Rockey et al (2005) as the sensitivity of the tests for detecting cancer (see Table 32), CTC is associated with an incremental cost and an incremental benefit in terms of life years saved when compared to DCBE. The incremental cost per life year saved of CTC compared to DCBE is $25,420 (see Table 37).

Table 37 Incremental cost-effectiveness of CTC vs DCBE and of colonoscopy vs DCBE in terms of cost/life year saved –- Base case

Strategy	Total average cost	Total Average effects	Incremental cost	Incremental Effects (life years)	ICER
DCBE	$788.38	22.638			
CTC (compared to DCBE)	$995.58	22.647	$207.20	0.00815	$25,420
Colonoscopy (compared to DCBE)	$1,042.50	22.675	$254.12	0.0364	$6,975

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

For this base case scenario, CTC is less costly but also less effective than colonoscopy. The incremental cost per life year saved for colonoscopy compared to CTC in this scenario is $1,659 (Table 38).

Table 38 Incremental cost-effectiveness of colonoscopy vs CTC in terms of cost/life year saved – Base case

Strategy	Total average cost	Total Average effects	Incremental cost	Incremental Effects (life years)	ICER
CTC	$995.58	22.647			
Colonoscopy (compared to CTC)	$1,042.50	22.675	$46.92	0.0283	$1,659

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

Sensitivity analyses base case – prevalence of lesions

Using the base case, sensitivity analyses around the prevalence of lesions were conducted. Assuming a low prevalence of cancer and of polyps ≥ 6 mm of 0.08% and of 17%, respectively, the incremental cost per life year saved of CTC compared to DCBE is $42,357 and higher than in the base case. Conversely, at a high prevalence of cancer and polyps ≥ 6 mm of 11% and 37%, CTC becomes more cost-effective and the incremental cost per life year saved of CTC compared to DCBE is $4,882 (see Table 39).

Table 39 Incremental cost-effectiveness of CTC vs DCBE and colonoscopy vs DCBE base case – sensitivity analysis on prevalence of lesions

Strategy	Total average cost	Total average effects (life years)	Incremental cost	Incremental effects (life years)	ICER
Low prevalence of lesions (cancer: 0.08%, polyps ≥ 6 mm: 17%)					
DCBE	$600.02	22.712			
CTC (compared to DCBE)	$802.74	22.717	$202.72	0.00479	$42,357
Colonoscopy (compared to DCBE)	$894.33	22.733	$294.31	0.0213	$13,827
High prevalence of lesions (cancer: 11%, polyps≥ 6 mm: 37%)					
DCBE	$2,516.05	21.678			
CTC (compared to DCBE)	$2,736.99	21.723	$220.94	0.0453	$4,882
Colonoscopy (compared to DCBE)	$2,655.99	21.884	$139.94	0.206	$680

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

For a low prevalence of lesions, CTC is less costly, but also less effective than colonoscopy and the incremental cost per life year saved of colonoscopy compared to CTC is $5,552. For a high prevalence of lesions, colonoscopy becomes less costly than CTC, and as it is also more effective, colonoscopy is the dominant of the two tests for this scenario (see Table 40).

Table 40 Incremental cost-effectiveness of colonoscopy vs CTC base case – sensitivity analysis on prevalence of lesions

Strategy	Total average cost	Total average effects (life years)	Incremental cost	Incremental effects (life years)	ICER
Low prevalence of lesions					
CTC	$802.74	22.717			
Colonoscopy (compared to CTC)	$894.33	22.733	$91.59	0.0169	$5,552
High prevalence of lesions					
CTC	$2,736.99	21.723			
Colonoscopy (compared to CTC)	$2,655.99	21.884	-$81.00	0.161	dominant

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

Sensitivity analyses base case – delay of diagnosis

When the delay of diagnosis of cancer after a false negative initial test is assumed to be low (as estimated by the Advisory Panel, see Table 31), the incremental cost per life year saved of CTC compared to DCBE increases to $42,243. When the high values for delay of diagnosis are assumed, the incremental cost per life year saved of CTC compared to DCBE is lowered to $14,422 (see Table 41).

Table 41 Incremental cost-effectiveness of CTC vs DCBE and colonoscopy vs DCBE base case – sensitivity analysis on delay of diagnosis

Strategy	Total average cost	Total average effects (life years)	Incremental cost	Incremental effects (life years)	ICER
Short treatment delay					
DCBE	$789.57	22.654			
CTC (compared to DCBE)	$996.51	22.659	$206.95	0.00490	$42,243
Colonoscopy (compared to DCBE)	$1,042.54	22.675	$252.97	0.021541	$11,744
Long treatment delay					
DCBE	$782.20	22.609			
CTC (compared to DCBE)	$990.71	22.623	$208.50	0.014457	$14,422
Colonoscopy (compared to DCBE)	$1,042.31	22.674	$260.11	0.065333	$3,981

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

For both a short and a long delay of diagnosis after a false negative initial test, CTC is less costly but also less effective than colonoscopy; the incremental cost per life year saved of colonoscopy compared to CTC ranges from $1,014 to $2,766 (see Table 42).

Table 42 Incremental cost-effectiveness of colonoscopy vs CTC base case – sensitivity analysis on delay of diagnosis

Strategy	Total average cost	Total average effects (life years)	Incremental cost	Incremental effects (life years)	ICER
Short treatment delay					
CTC	$996.51	22.659			
Colonoscopy (compared to CTC)	$1,042.54	22.675	$46.02	0.016642	$2,766
Long treatment delay					
CTC	$990.71	22.623			
Colonoscopy (compared to CTC)	$1,042.31	22.674	$51.60	0.050876	$1,014

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

Scenario 2 – all evidence available on sensitivity of cancer

In this scenario, all the evidence available about the sensitivity of the three tests in the detection of cancer is used. CTC is associated with an additional cost and an additional benefit in terms of life years saved when compared to DCBE. The incremental cost per life year saved of CTC compared to DCBE is $37,088 (see Table 43).

Table 43   Incremental cost-effectiveness of CTC vs DCBE and of colonoscopy vs DCBE in terms of cost/life year saved – scenario 2

Strategy	Total average cost	Total Average effects	Incremental cost	Incremental Effects (life years)	ICER
Barium Enema	$788.91	22.661			
CTC (compared to DCBE)	$996.04	22.666	$207.14	0.00559	$37,088
Colonoscopy (compared to DCBE)	$1,042.36	22.676	$253.45	0.0152	$16,685

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

This scenario represents the 'best case' in terms of the sensitivity of CTC for cancer, when compared to colonoscopy (CTC sensitivity 97% vs colonoscopy 100%). For this scenario, CTC is less costly than colonoscopy, but also less effective in terms of life years saved. The additional cost per life year saved of colonoscopy compared to CTC is $4,822 (see Table 44).

Table 44   Incremental cost-effectiveness of colonoscopy vs CTC in terms of cost/life year saved – scenario 2

Strategy	Total average cost	Total Average effects	Incremental cost	Incremental Effects (life years)	ICER
CTC	$996.04	22.666			
Colonoscopy (compared to CTC)	$1,042.36	22.676	$46.31	0.00961	$4,822

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

Sensitivity analysis scenario 2 – prevalence of lesions

On the basis of scenario 2, sensitivity analyses around the prevalence of lesions showed higher costs but more effects in terms of life years saved than DCBE for both the low and high values of prevalence of lesions. For the low values of prevalence of lesions (prevalence of cancer = 0.08%, prevalence of polyps ≥ 6 mm = 17%), the incremental cost per life year saved of CTC compared to DCBE is $59,301; at a high prevalence of lesions (prevalence of cancer = 11%, prevalence of polyps ≥ 6 mm = 37%), the ICER of CTC versus DCBE is $8,339/LYS (see Table 45).

Table 45 Incremental cost-effectiveness of CTC vs DCBE and colonoscopy vs DCBE scenario 2 – sensitivity analysis on prevalence of lesions

Strategy	Total average cost	Total average effects (life years)	Incremental cost	Incremental effects (life years)	ICER
Low prevalence of lesions (cancer: 0.08%, polyps ≥ 6 mm: 17%)					
DCBE	$600.30	22.724			
CTC (compared to DCBE)	$802.99	22.727	$202.69	0.00341	$59,301
Colonoscopy (compared to DCBE)	$894.26	22.734	$293.96	0.00996	$29,520
High prevalence of lesions (cancer: 11%, polyps ≥ 6 mm: 37%)					
DCBE	$2,519.91	21.840			
CTC (compared to DCBE)	$2,740.40	21.866	$220.49	0.0264	$8,339
Colonoscopy (compared to DCBE)	$2,654.94	21.890	$135.03	0.0502	$2,691

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

Testing a low prevalence of lesions, CTC is less costly but also less effective than colonoscopy and the incremental cost per life year saved of colonoscopy compared to CTC is $13,955. For a high prevalence of lesions, colonoscopy becomes less costly than CTC, and as it is also more effective, colonoscopy is the dominant of the two tests for this scenario (see Table 46).

Table 46 Incremental cost-effectiveness of colonoscopy vs CTC scenario 2 – sensitivity analysis on prevalence of lesions

Strategy	Total average cost	Total average effects (life years)	Incremental cost	Incremental effects (life years)	ICER
Low prevalence of lesions					
CTC	$802.99	22.727			
Colonoscopy (compared to CTC)	$894.26	22.734	$91.27	0.00654	$13,955
High prevalence of lesions					
CTC	$2,740.40	21.866			
Colonoscopy (compared to CTC)	$2,654.94	21.890	–$85.46	0.0237	dominant

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

Scenario 3 – evidence from the Rockey et al (2005) study

The only evidence available on the relative sensitivity of the three tests for the detection of cancer is from Rockey et al (2005), which also represents the 'worst case' in terms of the comparative sensitivity of CTC compared to DCBE (CTC sensitivity 78%, DCBE sensitivity 89%, colonoscopy sensitivity 100%).

For this scenario, CTC is dominated by DCBE, as it is both less effective and more costly than DCBE (see Table 47).

Table 47 Incremental cost-effectiveness of CTC vs DCBE and of colonoscopy vs DCBE in terms of cost/life year saved – Worst case

Strategy	Total average cost	Total Average effects	Incremental cost	Incremental Effects (life years)	ICER
DCBE	$788.88	22.660			
CTC (compared to DCBE)	$995.81	22.656	$206.93	–0.00409	(Dominated)
Colonoscopy (compared to DCBE)	$1,217.83	22.676	$428.94	0.0153	$16,603

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

For this scenario, CTC is less costly but also less effective than colonoscopy and the incremental cost per life year saved of colonoscopy compared to CTC is $2,405 (see Table 48).

Table 48 Incremental cost-effectiveness of colonoscopy vs CTC in terms of cost/life year saved – Worst case

Strategy	Total average cost	Total Average effects	Incremental cost	Incremental Effects (life years)	ICER
CTC	$995.81	22.656			
Colonoscopy (compared to CTC)	$1,217.83	22.676	$222.02	0.0194	$2,405

ICER = incremental cost-effectiveness ratio, rounded to nearest dollar for presentation.

Sensitivity in detecting cancer – threshold analysis

For the comparison of CTC with DCBE in this scenario, threshold analysis around the sensitivity of CTC to detect cancer was conducted to test at which value of sensitivity CTC becomes the more effective test. This analysis found that below or at a threshold value for CTC cancer sensitivity of 84.1%, DCBE is more effective than CTC and thus dominant, as it is also less costly. Above the threshold value, CTC saves more life years than DCBE (see Figure 8).

No threshold effect was found for costs. Over the range of CTC sensitivities for cancer tested in the analysis (78% to 97%), CTC remains the more expensive test.

Figure 8 Threshold analysis on the sensitivity of CTC for cancer and life years*
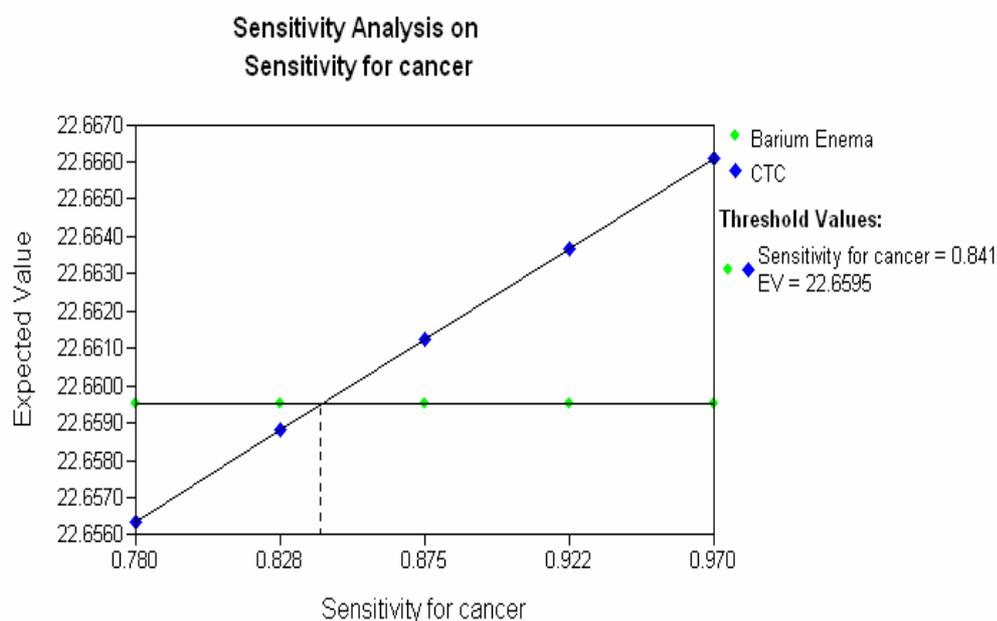
*Barium enema sensitivity kept at 0.89
Expected value: expected life years saved

Financial implications

The financial implications of a positive recommendation for CT Colonography as a replacement for DCBE in patients ineligible for colonoscopy were estimated. The calculations used information about requested interim Medicare items processed in the first 6 months after introduction (see Table 3) to derive an estimate of the annual number of patients that will receive CTC for this indication. Assuming that Medicare items in the remaining 6 months are claimed at the same rate as in October 2005 (6th month after introduction), 1,559 patients would receive CT Colonography in the first year of use. This would result in an annual expenditure on CT Colonography through the MBS of $600,215 in the first year of use. Considering the average incremental costs associated with CT colonography per patient estimated in the base case analysis, a net impact of CT Colonography on overall health care expenditure of an additional $323,025 per year was calculated. These numbers are likely to increase with likely increased uptake of the procedure and population growth in the following years.

It is not possible to estimate the number of colonoscopies currently performed in symptomatic and high-risk asymptomatic patients. However, in light of the introduction of a national colorectal cancer screening program using FOBT screening tests, the number of patients requiring a colonoscopy, or CTC if it was to be introduced, is likely to increase in the future with financial implications for Medicare and the overall health care system.

Limitations

Interpreting the results of this cost-effectiveness analysis, limitations of the model structure and uncertainties of model parameters, especially of test sensitivity, need to be considered.

The model is a simple decision-tree model. Unlike a Markov model, it calculates overall costs and effects over the patient's lifetime and does not consider the time of occurrence of costs and effects.

One model has been used to compare CTC with DCBE and colonoscopy in symptomatic patients. The model has been structured to reflect the course of diagnosis and treatment over the patient's lifetime for both patients that are eligible for colonoscopy and patients that are not eligible for colonoscopy. Potential differences between these patient groups are not considered.

More generally, the model does not consider the following:

- CTC may be used in staging of patients with positive findings with potential cost savings if an additional abdominal CT is avoided after the histopathological diagnosis is made. This might be especially beneficial in patients diagnosed with an obstructive cancer (ineligible for colonoscopy).

- The literature review has shown that CTC may be preferred over DCBE. However, this has not been considered as no data were available on whether and how this preference translates to a higher utility, which would have allowed measurement of health outcomes in terms of quality-adjusted life years.

Differences in health outcomes (life years saved) occur due to differences in the proportion of patients with a delay in diagnosis resulting from differences in sensitivity between the tests. This is one of the key variables in the model, but no published evidence has been available to estimate the length of delay of diagnosis. The figures used were estimated by the Advisory Panel and tested in the sensitivity analyses.

Further uncertainties exist around the relative accuracy of the tests, especially of CTC and DCBE. The impact of different scenarios of test sensitivity for cancer has been tested in this analysis. However, the analysis remains exploratory, as the true relative accuracy of the tests, which determines health outcomes, is not known.

Uncertainties around the costs associated with CTC, DCBE and colonoscopy exists, especially regarding the estimation of lifetime treatment costs of colorectal cancer. These costs were based on a paper published in 1998 and updated with current patterns of cancer care studies. It is not known whether this represents best practice, but a deviation from the chemotherapy regimens costed in this analysis may affect the incremental cost-effectiveness of CTC and its comparators.

Conclusions

Safety

CTC is a relatively safe procedure compared to DCBE and as least as safe as, or safer than, diagnostic colonoscopy. Both CTC and DCBE are associated with a very small risk of colonic perforation and expose patients to ionizing radiation. No perforations or deaths from CTC, DCBE or colonoscopy were reported in the studies reviewed (1,152 patients undergoing CTC), although a perforation rate of 0.06% following diagnostic colonoscopy has been reported in the literature (Tran et al 2001).

Effectiveness

CTC is generally highly sensitive and specific for the diagnosis or exclusion of lesions (cancers and polyps) ≥ 10 mm in symptomatic patients and asymptomatic patients at high risk of colorectal neoplasia. However, the variation observed between the studies reviewed demonstrates that CTC is less accurate in some population subgroups or settings. It is also only moderately sensitive for the detection of lesions 6-9 mm and poorly sensitive for lesions < 5 mm.

Lesions ≥ 10 mm

The overall evidence from 11 studies of variable quality show a median CTC sensitivity of 84% (range 55-100%); and a median CTC specificity of 97% (range 74-100%) for the detection of cancers and polyps ≥ 10 mm. Meta-analysis of four studies reporting on CTC accuracy for the detection of cancer provides a pooled estimate CTC sensitivity of 97% (95% CI 89-100%); and CTC specificity of 98% (95% CI 95-99%).

These findings are consistent with results from existing high-quality HTA reports (Ontario 2003) and systematic reviews (Mulhall et al 2005, Halligan et al 2005).

Patient characteristics, prevalence of disease, CTC techniques and the experience of those performing and interpreting the tests may contribute to the wide variation observed in CTC accuracy, but the extent to which these or other factors may influence CTC performance has not yet been clearly defined.

There is less evidence to compare the accuracy of CTC with DCBE and/or colonoscopy. One study of fair quality provides the best available evidence about the relative accuracy of the three tests (Rockey et al 2005). This study indicated that CTC is a more specific test than DCBE, but less sensitive and specific than colonoscopy for the detection of cancers and polyps ≥ 10 mm (see table 49). This study also suggested that CTC may be a more sensitive test than DCBE, but this difference did not reach statistical significance.

Table 49: Relative accuracy of CTC, DCBE and colonoscopy for the detection of cancers and polyps ≥ 10 mm (Rockey et al 2005)

Test	Sensitivity (95% CI)	p value[1]	Specificity (95% CI)	p value[1]
CTC	59% (46-71%)		96% (94-98%)	
DCBE	48% (35-61%)	0.11	90% (87-92%)	<0.0001
colonoscopy	98.3% (91-100%)	<0.0001	99.6% (99-100%)	<0.0001

1 p value CTC versus comparator test.

Two additional studies of fair quality also provided evidence that CTC is less sensitive and specific than colonoscopy for the detection of colorectal lesions ≥ 10 mm (Cotton et al 2004, Van Gelder et al 2004).

This review did not identify any studies that directly compared the relative accuracy of CTC versus DCBE in studies where CTC was observed to be highly sensitive. Expert opinion from the Advisory Panel suggests that it is unlikely that more direct comparative evidence of CTC with DCBE will become available.

Lesions < 10 mm

Six studies provide evidence that CTC is a moderately to poorly sensitive but moderately to highly specific test for the detection of lesions 6-9 mm (CTC sensitivity range 30-80%, median 61%; CTC specificity range 93-99%, median 96%). Four of these studies indicated that CTC accuracy was lower for the detection of lesions ≤ 5 mm (CTC sensitivity range 14-57%, median 34%; CTC specificity range 83- 97%, median 92%).

Evidence about the relative accuracy of CTC versus DCBE for the detection of lesions 6-9 mm from one fair-quality study demonstrated that CTC is statistically significantly superior to DCBE (Rockey et al 2005). No eligible studies reported on the relative accuracy of CTC and DCBE for detecting lesions ≤ 5 mm; however, individual studies of CTC and DCBE have consistently reported low sensitivities for both tests to detect lesions of this size.

Two studies have demonstrated that the accuracy of colonoscopy remains high for the detection of lesions < 10 mm (colonoscopy sensitivity 99%, colonoscopy specificity 99-100%) and is statistically significantly superior to CTC (Rockey et al 2005, Cotton et al 2004).

Overall colorectal disease

Two studies of fair quality suggested that CTC may be more accurate than DCBE for the detection of all colorectal disease but less sensitive than colonoscopy; however, no studies have directly compared these tests (Munikrishnan et al 2003, Durdey et al 1987).

Patient preferences and quality of life outcomes

Three studies of fair to high quality using different measurement instruments have reported a statistically significant difference in patient preference, satisfaction and experience of pain or discomfort in favour of CTC versus DCBE (Gluecker et al 2003, Taylor et al 2005, Taylor et al 2003).

Evidence from nine studies of fair quality also suggested that CTC was preferred over colonoscopy in patients who have had both procedures. However, these studies used different methods to assess patient preferences and the results may not apply to symptomatic patients in Australian practice. Preliminary results from a recent Australian study suggest patients with a positive FOBT prefer colonoscopy over CTC.

Eight studies comparing the pain and discomfort experienced by patients undergoing both tests reported mixed results; five studies reported in favour of CTC and three studies reported in favour of colonoscopy.

Additional considerations

CTC has been proposed as an alternative test to DCBE following an incomplete colonoscopy or in patients in whom colonoscopy cannot be performed. Four studies investigating the value of CTC following an incomplete colonoscopy provide evidence that CTC is successful in visualising the entire colon in at least 90% of patients following an incomplete colonoscopy. These studies reported that CTC yielded additional colorectal lesions in 18 to 27% of patients that were not identified at the initial incomplete colonoscopy (Neri et al 2002, Morrin et al 1999, Macari et al 1999, Minyue et al 2002). One study also observed that DCBE did not perform as well as CTC for visualising the proximal colon in patients with a distal obstruction (Morrin et al 1999).

CTC also offers the opportunity for detecting extracolonic lesions that cannot be identified at DCBE or colonoscopy. Six of the studies included in this review reported rates of clinically significant extracolonic findings between 1% and 13%. Three studies reported rates of incidental nonsignificant findings of between 19% and 63%. The consequences of extracolonic findings have not been assessed. Clinically significant findings may be expected to change patient management, whereas insignificant findings may result in additional unnecessary investigations and patient distress.

CTC also has a practical advantage over DCBE due to technical difficulties of coating the bowel wall with barium to conduct a DCBE following a colonoscopy.

No studies were designed to compare test failure rates for CTC versus DCBE and/or colonoscopy; however, comparison of median rates of failed CTCs (median 5%, 11 studies), failed DCBE (median 9%, 3 studies) and incomplete colonoscopies (median 8%, 18 studies) suggest that CTC failure rates are at least comparable or better than DCBE and colonoscopy.

Cost-effectiveness

Conclusions about the cost-effectiveness of CTC compared to colonoscopy and DCBE are based on an analysis using a decision-tree model that included one- and two-way sensitivity analyses of key parameters.

For the comparison of CTC with DCBE, the modelled analysis shows a cost of $25,420 per life year saved of CTC compared to DCBE in the base case scenario (CTC cancer sensitivity: 59%, DCBE cancer sensitivity: 48%). When the sensitivity in detecting cancer for CTC and DCBE is varied, the cost ranges from $37,088 per life year saved to a situation where CTC is dominated by DCBE. However, caution should be used in interpreting these results due to the uncertainty around the relative sensitivity of CTC

and DCBE. In particular, the point estimates reported by Rockey et al (2005) were surrounded by wide confidence intervals.

Further sensitivity analyses of the base case scenario and scenario 2 testing high and low values for the delay of diagnosis and prevalence of lesions result in incremental costs of CTC per life year saved between $4,882 and $59,301, when compared to DCBE.

For the three scenarios of test sensitivity for the detection of cancer, the analysis suggests that CTC is less costly, but also less effective than colonoscopy. The incremental cost of colonoscopy versus CTC per life year saved is $1,659 for the base case (CTC sensitivity for cancer of 59%, colonoscopy sensitivity for cancer of 98.4%). In the further two scenarios, an incremental costs per life year saved of colonoscopy versus CTC of $4,822 (scenario 2) and $2,405 (scenario 3) was found.

When sensitivity analyses are conducted around the base case, the highest cost per life year saved for colonoscopy compared to CTC is $5,552. When a high prevalence of lesions is assumed, colonoscopy is not only more effective than CTC, but also associated with less costs and is thus the dominant of the two tests. Similarly, when the prevalence of lesions is varied for scenario 2, which is the 'best case' for CTC relative to colonoscopy, the incremental cost per life year saved for colonoscopy ranges from $13,955 to a situation where colonoscopy is dominant, when compared to CTC.

Review Question 1: CTC versus DCBE and versus colonoscopy

CTC is a relatively safe test compared to DCBE and colonoscopy.

Evidence about CTC accuracy for the detection of cancers and polyps ≥ 10 mm compares favourably with DCBE. There is also some evidence to suggest that patients prefer CTC over DCBE. CTC is more costly than DCBE and an economic model suggests a base case incremental cost per life year saved for CTC compared to DCBE of $25,420; results of the sensitivity analysis ranged from a cost per life year saved of $4,882 for CTC compared to DCBE to a situation where CTC is dominated by DCBE (more costly and less effective).

CTC is less accurate than colonoscopy for the detection of cancers and polyps ≥ 10 mm. There is also some evidence to suggest that patients prefer CTC over colonoscopy. CTC is less costly than colonoscopy and an economic model found a base case incremental cost per life year saved of $1,659 for colonoscopy compared to CTC. The cost per life year saved for colonoscopy in sensitivity analyses ranged between $13,955 and a situation where colonoscopy is more effective and associated with less costs than CTC.

Review Question 2: CTC versus DCBE in patients ineligible for colonoscopy

There is little evidence for a comparison of CTC versus DCBE accuracy in patients following an incomplete colonoscopy. The evidence available indicates that CTC is successful in visualising the entire colon in at least 90% of patients following an incomplete colonoscopy. CTC also has demonstrated advantages over DCBE in visualising the proximal colon in patients with a distal obstruction, the detection of extracolonic disease, and patient preferences and tolerance of testing. Another consideration favouring the use of CTC is that it can be performed immediately after a

failed colonoscopy, whereas coating the bowel wall with barium can be difficult to achieve after colonoscopy.

CTC is more costly than DCBE. An economic analysis based on a general model of CTC compared to DCBE in symptomatic patients found a base case incremental cost per life year saved for CTC compared to DCBE of $25,420; results of the sensitivity analysis ranged from a cost per life year saved of $4,882 for CTC compared to DCBE to a situation where CTC is dominated by DCBE (more costly and less effective).

Recommendation

Computed tomography colonography (CTC) is a relatively safe procedure. CTC, double contrast barium enema (DCBE) and colonoscopy are associated with a small risk of complications.

Evidence in relation to the comparison of CTC with colonoscopy indicates that CTC is less effective. MSAC recommends that public funding for CTC as a substitute investigation for colonoscopy should not be supported.

On the basis of the strength of evidence pertaining to the effectiveness and cost-effectiveness, MSAC recommends that public funding for CTC for exclusion of colorectal neoplasia in symptomatic or high risk patients who are either ineligible for colonoscopy due to patient contraindications or where there is an inability to perform or complete a colonoscopy, should be supported.

- The Minister for Health and Ageing accepted this recommendation on 24 August 2006.

Appendix A   MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;

- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;

- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and

- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	Expertise or Affiliation
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Professor Syd Bell	pathology
Dr Michael Cleary	emergency medicine
Dr Paul Craft	clinical epidemiology and oncology
Dr Kwun Fong	thoracic medicine
Dr Debra Graves	medical administrator
Dr David Gillespie	gastroenterology
Professor Jane Hall	health economics
Professor John Horvath	Chief Medical Officer, Department of Health and Ageing
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Associate Professor Frederick Khafagi	nuclear medicine
Associate Professor Donald Perry-Keene	endocrinology
Dr Ray Kirk	health research

Member	Expertise or Affiliation
Dr Ewa Piejko	general practice
Ms Sheila Rimmer	consumer health issues
Ms Samantha Robertson	Acting Assistant Secretary, Department of Health and Ageing
Professor Ken Thomson	radiology
Dr Douglas Travis	urology
Dr Mary Turner	Australian Health Ministers" Advisory Council Representative
Dr David Wood	orthopaedics

Appendix B   Advisory Panel

Advisory panel for MSAC application 1095 CT Colonography

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Appendix C   Excluded studies

Studies excluded from the CTC search

Acar, B., Beaulieu, C. F., Gokturk, S. B., Tomasi, C., Paik, D. S., Jeffrey, R. B., Jr., Yee, J., Napel, S. 2002, 'Edge displacement field-based classification for improved detection of polyps in CT colonography', *IEEE Transactions on Medical Imaging*, 21 (12), 1461-1467.

Biancone, L., Fiori, R., Tosti, C., Marinetti, A., Catarinacci, M., De Nigris, F., Simonetti, G., Pallone, F. 2003, 'Virtual colonoscopy compared with conventional colonoscopy for stricturing postoperative recurrence in Crohn's disease', *Inflammatory Bowel Diseases*, 9 (6), 343-350.

Bruzzi, J. F., Moss, A. C., Brennan, D. D., MacMathuna, P., Fenlon, H. M. 2003, 'Efficacy of IV Buscopan as a muscle relaxant in CT colonography', *European Radiology*, 13 (10), 2264-2270.

Callstrom, M. R., Johnson, C. D., Fletcher, J. G., Reed, J. E., Ahlquist, D. A., Harmsen, W. S., Tait, K., Wilson, L. A., Corcoran, K. E. 2001, 'CT colonography without cathartic preparation: feasibility study', *Radiology*, 219 (3), 693-698.

Carr-Locke, D. L., Chang, K. J., Conn, M. I., Faigel, D. O., Leung, J., Mills, M., Nelson, D. B., Phillips, E., Tarnasky, P. R., Waxman, I., Laing, K. I. 1998, 'Technology status evaluation: Virtual colonoscopy', *Gastrointestinal Endoscopy*, 48 (6), 708-710.

Chen, S. C., Lu, D. S., Hecht, J. R., Kadell, B. M. 1999, 'CT colonography: value of scanning in both the supine and prone positions', *American Journal of Roentgenology*, 172 (3), 595-599.

Chung, D. J., Huh, K. C., Choi, W. J., Kim, J. K. 2005, 'CT colonography using 16-MDCT in the evaluation of colorectal cancer', *American Journal of Roentgenology*, 184 (1), 98-103.

Dachman, A. H., Kuniyoshi, J. K., Boyle, C. M., Samara, Y., Hoffmann, K. R., Rubin, D. T., Hanan, I. 1998, 'CT colonography with three-dimensional problem solving for detection of colonic polyps', *American Journal of Roentgenology*, 171 (4), 989-995.

Durkalski, V. L., Palesch, Y. Y., Pineau, B. C., Vining, D. J., Cotton, P. B. 2002, 'The virtual colonoscopy study: a large multicenter clinical trial designed to compare two diagnostic screening procedures', *Controlled Clinical Trials*, 23 (5), 570-583.

Fenlon, H. M., Nunes, D. P., Schroy, P. C., Barish, M. A., Clarke, P. D., Ferrucci, J.T. 1999, 'A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps', *New England Journal of Medicine,* 341 (20), 1496-1503.

Fenlon, H. M., Nunes, D. P., Clarke, P. D., Ferrucci, J. T. 1998, 'Colorectal neoplasm detection using virtual colonoscopy a feasibility study', *Gut*, 43 (6), 806-811.

Ferda, J., Mirka, H., Kreuzberg, B., Zdenek, P., Kozeluhova, J. 2004, 'Multidetector CT colonography: Comparing the results of virtual colonoscopy and optical colonoscopy', *Ceska Radiologie*, 58 (6), 364-371.

Fletcher, J. G., Johnson, C. D., Welch, T. J., MacCarty, R. L., Ahlquist, D. A., Reed, J. E., Harmsen, W. S., Wilson, L. A. 2000, 'Optimization of CT colonography technique: prospective trial in 180 patients', *Radiology*, 216 (3), 704-711.

Ginnerup, P. B., Christiansen, T. E., Bjerregaard, N. C., Ljungmann, K., Laurberg, S. 2003, 'Colonoscopy and multidetector-array computed-tomographic colonography: detection rates and feasibility', *Endoscopy*, 35 (9), 736-742.

Gluecker, T., Meuwly, J. Y., Pescatore, P., Schnyder, P., Delarive, J., Jornod, P., Meuli, R., Dorta, G. 2002, 'Effect of investigator experience in CT colonography', *European Radiology*, 12 (6), 1405-1409.

Hara, A. K., Johnson, C. D., Reed, J. E., Ahlquist, D. A., Nelson, H., MacCarty, R. L., Harmsen, W. S., Ilstrup, D. M. 1997, 'Detection of colorectal polyps with CT colonography: initial assessment of sensitivity and specificity', *Radiology*, 205 (1), 59-65.

Harvey, C. J., Amin, Z., Hare, C. M., Gillams, A. R., Novelli, M. R., Boulos, P. B., Lees, W. R. 1998, 'Helical CT pneumocolon to assess colonic tumors: radiologic-pathologic correlation', *American Journal of Roentgenology*, 170 (6), 1439-1443.

Hoppe, H., Quattropani, C., Spreng, A., Mattich, J., Netzer, P., Dinkel, H. P. 2004, 'Virtual colon dissection with CT colonography compared with axial interpretation and conventional colonoscopy: preliminary results', *American Journal of Roentgenology*, 182 (5), 1151-1158.

Iannaccone, R., Laghi, A., Catalano, C., Brink, J. A., Mangiapane, F., Trenna, S., Piacentini, F., Passariello, R. 2003, 'Detection of colorectal lesions: lower-dose multi-detector row helical CT colonography compared with conventional colonoscopy', *Radiology*, 229 (3), 775-781.

Iannaccone, R., Laghi, A., Catalano, C., Mangiapane, F., Lamazza, A., Schillaci, A., Sinibaldi, G., Murakami, T., Sammartino, P., Hori, M., Piacentini, F., Nofroni, I., Stipa, V., Passariello, R. 2004, 'Computed tomographic colonography without cathartic preparation for the detection of colorectal polyps', *Gastroenterology*, 127 (5), 1300-1311.

Johnson, C. D., Harmsen, W. S., Wilson, L. A., MacCarty, R. L., Welch, T. J., Ilstrup, D. M., Ahlquist, D. A. 2003, 'Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps', *Gastroenterology*, 125 (2), 311-319.

Kay, C. L., Kulling, D., Hawes, R. H., Young, J. W., Cotton, P. B. 2000, 'Virtual endoscopy - comparison with colonoscopy in the detection of space-occupying lesions of the colon', *Endoscopy*, 32 (3), 226-232.

Laghi, A., Iannaccone, R., Carbone, I., Catalano, C., Di Giulio, E., Schillaci, A., Passariello, R. 2002, 'Detection of colorectal lesions with virtual computed tomographic colonography, *American Journal of Surgery*, 183 (2), 124-131.

Lefere, P., Gryspeerdt, S., Marrannes, J., Baekelandt, M., Van Holsbeeck, B. 2005, 'CT Colonography After Fecal Tagging with a Reduced Cathartic Cleansing and a Reduced Volume of Barium', *American Journal of Roentgenology*, 184 (6), 1836-1842.

Lefere, P. A., Gryspeerdt, S. S., Dewyspelaere, J., Baekelandt, M., van Holsbeeck, B. G. 2002, 'Dietary fecal tagging as a cleansing method before CT colonography: initial results polyp detection and patient acceptance', *Radiology*, 224 (2), 393-403.

Lidofsky, S. 2005, 'Detection and prevention of colon cancer: colonoscopy, virtual colonoscopy, and DNA stool tests', *Medicine & Health, Rhode Island*, 88 (3), 82-85.

Lui, Y. W., Macari, M., Israel, G., Bini, E. J., Wang, H., Babb, J. 2003, 'CT colonography data interpretation: effect of different section thicknesses - preliminary observations', *Radiology*, 229 (3), 791-797.

Macari, M., Milano, A., Lavelle, M., Berman, P., Megibow, A. J. 2000, 'Comparison of time-efficient CT colonography with two- and three-dimensional colonic evaluation for detecting colorectal polyps', *American Journal of Roentgenology*, 174 (6), 1543-1549.

Macari, M., Green, J. C., Berman, P., Milano, A. 1999, 'Diagnosis of familial adenomatous polyposis using two-dimensional and three-dimensional CT colonography', *American Journal of Roentgenology*, 173 (1), 249-250.

Macari, M., Bini, E. J., Jacobs, S. L., Lui, Y. W., Laks, S., Milano, A., Babb, J. 2004, 'Significance of missed polyps at CT colonography', *American Journal of Roentgenology*, 183 (1), 127-134.

Mani, A., Napel, S., Paik, D. S., Jeffrey, R. B., Jr., Yee, J., Olcott, E. W., Prokesch, R., Davila, M., Schraedley-Desmond, P., Beaulieu, C. F. 2004, 'Computed tomography colonography: feasibility of computer-aided polyp detection in a "first reader" paradigm', *Journal of Computer Assisted Tomography*, 28 (3), 318-326.

McFarland, E. G., Pilgram, T. K., Brink, J. A., McDermott, R. A., Santillan, C. V., Brady, P. W., Heiken, J. P., Balfe, D. M., Weinstock, L. B., Thyssen, E. P., Littenberg, B. 2002, 'CT colonography: multiobserver diagnostic performance', *Radiology*, 225 (2), 380-390.

Mendelson, R. M., Foster, N. M., Edwards, J. T., Wood, C. J., Rosenberg, M. S., Forbes, G. M. 2000, 'Virtual colonoscopy compared with conventional colonoscopy: a developing technology', *Medical Journal of Australia*, 173 (9), 472-475.

Miao, Y. M., Amin, Z., Healy, J., Burn, P., Murugan, N., Westaby, D., Allen-Mersh, T. G. 2000, 'A prospective single centre study comparing computed tomography pneumocolon against colonoscopy in the detection of colorectal neoplasms', *Gut*, 47 (6), 832-837.

Ota, Y., Matsui, T., Ono, H., Uno, H., Matake, H., Tsuda, S., Sakurai, T., Yao, T. 2003, 'Value of virtual computed tomographic colonography for Crohn's colitis: comparison with endoscopy and barium enema', *Abdominal Imaging*, 28 (6), 778-783.

Park, S. H., Ha, H. K., Kim, M. J., Kim, K. W., Kim, A. Y., Yang, D. H., Lee, M. G., Kim, P. N., Shin, Y. M., Yang, S. K., Myung, S. J., Min, Y. I. 2005, 'False-negative results at multi-detector row CT colonography: multivariate analysis of causes for missed lesions', *Radiology*, 235 (2), 495-502.

Pescatore, P., Glucker, T., Delarive, J., Meuli, R., Pantoflickova, D., Duvoisin, B., Schnyder, P., Blum, A. L., Dorta, G. 2000, 'Diagnostic accuracy and interobserver agreement of CT colonography (virtual colonoscopy)', *Gut*, 47 (1), 126-130.

Pickhardt, P. J., Choi, J. R., Nugent, P. A., Schindler, W. R. 2004, 'The effect of diagnostic confidence on the probability of optical colonoscopic confirmation of potential polyps detected on CT colonography: prospective assessment in 1,339 asymptomatic adults', *American Journal of Roentgenology*, 183 (6), 1661-1665.

Pineau, B. C., Paskett, E. D., Chen, G. J., Espeland, M. A., Phillips, K., Han, J. P., Mikulaninec, C., Vining, D. J. 2003, 'Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps', *Gastroenterology*, 125 (2), 304-310.

Rex, D. K., Vining, D., Kopecky, K. K. 1999, 'An initial experience with screening for colon polyps using spiral CT with and without CT colonography (virtual colonoscopy)', *Gastrointestinal Endoscopy*, 50 (3), 309-313.

Rottgen, R., Fischbach, F., Plotkin, M., Lorenz, M., Freund, T., Schroder, R. J., Felix, R. R. 2005, 'CT colonography using different reconstruction modi', *Clinical Imaging*, 29 (3), 195-199.

Serracino-Inglott, F., Atkinson, H. D., Jha, P., Parker, I., Anderson, D. N. 2004, 'Early experiences with computed axial tomography colonography', *American Journal of Surgery*, 187 (4), 511-514.

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

Thomeer, M., Carbone, I., Bosmans, H., Kiss, G., Bielen, D., Vanbeckevoort, D., Van Cutsem, E., Rutgeerts, P., Marchal, G. 2003, 'Stool tagging applied in thin-slice multidetector computed tomography colonography', *Journal of Computer Assisted Tomography*, 27 (2), 132-139.

van Gelder, R. E., Venema, H. W., Florie, J., Nio, C. Y., Serlie, I. W., Schutter, M. P., van Rijn, J. C., Vos, F. M., Glas, A. S., Bossuyt, P. M., Bartelsman, J. F., Lameris, J. S., Stoker, J. 2004, 'CT colonography: feasibility of substantial dose reduction-comparison of medium to very low doses in identical patients', *Radiology*, 232 (2), 611-620.

Vos, F. M., van Gelder, R. E., Serlie, I. W., Florie, J., Nio, C. Y., Glas, A. S., Post, F. H., Truyen, R., Gerritsen, F. A., Stoker, J. 2003, 'Three-dimensional display modes for CT colonography: conventional 3D virtual colonoscopy versus unfolded cube projection', *Radiology*, 228 (3), 878-885.

Wang, Y., Gong, S.G., Zhang, W.G., Chen, J.H., Zhang, L.Y., Chen, J.P. 2004, 'Sensitivity and specificity of pneumocolon CT in detecting colorectal neoplasms', *World Chinese Journal of Digestology*, 12 (2), 359-362.

Wessling, J., Domagk, D., Lugering, N., Schierhorn, S., Heindel, W., Domschke, W., Fischbach, R. 2005, 'Virtual colonography: Identification and differentiation of colorectal lesions using multi-detector computed tomography', *Scandinavian Journal of Gastroenterology*, 40 (4), 468-476.

Wong, B. C., Wong, W. M., Chan, J. K., Lai, K. C., Hu, W. H., Chan, C. K., Lam, S. K., Carr-Locke, D. L. 2002, 'Virtual colonoscopy for the detection of colorectal polyps and cancers in a Chinese population', *Journal of Gastroenterology & Hepatology*, 17 (12), 1323-1327.

Yee, J., Akerkar, G. A., Hung, R. K., Steinauer-Gebauer, A. M., Wall, S. D., McQuaid, K. R. 2001, 'Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients', *Radiology*, 219 (3), 685-692.

Yee, J., Kumar, N. N., Hung, R. K., Akerkar, G. A., Kumar, P. R., Wall, S. D. 2003, 'Comparison of supine and prone scanning separately and in combination at CT colonography', *Radiology*, 226 (3), 653-661.

Yoshida, H., Nappi, J., MacEneaney, P., Rubin, D. T., Dachman, A. H. 2002, 'Computer-aided diagnosis scheme for detection of polyps at CT colonography', *Radiographics*, 22 (4), 963-979.

Studies excluded from DCBE search:

Aggarwal, V. 1995, 'A comparative study of double contrast barium enema and colonoscopy for evaluation of rectal bleeding in children', *Tropical gastroenterology : official journal of the Digestive Diseases Foundation*, 16 (2), 132-137.

Bartram, C. 2005, 'National audit of the sensitivity of double-contrast barium enema for colorectal carcinoma, using control charts', *Clinical Radiology*, 60 (5), 555-557.

Burtin, P. 1995, 'Colonic investigations in the elderly: Colonoscopy barium enema?', *Aging Clinical and Experimental Research*, 7 (4), 190-194.

Chen, Y. M., Ott, D. J., Gelfand, D. W., Munitz, H. A. 1988, 'Impact of the barium enema on patient management', *Gastrointestinal Radiology*, 13 (1), 81-84.

Ciatto, S., & Castiglione, G. 2002, 'Role of double-contrast barium enema in colorectal cancer screening based on fecal occult blood', *Tumori*, 88 (2), 95-98.

Ernstoff, J. J., Howard, D. A., Marshall, J. B., Jumshyd, A., McCullough, A. J. 1983, 'A randomized blinded clinical trial of a rapid colonic lavage solution (Golytely) compared with standard preparation for colonoscopy and barium enema', *Gastroenterology*, 84 (6), 1512-1516.

Gollub, M. J., & Flaherty, F. 1999, 'Barium enema following incomplete colonoscopy', *Clinical Imaging*, 23 (6), 367-374.

Hagenthau, P., Wagner, H. J., Stinner, B., Klose, K. J. 1995, 'Prospective evaluation of colon double-contrast enemas in patients with incomplete colonoscopy diagnostic', *Radiologe*, 35 (5), 356-360.

Jensen, J. 1990, 'Double contrast barium enema and flexible rectosigmoidoscopy: a reliable diagnostic combination for detection of colorectal neoplasm', *The British journal of surgery*, 77 (3), 270-272.

Kaude, J. V., Harty, R. F. 1982, 'Sensitivity of single contrast barium enema with regard to colorectal disease as diagnosed by colonoscopy', *European Journal of Radiology*, 2 (4), 290-292.

Knoepp, L. F. J., Suits, G. S. 1984, 'Comparison of barium enema and colonoscopy in the diagnosis of colon and rectal cancer', *Journal South Carolina Medical Association*, 80 (1), 7-9.

Maratia, F., Buccino, R. V., Sinisi, G., Spada, P., Fasano, G., Dileo, F., Campaniello, A. 1993, 'Opaque enema as the first test: is it always the right choice?', *Minerva Chirurgica*, 48 (20), 1197-1204.

Mirza, F. H., Shah, S. M. 1977, 'Barium enema and colonoscopy in diagnosis of colonic disorders', *Journal of the Arkansas Medical Society*, 74 (6), 217-220.

Nicholas, G. G., Miller, W. T., Fitts, W. T., Tondreau, R. L. 1972, 'Diagnosis of diverticulitis of the colon: role of the barium enema in defining pericolic inflammation', *Annals of Surgery*, 176 (2), 205-209.

Norfleet, R. G., Ryan, M. E., Wyman, J. B., Rhodes, R. A., Nunez, J. F., Kirchner, J. P., Parent, K. 1991, 'Barium enema versus colonoscopy for patients with polyps found during flexible sigmoidoscopy', *Gastrointestinal Endoscopy*, 37 (5), 531-534.

Smith, G. A., O'Dwyer, P. J. 2001, 'Sensitivity of double contrast barium enema and colonoscopy for the detection of colorectal neoplasms', *Surgical Endoscopy*, 15 (7), 649-652.

Stephenson, G., Robertson, A., Hecker, R. 1984, 'Barium enema in the diagnosis of colonic carcinoma', *Australian Clinical Review,* (13), 13-17.

Stringer, D. A., Sherman, P. M., Jakowenko, N. 1986, 'Correlation of double-contrast high-density barium enema, colonoscopy, and histology in children with special attention to disparities', *Pediatric Radiology*, 16 (4), 298-301.

Tedesco, F. J., Gottfried, E. B., Corless, J. K., Brownstein, R. E. 1984, 'Prospective evaluation of hospitalized patients with nonactive lower intestinal bleeding - timing and role of barium enema and colonoscopy', *Gastrointestinal Endoscopy*, 30 (5), 281-283.

Teefey, S. A., Carlson, H. C. 1983, 'The fluoroscopic barium enema in colonic polyp detection', *American Journal of Roentgenology*, 141 (6), 1279-1281.

Thoeni, R. F., Vandeman, F. 1984, 'Effect of glucagon on the diagnostic accuracy of double-contrast barium enema examinations', *American Journal of Roentgenology*, 142 (1), 111-114.

Thoeni, R. F., Venbrux, A. C. 1983, 'The value of colonoscopy and double-contrast barium-enema examinations in the evaluation of patients with subacute and chronic lower intestinal bleeding', *Radiology*, 146 (3), 603-607.

Thoeni, R. F., Menuck, L. 1977, 'Comparison of barium enema and colonoscopy in the detection of small colonic polyps', *Radiology*, 124 (3), 631-635.

Warden, M. J., Petrelli, N. J., Herrera, L., Mittelman, A. 1988, 'Endoscopy versus double-contrast barium enema in the evaluation of patients with symptoms suggestive of colorectal carcinoma', *American Journal of Surgery*, 155 (2), 224-226.

Appendix D   Studies included in the review

Studies included from the CTC search

Akerkar, G. A., Yee, J., Hung, R., McQuaid, K. 2001, 'Patient experience and preferences toward colon cancer screening: a comparison of virtual colonoscopy and conventional colonoscopy', *Gastrointestinal Endoscopy*, 54 (3), 310-315.

Bruzzi, J. F., Moss, A. C., Brennan, D. D., MacMathuna, P., Fenlon, H. M. 2004, 'Colonic surveillance by CT colonography using axial images only', *European Radiology*, 14 (5), 763-767.

Canadian Coordinating Office for Health Technology Assessment (CCOHTA). *Pre-Assessment Virtual Colonoscopy* [Internet]. Available at: http://www.ccohta.ca [Accessed on 6 June 2005].

Cohnen, M., Vogt, C., Beck, A., Andersen, K., Heinen, W., vom Dahl, S., Aurich, V., Haeussinger, D., Moedder, U. 2004, 'Feasibility of MDCT Colonography in ultra-low-dose technique in the detection of colorectal lesions: comparison with high-resolution video colonoscopy', *American Journal of Roentgenology*, 183 (5), 1355-1359.

Cotton, P. B., Durkalski, V. L., Pineau, B. C., Palesch, Y. Y., Mauldin, P. D., Hoffman, B., Vining, D. J., Small, W. C., Affronti, J., Rex, D., Kopecky, K. K., Ackerman, S., Burdick, J. S., Brewington, C., Turner, M. A., Zfass, A., Wright, A. R., Iyer, R. B., Lynch, P., Sivak, M. V., Butler, H. 2004, 'Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia.[see comment]', *JAMA*, 291 (14), 1713-1719.

Ginnerup Pedersen, B., Christiansen, T. E. M., Bjerregaard, N. C., Ljungmann, K., Laurberg, S. 2003, 'Colonoscopy and multidetector-array computed-tomographic colonography: detection rates and feasibility', *Endoscopy*, 35 (9), 736-742.

Gluecker, T., Dorta, G., Keller, W., Jornod, P., Meuli, R., Schnyder, P. 2002, 'Performance of multidetector computed tomography colonography compared with conventional colonoscopy', *Gut*, 51 (2), 207-211.

Gluecker, T. M., Johnson, C. D., Harmsen, W. S., Offord, K. P., Harris, A. M., Wilson, L. A., Ahlquist, D. A. 2003, 'Colorectal cancer screening with CT colonography, colonoscopy, and double-contrast barium enema examination: prospective assessment of patient perceptions and preferences', *Radiology*, 227 (2), 378-384.

Halligan, S., Altman, D. G., Taylor, S. A., Mallett, S., Deeks, J. J., Bartram, C. I., Atkin, W. 2005, 'CT colonography in the detection of colorectal polyps and cancer: systematic review, meta-analysis, and proposed minimum data set for study level reporting', *Radiology*, 237 (3), 893-904.

Hara, A. K., Johnson, C. D., MacCarty, R. L., Welch, T. J., McCollough, C. H., Harmsen, W. S. 2001, 'CT colonography: single- versus multi-detector row imaging', *Radiology*, 219 (2), 461-465.

Health Technology Advisory Committee, 2002. *Computed Tomographic Colonography (Virtual Colonoscopy)* [Internet], Minnesota Department of Health. Available at: http://www.health.state.mn.us/htac/colon.htm [Accessed on 6 June 2005].

Hoppe, H., Netzer, P., Spreng, A., Quattropani, C., Mattich, J., Dinkel, H. P. 2004, 'Prospective comparison of contrast enhanced CT colonography and conventional colonoscopy for detection of colorectal neoplasms in a single institutional study using second-look colonoscopy with discrepant results', *American Journal of Gastroenterology*, 99 (10), 1924-1935.

Iannaccone, R., Laghi, A., Catalano, C., Mangiapane, F., Piacentini, F., Passariello, R. 2003, 'Feasibility of ultra-low-dose multislice CT colonography for the detection of colorectal lesions: preliminary experience', *European Radiology*, 13 (6), 1297-1302.

Institute for Clinical Systems Improvement, 2004. *Computed Tomographic Colonography for Detection of Colorectal Polyps and Neoplasms. Technology Assessment Report* [Internet]. Available at: http://www.icsi.org/index.asp [Accessed on 6 June 2005].

Interventional Procedures Advisory Committee (IPAC), 2004. *Interventional procedures consultation document - Computed tomographic colonography (virtual colonoscopy)* [Internet]. National Institute for Clinical Excellence. Available at: http://www.nice.org.uk/page.aspx?o=233209 [Accessed on 6 June 2005].

Johnson, C. D., MacCarty, R. L., Welch, T. J., Wilson, L. A., Harmsen, W. S., Ilstrup, D. M., Ahlquist, D. A. 2004, 'Comparison of the relative sensitivity of CT colonography and double-contrast barium enema for screen detection of colorectal polyps', *Clinical Gastroenterology & Hepatology*, 2 (4), 314-321.

Johnson, C. D., Toledano, A. Y., Herman, B. A., Dachman, A. H., McFarland, E. G., Barish, M. A., Brink, J. A., Ernst, R. D., Fletcher, J. G., Halvorsen, R. A. J., Hara, A. K., Hopper, K. D., Koehler, R. E., Lu, D. S., Macari, M., MacCarty, R. L., Miller, F. H., Morrin, M., Paulson, E. K., Yee, J., Zalis, M., American College of Radiology Imaging Network 2003, 'Computerized tomographic colonography: performance evaluation in a retrospective multicenter setting, *Gastroenterology*, 125 (3), 688-695.

Iannaccone, R., Bria, E., Carbone, I., Trasatti, L., Piacentini, F., Lauro, S., Vecchione, A., Passariello, R. 2003, 'Contrast-enhanced computed tomographic colonography in the follow-up of colorectal cancer patients: a feasibility study', *European Radiology*, 13 (4), 883-889.

Iannaccone, R., Carbone, I., Catalano, C., Panebianco, V., Di Giulio, E., Schillaci, A., Passariello, R. 2002, 'Computed tomographic colonography (virtual colonoscopy): blinded prospective comparison with conventional colonoscopy for the detection of colorectal neoplasia', *Endoscopy*, 34 (6), 441-446.

Macari, M., Bini, E. J., Xue, X., Milano, A., Katz, S. S., Resnick, D., Chandarana, H., Krinsky, G., Klingenbeck, K., Marshall, C. H., Megibow, A. J. 2002, 'Colorectal neoplasms: prospective comparison of thin-section low-dose multi-detector row CT colonography and conventional colonoscopy for detection', *Radiology*, 224 (2), 383-392.

Medical Services Advisory Committee, 2002. Horizon Scanning 001: Virtual Colonoscopy. Department of Health and Ageing, Canberra.

Morrin, M. M., Farrell, R. J., Kruskal, J. B., Reynolds, K., McGee, J. B., Raptopoulos, V. 2000, 'Utility of intravenously administered contrast material at CT colonography', *Radiology*, 217 (3), 765-771.

Mulhall, B. P., Veerappan, G. R., Jackson, J. L. 2005, 'Meta-analysis: computed tomographic colonography', *Annals of Internal Medicine*, 142 (8), 635-650.

Munikrishnan, V., Gillams, A. R., Lees, W. R., Vaizey, C. J., Boulos, P. B. 2003, 'Prospective study comparing multislice CT colonography with colonoscopy in the detection of colorectal cancer and polyps', *Diseases of the Colon & Rectum*, 46 (10), 1384-1390.

Ristvedt, S. L., McFarland, E. G., Weinstock, L. B., Thyssen, E. P. 2003, 'Patient preferences for CT colonography, conventional colonoscopy, and bowel preparation', *American Journal of Gastroenterology*, 98 (3), 578-585.

Rockey, D. C., Paulson, E., Niedzwiecki, D., Davis, W., Bosworth, H. B., Sanders, L., Yee, J., Henderson, J., Hatten, P., Burdick, S., Sanyal, A., Rubin, D. T., Sterling, M., Akerkar, G., Bhutani, M. S., Binmoeller, K., Garvie, J., Bini, E. J., McQuaid, K., Foster, W. L., Thompson, W. M., Dachman, A., Halvorsen, R. 2005, 'Analysis of air contrast barium enema, computed tomographic colonography, and colonoscopy: prospective comparison ', *Lancet*, 365 (9456), 305-311.

Rottgen, R., Fischbach, F., Plotkin, M., Herzog, H., Freund, T., Schroder, R. J., Felix, R. 2005, 'Colon dissection: a new three-dimensional reconstruction tool for computed tomography colonography', *Acta Radiologica*, 46 (3), 222-226.

Sosna, J., Morrin, M. M., Kruskal, J. B., Lavin, P. T., Rosen, M. P., Raptopoulos, V. 2003, 'CT colonography of colorectal polyps: a metaanalysis', *AJR*, American Journal of Roentgenology, 181 (6), 1593-1598.

Svensson, M. H., Svensson, E., Lasson, A., Hellstrom, M. 2002, 'Patient acceptance of CT colonography and conventional colonoscopy: prospective comparative study in patients with or suspected of having colorectal disease', *Radiology*, 222 (2), 337-345.

Taylor, S. A., Halligan, S., Burling, D., Bassett, P., Bartram, C. I. 2005, 'Intra-individual comparison of patient acceptability of multidetector-row CT colonography and double-contrast barium enema', *Clinical Radiology*, 60 (2), 207-214.

Taylor, S. A., Halligan, S., O'Donnell, C., Morley, S., Mistry, H., Saunders, B. P., Vance, M., Bassett, P., Windsor, A., Stern, Y., Bethel, H., Atkin, W., Bartram, C. I. 2003, 'Cardiovascular effects at multi-detector row CT colonography compared with those at conventional endoscopy of the colon', *Radiology*, 229 (3), 782-790.

Taylor, S. A., Halligan, S., Saunders, B. P., Bassett, P., Vance, M., Bartram, C. I. 2003, 'Acceptance by patients of multidetector CT colonography compared with barium enema examinations, flexible sigmoidoscopy, and colonoscopy', *American Journal of Roentgenology*, 181 (4), 913-921.

Taylor, S. A., Halligan, S., Saunders, B. P., Morley, S., Riesewyk, C., Atkin, W., Bartram, C. I. 2003, 'Use of multidetector-row CT colonography for detection of colorectal neoplasia in patients referred via the Department of Health "2-Week-wait" initiative', *Clinical Radiology*, 58 (11), 855-861.

Technology Evaluation Centre, Blue Cross and Blue Shield Association, 2004. '*CT Colonography ("Virtual Colonography") for Colon Cancer Screening*'. Assessment Program, 19 (6) Available at: http://www.bcbs.com/tec/vol19/19_06.html [Accessed on 6 June 2005].

The Medical Advisory Secretariat, 2003. *Computed Tomographic Colonography [Virtual Colonoscopy] Health Technology Literature Review*, Ministry of Health and Long-Term Care, Ontario, Canada.

Thomeer, M., Bielen, D., Vanbeckevoort, D., Dymarkowski, S., Gevers, A., Rutgeerts, P., Hiele, M., Van Cutsem, E., Marchal, G. 2002, 'Patient acceptance for CT colonography: what is the real issue?', *European Radiology*, 12 (6), 1410-1415.

van Gelder, R. E., Birnie, E., Florie, J., Schutter, M. P., Bartelsman, J. F., Snel, P., Lameris, J. S., Bonsel, G. J., Stoker, J. 2004, 'CT colonography and colonoscopy: assessment of patient preference in a 5-week follow-up study', *Radiology*, 233 (2), 328-337.

van Gelder, R. E., Nio, C. Y., Florie, J., Bartelsman, J. F., Snel, P., De Jager, S. W., Van Deventer, S. J., Lameris, J. S., Bossuyt, P. M. M., Stoker, J. 2004, 'Computed tomographic colonography compared with colonoscopy in patients at increased risk for colorectal cancer', *Gastroenterology*, 127 (1), 41-48.

van Gelder, R. E., Venema, H. W., Serlie, I. W. O., Nio, C. Y., Determann, R. M., Tipker, C. A., Vos, F. M., Glas, A. S., Bartelsman, J. F. W., Bossuyt, P. M. M., Lameris, J. S., Stoker, J. 2002, 'CT colonography at different radiation dose levels: feasibility of dose reduction', *Radiology*, 224 (1), 25-33.

Vogt, C., Cohnen, M., Beck, A., vom Dahl, S., Aurich, V., Modder, U., Haussinger, D. 2004, 'Detection of colorectal polyps by multislice CT colonography with ultra-low-dose technique: comparison with high-resolution videocolonoscopy', *Gastrointestinal Endoscopy*, 60 (2), 201-209.

Studies included from the DCBE search:

de Zwart, I. M., Griffioen, G., Shaw, M. P., Lamers, C. B., de Roos, A. 2001, 'Barium enema and endoscopy for the detection of colorectal neoplasia: sensitivity, specificity, complications and its determinants', *Clinical Radiology*, 56 (5), 401-409.

Durdey, P., Weston, P. M., Williams, N. S. 1987, 'Colonoscopy or barium enema as initial investigation of colonic disease', *Lancet*, 2 (8558), 549-551.

Irvine, E. J., O'Connor, J., Frost, R. A., Shorvon, P., Somers, S., Stevenson, G. W., Hunt, R. H. 1988, 'Prospective comparison of double contrast barium enema plus flexible sigmoidoscopy v colonoscopy in rectal bleeding: barium enema v colonoscopy in rectal bleeding', *Gut*, 29 (9), 1188-1193.

Rockey, D. C., Koch, J., Yee, J., McQuaid, K. R., Halvorsen, R. A. 2004, 'Prospective comparison of air-contrast barium enema and colonoscopy in patients with fecal occult blood: a pilot study', *Gastrointestinal Endoscopy*, 60 (6), 953-958.

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Table 50   HTA reviews of CTC

Author, year & country	Objective	Inclusion and quality criteria	Quality assessment of review	
BlueCross BlueShield Association 2004 USA	To assess the effectiveness of CTC versus colonoscopy as a screening test for colorectal cancer.	**Study design:** prospective study, $n \geq 50$ **Population:** not specified **Interventions:** CTC **Comparators:** not specified **Reference standard:** colonoscopy **Outcomes:** effectiveness (diagnostic performance+health outcomes) **Quality criteria:** not reported **Methods:** Search described, but no details on selection, number of reviewers, quality assessment or data extraction provided.	Were inclusion/exclusion criteria reported that addressed the review question? Was the search adequate? Was the validity of the included studies assessed? Are sufficient details about the individual included studies presented?	YES YES NO YES
	Results: 11 clinical studies were included, one of asymptomatic average risk patients, the others of high-risk, followup- and/or symptomatic patients. **Conclusions:** • The evidence does not allow conclusions on the comparative efficacy of CTC and colonoscopy, or on the effect of CTC in improving health outcomes. • CTC fails to meet criteria to be accepted as screening test as alternative to colonoscopy			
Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 2004 Canada	To conduct a pre-assessment of CTC versus conventional technologies that image the colon.	**Study design:** controlled trials/comparative studies **Population:** not specified **Interventions:** CTC **Comparators:** conventional technologies **Outcomes:** not specified **Quality criteria:** not reported **Methods:** Search described, but no details on selection, number of reviewers, quality assessment, data extraction provided.	Were inclusion/exclusion criteria reported that addressed the review question? Was the search adequate? Was the validity of the included studies assessed? Are sufficient details about the individual included studies presented?	NO YES NO NO
	Results: 17 studies were included (2 systematic reviews/meta-analysis, 8 diagnostic accuracy studies, 2 cost- or cost-effectiveness studies, 5 studies on patient acceptance). Patient population assessed is mixed patient group **Conclusion:** because review is undertaken in Ontario, CCOHTA will not assess CTC at this time			

Author, year & country	Objective	Inclusion and quality criteria	Quality assessment of review	
National Institute of Clinical Excellence,, Interventional Procedures Advisory Committee (IPAC) 2004 UK	To conduct a rapid review (no definitive assessment) of safety and efficacy of CTC, to assist members of IPAC (Interventional procedures overview)	**Study design:** clinical studies included **Population:** diagnosis, (average and high-risk) screening population **Interventions:** CTC **Comparators:** not specified **Outcomes:** Safety and/or efficacy **Quality criteria:** not specified **Methods:** Search and selection, described, but no details on number of reviewers, quality assessment, data extraction provided.	Were inclusion/exclusion criteria reported that addressed the review question?	YES
			Was the search adequate?	YES
			Was the validity of the included studies assessed?	NO
			Are sufficient details about the individual included studies presented?	YES
Results: 7 studies were included (one systematic review with meta-analysis of 14 studies, 2 HTA reports, 4 clinical studies). One of the studies reports on the use of CTC in diagnosis, all others in screening (3 in high-risk patients) All but two studies used colonoscopy as comparator; one study compared CTC with DCBE, another one CTC and colonoscopy with CTC and DCBE. **Conclusion** from separate "interventional procedures consultation document": Current evidence on safety and efficacy of CTC seems adequate to support the use of the procedure, provided that normal arrangements for consent, audit, clinical governance are in place.				
Technology Assessment Committee, Institute for Clinical Systems Improvement 2004 USA	To assess the safety and efficacy of CTC for detection of colorectal polyps and neoplasms.	**Study design:** not specified **Population:** not specified **Interventions:** CTC **Comparators:** not specified **Outcomes:** not specified **Quality criteria:** evidence grading system based on classes of research reports **Methods:** Search and selection, described, but no details on number of reviewers, quality assessment, data extraction provided.	Were inclusion/exclusion criteria reported that addressed the review question?	NO
			Was the search adequate?	YES
			Was the validity of the included studies assessed?	NO
			Are sufficient details about the individual included studies presented?	YES

Author, year & country	Objective	Inclusion and quality criteria	Quality assessment of review
	Results: 22 studies were reviewed. These included average risk, high-risk and symptomatic patients. 16 studies investigated accuracy (1 meta-analysis), 1 extracolonic findings, 2 patient outcomes and 3 were cost-effectiveness studies (1 systematic review in screening, only one study examined cost-effectiveness of CTC) **Conclusions:** • CTC is a safe procedure with minor side effects. • CTC is potentially useful for patients unwilling to undergo conventional colonoscopy or other procedures, who have failed conventional colonoscopy (incomplete examination), or who cannot be sedated. • CTC seems superior to no examination, fecal occult blood test, DCBE and flexible sigmoidoscopy, but it is unclear how CTC compares with conventional colonoscopy in a screening population.		
Medical Services Advisory Secretariat 2003 Ontario, Canada	To assess the safety and effectiveness of CTC versus colonoscopy as a screening test for colon cancer and polyps.	**Study design:** studies addressing technical, educational, and other aspects of CTC excluded **Population:** diagnosis or screening population, n > 30 **Interventions:** CTC **Comparators:** Conventional colonoscopy **Outcomes:** safety and effectiveness **Quality criteria:** Levels of evidence assigned according to Goodman's (1985) hierarchy. **Methods:** Search, selection, quality assessment described, but no details on number of reviewers or data extraction provided.	Were inclusion/exclusion criteria reported that addressed the review question? YES Was the search adequate? YES Was the validity of the included studies assessed? YES Are sufficient details about the individual included studies presented? YES
	Results: 18 clinical studies were included. Two of the studies included asymptomatic patients (6% of population), one included symptomatic patients only, most studies were in a mixed high-risk asymptomatic and symptomatic population (with personal or family history). Subgroup analyses to investigate the variability of results were conducted. Results varied when looking at earlier vs recent studies, multi-slice vs single-slice scanning, dual vs supine positioning and radiologist's experience. For detection of cancer: CTC sensitivity 25-100%, CTC specificity 74-100% (12 studies). **Conclusions:** • CTC cannot be recommended for population-based colorectal cancer screening nor for screening of patients with colonic symptoms or a personal/family history of polyps. • CTC equivalent to DCBE for detection of lesions greater than 5 mm in patients with incomplete colonoscopy. • CTC can be considered: for preoperative evaluation of CRCs; for diagnosis in patients where colonoscopy is clinically contraindicated; or for patients who had incomplete colonoscopy because of stenosis or obstruction of the colon.		

Author, year & country	Objective	Inclusion and quality criteria	Quality assessment of review
Health Technology Advisory Committee 2002 Minnesota, USA	To assess CTC as an emerging technology for colorectal cancer screening	**Study design:** not specified **Population:** not specified **Interventions:** CTC **Comparators:** not specified **Outcomes:** not specified **Quality criteria:** not specified **Methods:** Search strategy reported, selection, number of reviewers, data extraction, quality assessment not reported	Were inclusion/exclusion criteria reported that addressed the review question?　　NO Was the search adequate?　　YES Was the validity of the included studies assessed?　　NO Are sufficient details about the individual included studies presented?　　YES
Results: 17 clinical studies were reviewed. Most of these included high-risk or symptomatic patients. 10 studies investigated accuracy (7 of these were tabulated for sens/spec of 10 mm, 5 mm, < 5 mm), 1 extracolonic findings, 4 patient outcomes and 2 were cost-effectiveness studies (only one examined CE of CTC). **Conclusions:** • CTC is a safe procedure • CTC was found useful in patients unable to complete colonoscopy or DCBE, at increased risk of perforation, for viewing extracolonic tissues and organs, for preoperative colorectal cancer staging. • One CE-study of CTC was reviewed that found that CTC is not cost-effective compared to colonoscopy in a screening population. • CTC should not be recommended as a screening tool at this stage.			
Medical Services Advisory Committee 2001 Australia	To assess the current state of development of CTC, present use and potential application.	**Study design:** not specified **Population:** diagnosis or screening population **Interventions:** CTC **Comparators:** not specified **Outcomes:** Accuracy of lesions >/< 10 mm **Quality criteria:** not specified **Methods:** Search and selection described, but number of reviewers, data extraction, quality assessment not reported	Were inclusion/exclusion criteria reported that addressed the review question?　　YES Was the search adequate?　　YES Was the validity of the included studies assessed?　　NO Are sufficient details about the individual included studies presented?　　NO

Author, year & country	Objective	Inclusion and quality criteria	Quality assessment of review
	Results: 19 studies were included (15 clinical studies, 2 HTAs, 1 horizon scanning). No details on patient population provided **Conclusions:** • When used in diagnosing colorectal cancer, CTC appears to be safe, evidence about patient tolerance not consistent • CTC is an appropriate test in the following clinical situations: rectal bleeding where conventional colonoscopy is contraindicated, in patients who are unfit for sedation, where preceding conventional colonoscopy was incomplete or difficult and in patients with a nontraversable stricture due to diverticular disease or malignancy, obstructed colon, megacolon or fistulous disease. • CTC as a screening tool has not yet been adequately evaluated.		

Table 51   Systematic reviews/meta-analyses of CTC

Author, year & country	Study question	Inclusion and quality criteria	Quality assessment of review
Halligan et al 2005 U.K.	To assess the methodological quality of available data in published reports of CTC by performing systematic review and meta-analysis.	**Study design:** studies with focus on detection of colorectal polyps, full reports with original data, peer-reviewed Published: 1994 – December 2003 **Population:** n $\geq$ 30, excluded studies that selected patients with a known high prevalence of abnormality (eg prior positive test), excluded studies if $\geq$ 50% patients underwent CTC because of incomplete colonoscopy. **Intervention:** CTC with full bowel preparation, double imaging, helical scanners, no IV contrast material routinely, software commercially available **Ref Standard:** conventional endoscopy or surgical findings **Outcomes:** not specified **Quality criteria:** six criteria specified for technical aspects of CTC and reference test based on STARD criteria and QUADAS tool. **Methods:** Search, selection, data extraction, reviewers and quality assessment (QUADAS tool) described.	HIGH QUALITY Were inclusion/exclusion criteria reported that addressed the review question? YES Was the search adequate? YES Was the validity of the included studies assessed? YES Are sufficient details about the individual included studies presented? YES

Results:

24 studies were included (4,181 patients).

Prevalence of abnormality 15-72%. 23 of these studies included symptomatic/high-risk asymptomatic patients, one in average risk patients only

Mean age: not reported

Pooled per-patient sensitivity:

Cancer (not pooled, but treated as from one study): 96% (91%-99%)

Polyps 10 mm or larger: 93% (73-98%); polyps 6-9 mm: 86% (75-93%); 5 mm or smaller: not pooled, studies were heterogeneous

Pooled per-patient specificity:

Polyps larger than 10 mm: 97% (95-99%); polyps 6-9 mm: 86% (76-93%); 5 mm or smaller: not pooled, studies were heterogeneous

Pooled per-polyp sensitivity:

Polyps 10 mm or larger: 77% (70-83%); polyps 6-9 mm: 70% (63-76%); 5 mm or smaller: not pooled, studies were heterogeneous

Conclusions:
- CTC seems sufficiently sensitive and specific in the detection of large and medium polyps and is especially sensitive in the detection of symptomatic cancer.
- Studies are poorly reported and a minimum data set for study reporting is proposed

Author, year & country	Study question	Inclusion and quality criteria	Quality assessment of review
Mulhall et al 2005 USA	To assess the test performance of CTC versus colonoscopy or surgery and to assess variables that may affect test outcome (Meta-analysis)	**Study design:** prospective, blinded Published: 1975 – February 2005 **Population:** adult patients undergoing CTC with full colorectal preparation, followed by complete colonoscopy or surgery, colon insufflation by air or carbon dioxide, both 2D and 3D, slice thickness ≥ 5 mm, at least a single-detector helical CT **Intervention:** CTC **Ref Standard:** complete colonoscopy or surgery **Outcomes:** Sensitivity/Specificity of all polyps or > 9/6-9 mm/ < 6 mm in size, on per-patient/per-polyp basis **Quality criteria:** disease severity & prevalence, prospective study design, relevant clinical sample, consecutive patients, performance and interpretation of CTC and reference test. **Methods:** Search, selection, data extraction, reviewers, quality assessment described	HIGH QUALITY Were inclusion/exclusion criteria reported that addressed the review question? YES Was the search adequate? YES Was the validity of the included studies assessed? YES Are sufficient details about the individual included studies presented? YES

Results:

33 studies were included (6,393 patients).

Mean age: 61.9 years.

Patient group: 23 studies (74% of patients) in high-risk populations (includes symptomatic, family history, surveillance), 3 studies in average risk patiens only, 7 studies in mixed high-risk/low-risk populations.

16 of included studies used single-slice scanning, 13 used multi-slice and four studies used both single- and multi-slice scanning.

Pooled per-patient sensitivity:

Overall: 70% (53-87%)

Polyps > 9 mm: 85% (79-91%); polyps 6-9 mm: 70% (55-84%); < 6 mm: 48% (25-70%)

Statistical heterogeneity (p < 0.001) – mainly between-study heterogeneity;

Slice thickness, type of scanner, type of imaging could partly explain heterogeneity, but not eg patient characteristics

Pooled per-patient specificity:

Overall: 86% (84-88%)

Polyps > 9 mm: 97% (96-97%); polyps 6-9 mm: 93% (91-95%); < 6 mm: 91% (89-95%)

Statistically homogeneous

Conclusions:

- CTC is highly specific, but reported sensitivities vary widely, even for larger polyps

- Variability could not be clearly explained in meta-analysis

- CTC needs further refinement before it can be recommended for general use in screening for colorectal cancer

Author, year & country	Study question	Inclusion and quality criteria	Quality assessment of review
Sosna et al 2003 USA	To assess the accuracy of CTC versus colonoscopy for detecting colorectal polyps (Meta-analysis)	**Study design:** prospective studies, blinded to colonoscopy Result Published: 1994 – July 2002 **Population:** patients undergoing CTC with full colorectal preparation, evaluation of entire colon, dual positioning, both 2D and 3D, slice thickness $\geq$ 5 mm, at least a single-detector helical CT **Intervention:** CTC **Ref Standard:** complete colonoscpoy **Outcomes:** Sensitivity/Specificity of all polyps or 10 mm / 5 mm / < 5 mm in size, on per-patient/per-polyp basis **Quality criteria:** not specified **Methods:** Search, selection, data extraction, reviewers described, no details on quality assessment of studies.	FAIR QUALITY Were inclusion/exclusion criteria reported that addressed the review question?　YES Was the search adequate?　YES Was the validity of the included studies assessed?　NO Are sufficient details about the individual included studies presented?　NO

Results:

14 studies were included (1,324 patients).

Mean age: not reported

Twelve of these studies were in high-risk patients, two in low-risk patients

Pooled per-patient sensitivity:

Polyps 10 mm or larger: 88% (84-93%); polyps 6-9 mm: 84% (80-89%); 5 mm or smaller: 65% (57-73%)

Pooled per-patient specificity:

Polyps larger than 10 mm: 95% (94-97%)

Pooled per-polyp sensitivity:

Polyps 10 mm or larger: 81% (76-85%); polyps 6-9 mm: 62% (58-67%); 5 mm or smaller: 43% (39-47%)

Conclusions:

- CTC is accurate tool for detecting clinically important colorectal polyps (polyps 10 mm or larger)
- The extrapolation of results to screening populations needs to await larger-scale studies

Table 52   Systematic reviews/meta-analyses of DCBE versus colonoscopy

Author, year & country	Study question	Inclusion and quality criteria	Quality assessment of review
De Zwart et al 2001 The Netherlands	To analyse sensitivity, specificity and complication rate of colonoscopy and barium enema for the detection of colorectal neoplasia (systematic review)	**Study design:** not specified **Population:** not specified **Interventions:** DCBE, colonoscopy **Ref Standard:** not specified **Outcomes:** Sensitivity and specificity for polyps of different sizes, complication rates **Quality criteria: selection, verificiation and reference standard** bias assessed **Methods:** Search described, but no details on selection, data extraction, reviewers or quality assessment of studies.	LOW QUALITY Were inclusion/exclusion criteria reported that addressed the review question? YES Was the search adequate? YES Was the validity of the included studies assessed? YES, but case referent and retrospective studies included Are sufficient details about the individual included studies presented? NO

Results:

Overall, 28 studies were included: 25 studies of DCBE accuracy and 16 studies of endoscopic colonoscopy accuracy, 13 studies assessed both DCBE and endoscopic colonoscopy accuracy.

DCBE:

25 studies assessing the sensitivity (and specificity (4 studies)) of DCBE for detection of colorectal polyps (16 studies) and/or carcinomas (15 studies) were included. All of these studies were in high-risk, symptomatic populations.

Sensitivity: Polyps > 1 cm: 48 – 100%; polyps < 1 cm: 53-96%; CRC: 62-100%

Specificity: all sizes: 67-85%

Caecum reached in 95% of all colonoscopies

Very small risk of complications, mostly due to use of rectal retention balloons which can cause perforation at insertion, or by overinflation, in 0.0001-0.004% of all cases

Endoscopic colonoscopy:

16 studies assessing the sensitivity (and specificity (3 studies) of endoscopic colonoscopy for detection of colorectal polyps (11 studies) and/or carcinomas (9 studies) were included. All of these studies were in high-risk, symptomatic populations.

Sensitivity: Polyps > 1 cm: 79% – 100%; polyps < 1 cm: 75%-85%; CRC: 79-100%

Specificity: all sizes: 78-99%

Caecum reached in 54-98% of all colonoscopies

Complications usually related to sedation (0.2-0.5%). Perforation (0.08%) and cardiac complications are mentioned, but these are rare.

Conclusion:

- Barium enema has a lower complication rate than endoscopy.
- In high-risk populations, endoscopic colonoscopy is the examination of choice for the detection of colorectal polyps and cancer, due to its superior sensitivity and therapeutic options, as compared to DCBE.
- It is not clear which examination should be preferred for screening of average-risk, asymptomatic populations.

Table 53   Summary of study characteristics and quality appraisal of accuracy studies CTC versus DCBE and versus colonoscopy

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test and comparator	Study quality, applicability and comparison
Rockey et al 2005 USA	II	**Objective:** To compare the accuracy of CTC, DCBE and colonoscopy for detection of large colon polyps and cancers in patients at high risk for colorectal neoplasia. **Patient enrolment:** Dec 2000 – Feb 2004, multi-centre study. **Endpoints:** Sensitivity per lesion/patient/histology, specificity per patient. **Reference standard:** • Initial colonoscopy (comparator) • segmental unblinding and second-look colonoscopy if discrepant result on initial colonoscopy • Ref standard established by reconciliation of all tests; repeat blind review of DCBE/CTC if lesion > 6 mm on CTC/DCBE not found on colonoscopy; repeat all 3 tests if discordant results after repeat blind review. **Comparison of CTC/DCBE detected lesion with Ref standard:** same lesion if within one of six colon segments and within 50% of size of lesion identified by colonoscopy	**n = 614** **Exclusions:** • 161 of 775 enrolled excluded (21%) • Exclusions due to test failures: 18/775 (2%) **Male:** 70% **Mean age** (SD): 57 (10) yrs **Inclusion criteria:*** • ≥ 1 positive FOBT (38%) • ≥ 1 episodes of rectal bleeding (42%) • iron-deficiency anaemia (8%) • family history of colon cancer or adenoma (32%) **Exclusion criteria:** • active gastrointestinal haemorrhage, previous colon surgery, normal colonoscopy within the previous 2 years, known IBD • test contraindications * Subjects could meet more than 1 inclusion criterion	**CTC** *Scanning:* Supine and prone positioning; 4-slice or 8-slice MDCT scanners; Other parameters: slice thickness: 2.5 mm; reconstruction int.: 1 mm; table speed: 7.5-15 mm/s *Imaging:* primary 2D reading with 3D problem-solving **DCBE** *Imaging:* high-density barium (100% w/v); Spot films of all colon segments+ overhead radiographs in prone 35 degrees angled, supine, left and right lateral decubitus, and left lateral positions with the rectal tube. *Diagnostic Review:* reading by experienced radiologist (CTC: > 50 cases read or prior training module; DCBE: 19 yrs)	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC/DCBE appropriately described • Definition of true match given **Presentation of results:** • Reasons for exclusions reported • Test failures excluded • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Appropriate CTC techniques **COMPARISON:** • Direct comparison with colonoscopy and DCBE

Table 54   Summary of study characteristics and quality appraisal of accuracy studies of CTC versus DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test and comparator	Study quality, applicability and comparison
Johnson et al 2004 USA	III-2	**Objectives:** (1) To compare the accuracy of CTC with DCBE for the detection of colorectal polyps in asymptomatic low-prevalence population and (2) to assess the value of double reading of CTC. **Patient enrolment:** Prospective, Jan 1998 – Feb 2001, single-centre outpatients prescheduled for DCBE **Endpoints:** Sensitivity per lesion/patient; Specificity per patient, double-read CTC of lesions ≥ 5 mm **Reference standard:** Endoscopy (colonoscopy (17%), flexible sigmoidoscopy (to confirm polyps in rectum, sigmoid, descending colon) (84%), or proctoscopy (to confirm rectal polyps) (13%) +/- histopathology, or surgery (0.4%) **Comparison of CTC/DCBE detected lesion with Ref standard:** Same lesion if similar size and within one of eight colon segments of lesion identified on ref standard	**n = 691** **Exclusions:** 146 of 837 enrolled excluded (17%). These patients did not have reference standard but reasons n.r. **Male:** 51% **Mean age** (SD/range): 63.4 (7.2/50-86) yrs **Inclusion criteria:** • Prior history of colorectal neoplasia (33%) OR • First-degree family member with a history of colorectal cancer (64%) OR • New onset of asymptomatic iron-deficiency anemia (3%) AND • 50 years or older **Exclusion criteria**: Melena, hematochezia, IBD, familial polyposis	**CTC:** *Additional preparation:* 1 mg glucagon in 89% of patients *Scanning:* supine and prone; Single-slice (12%) or 4-slice helical CT scanner (88%); Other parameters*: slice thickness: 5 mm; reconstruction int.: 3 mm; table speed: 15 mm/s (6.5 mm/pitch of 1.3), 80 mA (70), 120 kV (p), 0.7-second rotation time (1s) *Imaging:* primary 2D (axial) reading; suspected abnormalities evaluated further with multiplanar reformatted images and 3-dimensional endoluminal images *Diagnostic Review:* individual and double reading by 3 experienced radiologists (>150 CTC interpretations) **DCBE:** performed according to Standard of American College of Radiology *Imaging:* high-density barium (80% w/v); fluoroscopic guidance spot films of rectum, sigmoid, both colonic flexures, and caecum; + overhead radiographs in prone and supine views *Diagnostic Review:* individual reading by one of 3 experienced radiologists (> 10 yrs experience) * values for multi-slice scanning (differing single-slice values in brackets)	**LOW QUALITY** **Patient selection:** • Selection criteria clearly described • Representative sample - prospective, consecutive **Reference Standard:** • Reference standard not valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received a reference standard but selection of type of reference standard depended on index test results • Blinding of colonoscopy to CTC/DCBE results: n.r. **Test and its interpretation:** • Blinding of CTC/DCBE to colonoscopy results • CTC/DCBE appropriately described • Definition of true match given **Presentation of results:** • Reasons for exclusions not reported • No excluded test failures reported • 2 × 2 table not reconstructable **APPLICABILITY:** • Relevant patient spectrum • 12% of patients single-slice CTC only **COMPARISON:** • No comparison with colonoscopy • Comparison with DCBE

Table 55   Summary of study characteristics and quality appraisal of accuracy studies of CTC compared to colonoscopy

Author, Year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Cotton et al 2004 USA and UK	II	**Objectives:** To compare CTC versus colonoscopy for: • test accuracy • patient preferences To assess the association between CTC accuracy and reader experience. **Patient enrolment:** Prospective, consecutive, Apr 2000-Oct 2001, Multi-centre (8 US, 1 UK centres). **Endpoints:** Sensitivity and specificity of CTC and colonoscopy for the detection of lesions: ≥ 10 mm, ≥ 6 mm, 6-9 mm, 1-5 mm, Patient preferences **Reference standard:** • Colonoscopy (comparator) +/- histopathology • Segmental unblinding and second-look colonoscopy if discrepant results • Results of additional diagnostic tests performed at a later date when clinically indicated **Comparison of CTC detected lesion with ref standard:** Same lesion if detected lesion located in same or adjacent segments of colon and sizes agreed within 50%.	**n = 600** **Exclusions:** 15 of 615 excluded (2.4%) due to CTC not performed (12), and/or colonoscopy not performed (13). Reasons not reported. **Male:** 45% **Mean age** (SD): 61 (8.34) yrs **Inclusion criteria:** clinically indicated colonoscopy: • symptoms (overt or occult rectal bleeding, change in stool habit, abdominal pain) (86.5%) • surveillance after polypectomy (13.5%) **Exclusion criteria:** • Screening patients • colonoscopy within 3 years	**CTC:** *Preparation:* standard *Scanning:* prone and supine positioning; 2-section and 4-section CT scanner; Other parameters: slice width: 2.5/5 mm; table feed: 8 mm/s, 120 kVp; reconstruction increment: 1.5/1.0 mm *Imaging:* 2D slices, and when necessary by focal 3D snapshot reconstructions; independent 3-D fly through evaluation at later stage *Diagnostic Review:* individual reading by radiologist (having performed at least 10 CTC procedures and five recorded procedures checked for quality)	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Representative sample - prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • Reasons for exclusions reported, but unclear • Unclear if test failures excluded • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Radiologists with experience in at least 10 prior CTC **COMPARISON:** • Comparison with colonoscopy • No comparison with DCBE

Author, Year & setting	Level of evidence	Study objective,design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Ginnerup Pedersen et al 2003 Denmark	II/III-1 (if sample representative/not representative)	**Objective:** to assess multi-detector-array CTC accuracy versus colonoscopy for the detection of lesions ≥ 6 mm. **Patient enrolment:** n.r., single-centre **Endpoints:** CTC Sensitivity and specificity, colonoscopy sensitivity Quality of examinations (bowel preparation, colonic distension) **Reference standard:** • Colonoscopy (comparator) +/- histopathology • Second-look colonoscopy if discordant findings at original colonoscopy • Repeat colonoscopy or DCBE if incomplete colonoscopy **Comparison of CTC detected lesion with ref standard:** same polyp if CTC polyp in same part of colonic segment, with same morphology and within +/- 2 mm of size of polyp identified at colonoscopy	**n = 148** **Exclusions:** 10 of 158 patients excluded (6.3%) Exclusions due to test failure: 5.1% (8/185) (noncompliance with bowel preparation (3), mechanical difficulties with CT scanner (2), not possible to obtain satisfactory colonic distension at CTC (3)) **Male:** 48% **Median age** (range): 60 (25-86) yrs **Inclusion criteria:** • symptoms (44%) (rectal bleeding (17%); altered bowel habits (14%); abdominal pain (9%); mucus per rectum, weight loss, or anemia (4%); abdominal tumor (0%)) • history of neoplastic polyps or CRC (51%) • CRC, preoperative colonoscopy (5%) **Exclusion criteria:** • Suspicion of active IBD, bowel ischemia; clinical/radiological signs of obstruction; tumour located < 10 cm from anal verge; colostomy; Severe heart, lung, or renal failure, pregnancy • Logistics (paired CTC/colonoscopy could not be arranged)	**CTC:** *Preparation:* included IV glucagon *Scanning:* supine and prone positioning; Multi-slice CT scanner Other parameters: slice thickness: 3.2 (4 x 2.5 mm); increment: 1.6 mm; pitch 1.25; 120 kV; 70 mAs; rotation time: 0.5s *Imaging:* 2D axial and multiplanar reformatted images and 3D endoscopic views for problem-solving *Diagnostic Review:* CTC read by 1 radiologist (experience: ~100 studies read)	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Not clear if representative sample **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • 97% (144/148) of patients received reference standard. 4 patients with incomplete colonsocopy received DCBE as reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results (CTC read prior to colonoscopy) • CTC appropriately described • Definition of true match given **Presentation of results:** • Reasons for exclusions reported • 5% (8/185) exclusions due to test failure • 2 × 2 table reconstructable **APPLICABILITY:** • Patient spectrum 5% patients had known CRC • Patients received IV Glucagon • CTC reviewer had experience in reading ~ 100 CTC **COMPARISON:** • Comparison with colonoscopy sensitivity • No comparison with DCBE

Author, Year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Hoppe et al, 2004, Switzerland	II	**Objective:** to prospectively compare CTC w conventional colonoscopy for detection of colorectal neoplasms **Patient enrolment:** n.r., single centre **Endpoints:** Sensitivity (per-polyp, per patient) and specificity of CTC **Reference standard:** • Conventional colonoscopy (comparator) +/-histopathology • Segmental unblinding: second-look colonoscopy if negative initial CC after positive CTC **Comparison of CTC detected lesion w ref standard:** same polyp if CTC polyp in same or adjacent colonic segment in each study and within 50% of size of polyp on Colonoscopy	**n = 92** **Exclusions:** • 8 of 100 patients excluded (8%) • Exclusions due to test failure: 1 (1%) (Residual stool and fluid) • Exclusions due to failure to complete CC: 6 (6%) (impassable stenosis) **Male (of n=100):** 62% **Mean age** (range): 66 (20-91) yrs **Other characteristics:** Patients not known to have polyps **Inclusion criteria:** Evaluation of symptoms: • Hematochezia OR • Positive hemoccult test • Personal or family history of colonic neoplasms **Exclusion criteria:** n.r.	**CTC:** *Additional preparation:* IV contrast in 68/92 (74%) before supine scan *Scanning:* prone and supine positioning; Four channel multi-detector CT scanner; Other parameters: 4×2 collimation; pitch 1.375; 0.75-second gantry rotation; 120 kV;200 mA; reconstruction: slice width: 2 mm, interval: 1 mm *Imaging:* combination of 2D and 3D reformatted images, 3D virtual endoscopic images reformatted with a surface rendering algorithm, interactive software *Diagnostic Review:* CTC by 3 radiologists, experience: 30-60 studies read	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Representative sample - prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results (CTC read prior to colonoscopy) • CTC appropriately described • Definition of true match given **Presentation of results:** • Reasons for exclusions reported • Exclusions due to test failure • 2×2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • CTC techniques included IV contrast for supine position scans in 68 patients **COMPARISON:** • Direct comparison with colonoscopy • No comparison with DCBE

Author, Year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Taylor et al 2003, UK	II	**Objective:** to assess CTC accuracy as a first-line investigation for those referred under the 2-week-wait initiative* **Patient enrolment:** May 2001 – June 2002, single-centre **Endpoints:** CTC sensitivity and specificity for polyps < 10 mm and > 10 mm + cancer; Presence of diverticular disease **Reference standard:** • Colonoscopy (comparator) +/- histopathology • Second colonoscopy if positive CTC after negative initial colonoscopy • Follow-up (described in results section) **Comparison of CTC detected lesion with ref standard:** • Same polyp if in same segment and if estimated size agreed with colonoscopy size: +/- 90% if polyps < 6 mm; +/- 70% if polyps 6-9 mm; +/- 50% if polyps >= 10 mm • Per-patient analysis: at least one matched polyp per patient on CTC and colonoscopy, or both normal *under "2-week'wait" initiative, UK government proposed that everyone with suspected cancer would be able to see a specialist within 2 weeks of their GP deciding that they should be seen urgently and requesting an appointment	**n = 54** **Exclusions:** No exclusions reported **Male:** 41% **Median age** (range): 69 (42-85) yrs **Other characteristics:** n.r. **Inclusion criteria:** • Rectal bleeding with change in bowel habit (17%) OR • Change of bowel habit and age over 60 (33%) OR • Rectal bleeding w/o anal symptoms and age over 60 (22%) OR • Abdominal mass (4%) OR • Iron deficiency anaemia (7%) • No specified criterion, but referral for CC (17%) **Exclusion criteria:** n.r.	**CTC:** *Preparation:* included buscopan 81% *Scanning:* Supine and prone positioning, Multi-slice (4-detector) scanner Other parameters: 1.25/2.5 mm collimation; pitch: 6; 120 kVp; 50-100 mA; Reconstruction: with half the normal slice thickness *Imaging:* 2D (axial prone and supine; multiplanar reformats) + surface rendered 3-D endoluminal view to confirm abnormalities and problem solving *Diagnostic Review:* CTC assessment by 1 radiologist, level of experience n.r.	**HIGH QUALITY** **Patient selection:** • Eligibility criteria clearly described • Representative sample – consecutive, prospective **Reference standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results Test and its interpretation: • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • No exclusions reported • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • 81% of patients received IV buscopan • Level of CTC reviewer experience n.r. **COMPARISON:** • Comparison with colonoscopy: colonoscopy + additional info on clinical follow-up vs colonoscopy • No comparison with DCBE

Author, Year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Van Gelder et al 2004 Netherlands	III-2/II (if no blinding/blinding of CC to CTC)	**Objective:** To assess CTC accuracy to detect patients with polyps ≥ 10 mm **Patient enrolment:** Oct 2000 – Sep 2002, 2 centres **Endpoints:** • Sensitivity and specificity of CTC for polyps • Cause of false positives, interobserver analysis **Reference standard:** • Colonoscopy (comparator) +/- histopathology • Second-look colonoscopy if large FP polyp (> 10 mm) on CTC (after mean of 13 mo) **Comparison of CTC detected lesion with reference standard:** Per-patient assessment: true-positive CTC if at least one true-positive polyp on CTC in the patient	**n = 249** **Exclusions:** 39 of 288 excluded (14%) Exclusions due to test failures: insufficient bowel preparation (12/4%), CT inadequate (20/7%); unsatisfactory bowel insufflation (8/3%), severe breathing artefacts (3/1%), artefacts due to spondylodesis (2/1%), technical problems during scanning (7/2%) Exclusions due to failed CC: 5/2% (failed to reach caecum) **Male:** 59% **Mean age** (SD): 56 (13) yrs **Other characteristics:** History of mild abdominal symptoms 8% (mild abdominal pain, hematochezia, altered bowel habits) **Inclusion criteria:** • Personal history of colorectal polyps or cancer (64%) • Family history of colorectal polyps or cancer (36%) **Exclusion criteria:** • Age < 18 yrs • Colorectal polyps or cancer diagnosed during recent examination of the colon • Colostomy after colorectal surgery	**CTC:** *Preparation:* included IV buscopan or glucagon *Scanning:* Supine and prone positioning, Multi-slice CT scanner Other parameters: collimation: 4 × 2.5 mm; pitch: 1.25; rotation time: 0.75 s; 120 kV; reconstruction interval: 1.6 mm *Imaging:* 3D display mode, additional 2-D displays for further inspection of suspected lesions. *Diagnostic Review:* CTC assessment independent by 2 radiologists (experience: > 50 CTC evaluations)	**FAIR QUALITY** **Patient selection:** • Eligibility criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results n.r. **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • Exclusions and reasons reported • Exclusions due to test failure • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Patients received muscle relaxant • CTC reviewers had prior experience in > 50 CTC cases **COMPARISON:** • Comparison with colonoscopy: initial+ 2nd-look colonoscopy vs initial colonoscopy • no comparison with DCBE

Table 56   Summary of study characteristics and quality appraisal of studies of CTC accuracy (no comparator)

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Bruzzi et al 2004, Ireland (see also Bruzzi et al 2003: assessed as overlapping study population)	II/III-2 (if blinding/no blinding)	**Objectives:** to assess CTC as a screening test for populations at increased risk of colonic neoplasia using axial image interpretation only **Patient enrolment:** Prospective, single centre, dates n.r. **Endpoints:** CTC sensitivity & specificity for the detection of polyps ≥ 10 mm, 6-9 mm, ≤ 5 mm **Reference standard:** Colonoscopy +/- histopathology **Comparison of CTC detected lesion with ref standard:** Same polyp if of similar size and in same segment as or in contiguous section of adjacent segment to lesion seen on colonoscopy	**n = 82** **Exclusions:** Not completed reference standard 12% (10/82) **Male:** 48% **Mean age** (range): 57 (26-81) yrs Inclusion criteria: • Surveillance following polypectomy of colonic adenomas (41.5%) • History of colon cancer (8.5%) • Strong family history of colon cancer* (50%) **Exclusion criteria**: n.r. *At least one 1st degree relative with a history of colon cancer at age < 60 yrs or two 2nd degree relatives with a history of colon cancer at age < 50 yrs.	**CTC:** *Scanning:* Supine and prone positioning, 4-detector multi-slice CT scanner; Other parameters: collimation: 4 × 2.5 mm; table feed: 12.5 mm/s (pitch of 1.25), 100 mAs, 120 kVp; reconstruction w slice width: 3 mm and increment: 1.5 mm *Imaging:* 2D axial images, 'colon-tracking' technique *Diagnostic Review:* independent reading by 2 radiologists (experience > 50 CTC readings), consensus reading if discrepant	**QUALITY NOT ASSESSABLE (fair or low quality, blinding not reported)** **Patient selection:** • Inclusion criteria clearly described • Not clear if representative sample **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results n.r. **Test and its interpretation:** • Blinding of CTC to colonoscopy results n.r. • CTC appropriately described • Definition of positive test result unclear **Presentation of results:** • Reasons for exclusions reported • No exclusions due to CTC failure • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Nonstandard CTC techniques (axial imaging only) **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Cohnen et al (2004), Germany	II/III-2 (if blinding/no blinding of colonoscopy)	**Objectives:** to assess CTC accuracy using an ultra-low-dose technique. **Patient enrolment:** Prospective, single centre, dates n.r. **Endpoints:** CTC sensitivity & specificity for the detection of polyps ≥ 10 mm, 5-9 mm, < 5 mm **Reference standard:** High-resolution video colonoscopy +/- histopathology (98% of lesions) **Comparison of CTC detected lesion with reference standard:** Same lesion if detected lesion located in same or adjacent segments and size +/- 2 mm of lesion on colonoscopy.	**n = 137** **Exclusions:** None reported **Male:** 56% **Mean age** (SD): 57.1 (11.3) yrs **Inclusion criteria:** • Changing bowel habits (22.6%) • Abdominal pain (31.4%) • Heme-positive stools (19%) • Surveillance after previous polypectomy (27%) **Exclusion criteria:** n.r.	**CTC:** Ultra-low-dose CTC *Scanning:* Supine positioning; 4-detector CT scanner (Somatom Plus 4 Volume Zoom); Tube current at lowest possible: 10 effective mA~40 electric mA Other parameters: detector collimation: 4 × 1 mm; table feed: 8 mm/s, 120 kVp; reconstruction: slice width of 1.25 mm and increment of 0.7 mm *Imaging:* noise-reduction algorithm, 2D multiplanar images and high-resolution interactive real-time 3D simultaneously *Diagnostic Review:* reading by 'experienced' radiologist + gastroenterologist	**FAIR QUALITY** **Patient selection:** • Inclusion criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results n.r. **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • No exclusions reported • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • No standard CTC techniques (ultra-low-dose CTC, supine positioning only) • Level of experience of radiologist n.r. **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Gluecker et al 2002, Switzerland	II/III-1 (if representative/not representative sample)	**Objectives:** to assess CTC accuracy **Patient enrolment:** Prospective, single centre, dates n.r. **Endpoints:** CTC sensitivity per-polyp& specificity per-patient for the detection of polyps ≥ 10 mm, 5-9 mm, < 5 mm **Reference standard:** Colonoscopy +/- histopathology **Comparison of CTC detected lesion with reference standard:** True match of lesion found on CTC according to size only (definition not explicit)	**n = 50** **Exclusions:** 1 of 51 (2%) excluded, due to test failure (Did not follow instructions for bowel preparation) **Male %**: n.r. Age range: 50-75 yrs **Other characteristics:** n.r. **Inclusion criteria:** • History of prior polyps or cancer • Unexplained abdominal pain • Iron deficiency anaemia **Exclusion criteria:** Patient refusal, inability to participate	**CTC** *Preparation:* included IV buscopan *Scanning:* prone and supine positioning; Multi-detector CT scanner; Other parameters: beam collimation 5mm; table feed: 15 mm/s (pitch 3:1), 120 kVp;90 mA; reconstructions: slice thickness 2.5 mm, intervals: 2.0 mm *Imaging:* 2D supine axial images, lesions found re-evaluated on further 2D and 3D reconstructions *Diagnostic Review:* radiologist with experience in reading ~ 60 CTC and experienced gastroenterologist reviewed CTC together.	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Not clear if representative sample – prospective, consecutive (n.r.) **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match not adequately described **Presentation of results:** • Reasons for exclusions reported • Test failures excluded (but ineligible for CTC and colonoscopy) • 2 × 2 table not reconstructable **APPLICABILITY:** • Relevant patient spectrum • Patients received buscopan • Radiologist experience ~60 CTC **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Hara et al 2001, USA	II/III-2 (if blinding/no blinding)	**Objective:** to compare CTC performance using single- and multi-detector row systems **Patient enrolment:** Prospective, single centre, Jan 1998 – March 1999 **Endpoints**: CTC sensitivity and specificity for the detection of polyps: ≥ 10 mm, 6-9 mm, ≥ 6 mm, ≤5 mm; Colonic distension, respiratory artefacts **Reference standard:** colonoscopy, videotaped **Comparison of CTC detected lesion with reference standard:** • Positive if either of two radiologists found positive result • True match if polyp at colonoscopy within one segment of location at CTC and similar size.	*For patients receiving multidetector CTC* **n = 160** (of total 237 patients receiving either single or multidetector CTC) **Exclusions** No exclusions reported **Male:** 64% **Mean age (SD):** 63.5 yrs (6.5)0; age range 41-75yrs **Other characteristics:** n.r. **Inclusion criteria:** • History of colon polyps or cancer in first-degree relative OR • Personal history of prior polyps or colon cancer OR • Recent onset of iron deficiency anaemia AND • Received subcutaneously administered glucagon • 40-80 yrs of age • Able to provide written consent **Exclusion criteria**: Colostomy, IBD, acute diverticulitis, colonic biopsy in previous 72 hrs; polypectomy in previous 6 weeks, pregnancy, claustrophobia	**CTC** *Preparation:* included glucagon *Scanning:* prone and supine positioning; Multi-detector CT scanner; Other parameters: collimation 5 mm; table speed: 18.8 mm/s (pitch 0.75), 120 kVp;50 mA; reconstruction interval: 3.0 mm *Imaging:* supine and prone axial images, fully interactive 2D and 3D endoluminal CTC images *Diagnostic Review:* CTC by 3 radiologists, each study independent by 2 reviewers (level of experience not reported);	**QUALITY NOT ASSESSABLE: FAIR OR LOW QUALITY** (blinding not reported) **Patient selection:** • Selection criteria clearly described • Representative sample – prospective, consecutive **Reference standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results n.r. **Test and its interpretation:** • Blinding of CTC to colonoscopy results n.r. • CTC appropriately described • Definition of true match given **Presentation of results:** • No exclusions reported • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Patients received glucagon • CTC reviewers described as 'experienced' but level of experience n.r. **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Iannaccone et al, 2002, Italy	II/III-1 (if sample represen-tative/not represen-tative)	**Objective:** to assess the accuracy of ultra-low-dose scanning for multislice CTC for the detection of colorectal lesions **Patient enrolment:** Prospective, single centre, dates n.r. **Endpoints:** CTC sensitivity& specificity per-polyp for the detection of polyps: ≥ 10 mm, 6-9 mm **Reference standard:** Colonoscopy +/- histopathology **Comparison of CTC detected lesion with ref standard:** n.r.	**n = 27** **Exclusions:** No exclusions reported **Male:** 52% **Mean age** (range): 62 (48-80) yrs **Inclusion criteria:** Clinical indication for colon: • Positive FOBT (52%) OR • History of polyps (33%) OR • History of colorectal cancer resection (15%) **Exclusion criteria:** Known or suspected IBD, acute abdominal symptoms, pregnancy	**CTC:** *Preparation:* includes IV buscopan; IV contrast material if lesion > 20 mm on axial slices (additional supine scan followed) *Scanning:* prone and supine positioning; Multislice spiral CT scanner; Other parameters: 2.5 collimation; slice thickness: 3.0 mm; table speed: 17.5 mm/s; standard reconstruction kernel; 140 kVp; 10 mAs; reconstruction: interval: 1 mm *Imaging:* combination of 2D axial and multiplanar reconstructions, and 3D images for problem-solving *Diagnostic Review:* CTC by 2 independent radiologists (experience: > 200 studies read), consensus reading if controversial image;	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Not clear if representative sample **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match not given **Presentation of results:** • No exclusions reported • 2 × 2 table not reconstructable **APPLICABILITY:** • Relevant patient spectrum • Patients received IV buscopan +/- IV contrast • CTC reviewers had experience in reading > 200 CTC **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Johnson et al 2003 USA (Possible overlap with patients in Johnson et al 2004)	III-1	**Objective:** to assess CTC accuracy for detecting lesions ≥ 10 mm **Patient enrolment:** Retrospective, multi-centre Jan 1997 – April 2000 **Endpoints:** Diagnostic accuracy (area under ROC curves); Sensitivity and specificity for the detection of lesions: ≥ 10 mm, ≥ 5 mm; Investigate effects of reader variability and software platform performance **Reference standard:** Colonoscopy +/- histopathology **Comparison of CTC detected lesion with ref standard:** • True positive patient if having 1 or more proven polyps ≥ 10 mm in diameter • True match when CTC lesion (≥ 10 mm only) within 1 colonic segment of endoscopically proven polyp	**n = 93** **Exclusions:** 24 of 117 excluded Exclusion due to test failure 15.4% (18/117): Bowel prepation failures, incomplete distension (9.4% (11/117)); unreadable electronic data (6% (7/117), **Male:** 56% **Mean age:** 62 years **Inclusion criteria:** • Minimum standard CT acquisition parameters • Complete colonoscopy reports by experienced endoscopist (= 5 yrs) within 30 days after CTC • Pathology reports of all excised colorectal lesions **Exclusion criteria:** • Incomplete colonoscopy • Nondiagnostic CTC examination **Characteristics of study pop:** • High risk of CRC (first-degree relative with, personal history of, colorectal neoplasia) (74%) • Colorectal symptoms (40%)	**CTC** *Preparation:* n.r. *Scanning:* prone and supine positioning Other parameters: n.r. (only minimum standard defined (see Inclusion criteria) *Imaging:* axial images, w 2-dimensional multiplanar and 3-dimensional endoluminal views to confirm and problem-solve, 3 different software platforms *Diagnostic Review:* CTC read independently by 18 radiologists, experience varied ≤ 10 + instruction up to 500 studies read	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Representative sample unclear – retrospective **Reference Standard:** • Reference standard valid • reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results assumed based on reported methods. • CTC appropriately described • Definition of true match not given **Presentation of results:** • No exclusions reported • 2 × 2 table not reconstructable **APPLICABILITY:** • Relevant patient spectrum • Standard CTC techniques • 14/16 CTC reviewers had experience in reading ≥ 10 CTC, 2/16 received instruction **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison

Laghi et al 2003
 	
Italy
	II/III-1 (if rep/nonrep sample)	**Objective:** to assess contrast-enhanced CTC for follow-up of patients with past history of CRC
		
		To compare CTC with colonoscopy for patient tolerance and patient preferences
		
		Patient enrolment: Prospective, single centre, enrolment dates n.r.
		
		Endpoints: CTC Sensitivity & specificity for the detection of cancer; Patient tolerance; Patient preference; Extra-colonic findings
		
		Reference standard:
		• Colonoscopy +/- histopathology
		• Incomplete CC: barium enema or second CC (0)/ clinical f/u (8)
		
		Comparison of CTC detected lesion with reference standard: n.r.
			n = 35
			Exclusions:
			no exclusions reported
			Male: 51%
			Mean age (range): 62 (43-78) yrs
			Inclusion criteria:
			Follow-up for CRC:
			  • Surgically treated for colorectal cancer
			AND
			  • No known recurrence of disease
			AND
			• Normal CEA serum assay level
			Exclusion criteria: n.r.
				CTC
				Preparation: included IV buscopan
				Scanning: Supine and prone positioning, Multislice spiral CT scanner;
				Other parameters: slice collimation: 1 mm; table feed: 8 mm/s; 120 kVp; 80/120 mAs; reconstruction interval: 1 mm; scan time: 25-32s;
				IV contrast material (130 ml) in supine acquisition
				Imaging: 2D axial and multiplanar reconstructions (reformatted coronal and sagittal images), and 3D images for problem-solving
				Diagnostic Review: CTC independently reviewed by 2 experienced radiologists
					FAIR QUALITY
					Patient selection:
					• Inclusion criteria clearly/ exclusion criteria not clearly described
					• not clear if representative sample
					Reference Standard:
					• Reference standard valid
					• Reference standard does not include 2nd-look colonoscopy
					• Reference standard independent
					• 77% (27/35) of patients received reference standard (incomplete colonoscopy in 23% (8/35)
					• Blinding of colonoscopy to CTC results
					Test and its interpretation:
					• Blinding of CTC to colonoscopy results (CTC read prior colonoscopy)
					• CTC appropriately described
					• Definition of true match not adequately described
					Presentation of results:
					• No exclusions reported
					• 2 × 2 table reconstructable
					APPLICABILITY:
					• Relevant patient spectrum
					• Non standard CTC techniques (patients received contrast-enhanced, buscopan)
					• Level of radiologist experience n.r.
					COMPARISON:
					• No comparison with colonoscopy
					• No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Laghi et al 2002, Italy	II/III-1 (if rep/nonrep sample)	**Objective:** to assess CTC accuracy for the detection of suspected colorectal neoplasia **Patient enrolment:** Prospective, single centre, dates n.r. **Endpoints:** CTC sensitivity & specificity for the detection of Cancer, All lesions; CTC sensitivity reported per-polyp for lesions ≥ 10, 6-9, ≤ 5 mm **Reference standard:** • Colonoscopy +/- histopathology • Surgical palpation if incomplete colonoscopy **Comparison of CTC detected lesion with reference standard:** • Same lesion if exactly matched location and size of lesion on colonoscopy • Per-patient analysis: at least one polyp per patient on CTC confirmed on CC, regardless of other missed lesions	**n = 66** **Exclusions:** no exclusions reported **Male:** 53% **Mean age** (range): 61 (30-84) yrs **Inclusion criteria:** Referred for colonoscopy: • Positive FOBT (39%) OR • Altered bowel habits (24%) OR • Rectal bleeding (17%) OR • Anaemia of unknown origin (9%) OR • Previous history of colon cancer undergoing clinical f/u (11%) **Exclusion criteria:** • Suspected IBD • Pregnancy	**CTC** *Preparation:* included buscopan *Scanning:* Supine positioning, prone position if residual fluids were present Multislice spiral CT scanner; Other parameters: 3 mm collimation; slice thickness: 3.0 mm; table speed: 6 mm/s (pitch 1.5); 130 kVp; 120 mAs; reconstruction: interval: 2 mm *Imaging:* 2D axial and multiplanar images, and 3D images *Diagnostic Review:* CTC by 1 radiologists (level of experience: n.r.)	**FAIR QUALITY** **Patient selection:** • Selection criteria clearly described • Not clear if representative sample **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • No exclusions reported • 2 × 2 table reconstructable • Level of radiologist CTC experience not reported **APPLICABILITY:** • Relevant patient spectrum • No standard CTC techniques (supine position only) **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Macari et al 2002, USA	II	**Objective:** to prospectively compare thin-section low-dose multi-detector row CTC with CC for the detection of colorectal neoplasms **Patient enrolment:** Prospective, single centre, Sep 2000 – June 2001 **Endpoints:** CTC Sensitivity & specificity for the detection of: Overall polyps, Radiation dose **Reference standard:** • Colonoscopy +/- histopathology within 1 month of CTC • If CTC depicts same lesion as colonoscopy but size differs, gastroenterologist and radiologist review all images to determine actual size **Comparison of CTC detected lesion with reference standard:** Same lesion if similar size (+/-4 mm) and morphologic features and in same segment as colonoscopy finding	**n = 105** **Exclusions:** no exclusions reported **Male:** 97% **Mean age** (range): 58 (49-79) yrs Other characteristics: no patient known to have polyps **Inclusion criteria:** Referred for colonoscopy: • Positive FOBT OR • Hematochezia OR • Iron deficiency anemia OR • Previous history of polyps **Exclusion criteria:** n.r.	**CTC** *Preparation:* standard *Scanning:* Supine and prone positioning, prone position if residual fluids were present, 4-slice CT scanner; Other parameters: 1 mm collimation; slice thickness: 3.0 mm; 0.5-second gantry rotation; pitch: 6-7; 120 kv; 50 mAs; reconstruction: thickness: 1.25 mm, interval: 1 mm *Imaging:* 2D transverse plane imaging as primary display method; multiplanar reformatted and volume-rendered endoluminal CT views to verify suspected lesion *Diagnostic Review:* CTC reading by 1 radiologist (experience in CTC reading: 4 yrs)	**FAIR QUALITY** **Patient selection:** • Inclusion criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • No exclusions reported • 2 × 2 table reconstructable • Radiologist CTC experience 4 years **APPLICABILITY:** • Relevant patient spectrum • Nonstandard CTC techniques – low dose **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Morrin et al 2000, USA	III-2/II (if no blinding / blinding of colonoscopy)	**Objective:** to assess CTC accuracy in the detection of colorectal polyps and cancer To assess whether CTC + iv contrast improves overall reading **Patient enrolment:** Prospective, single centre, Oct 1997 – June 1999 **Endpoints**: CTC sensitivity and specificity for the detection of: Colorectal masses ≥20mm, Polyps 10-19 mm, 5-9 mm, <5 mm; Reader confidence, bowel preparation, degree of colonic distension **Reference standard:** • Colonoscopy +/- histopathology • Surgical findings **Comparison of CTC detected lesion with ref standard:** n.r.	**n = 81** **Exclusions:** 119 of 200 excluded (60%) No exclusions due to test failure Exclusions due to: incomplete colonoscopy (103), colonoscopy contra-indication (6), refused colonoscopy (6) **Male:** 44% **Mean age** (SD): 62.1 (17.1) yrs **Other characteristics:** n.r. **Inclusion criteria:** Referred for colonoscopy: • Positive FOBT (38%) OR • Anaemia (32%) OR • Altered bowel habit (12%) OR • Weight loss (10%) OR • Previous history of colorectal polyps (7%) **Exclusion criteria:** n.r.	**CTC** *Preparation:* included IV glucagon in 40% patients, IV contrast in 59% patients *Scanning:* Supine and prone positioning, Single-and multi-slice 10% (20/200) CT scanner Other parameters: (values for multi-slice scanning, differing single-slice values in brackets) 2.5-5.0 (3) mm collimation; table speed: 11.25-15.00 (6) mm/sec; 120 kVp; 200 (120) mA; *Imaging:* multiplanar reformation and endoluminal perspective *Diagnostic Review:* CTC reading independently by 2 radiologists (experience in CTC reading: 18 mths), differences resolved by consensus	**FAIR QUALITY** **Patient selection:** • Inclusion criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results n.r. **Test and its interpretation:** • Blinding of CTC to colonoscopy results (CTC read prior to colonoscopy) • CTC appropriately described • Definition of true match not given **Presentation of results:** • Exclusions and reasons reported • No exclusions due to test failure • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Not all patients with standard CTC techniques (single- and multi-slice scanning, IV glucagon and contrast in some patients) • CTC reader experience > 18 months **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Munikrishnan et al 2003, UK	II/III-2 (blinding / no blinding)	**Objective:** to assess CTC accuracy in detecting colorectal cancers and polyps in symptomatic patients **Patient enrolment:** Prospective, single centre, June 2000 - Dec 2001 **Endpoints:** CTC Sensitivity & specificity for: • Cancer • Polyps ≥ 10 mm • Polyps 6-9 mm • Polyps ≤ 5 mm • Diverticulosis and colitis **Reference standard:** Colonoscopy +/- histopathology **Comparison of CTC detected lesion with ref standard:** Per-patient assessment: true-positive CTC if at least one polyp on CTC seen on colonoscopy	**n = 80** **Exclusions:** None reported **Male:** 56% **Median age** (range): 68 (29-83) yrs **Other characteristics:** n.r. **Inclusion criteria:** • Change in bowel habit 58% • Rectal bleeding 48% • Abdominal pain 30% • Loss of weight 11% • Rectal mass 24% (patients may meet ≥ 1 criterion) **Exclusion criteria:** Impending large bowel obstruction, barium studies within the previous 14 days, pregnancy	**CTC** *Preparation:* included iv buscopan, iv contrast *Scanning:* Supine and prone positioning, Multi-slice (4-detector CT scanner) Other parameters: 1 mm collimation; variable table speed; 120 kVp; 120-200 mA; *Imaging:* two-dimensional, multiplanar image display technique with three-dimensional endoscopic reconstructions *Diagnostic Review:* CTC reading by 2 radiologists (experience in CTC reading: n.r.), final report by consensus	**QUALITY NOT ASSESSABLE: FAIR OR LOW QUALITY** (blinding not reported) **Patient selection:** • Eligibility criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results n.r. **Test and its interpretation:** • Blinding of CTC to colonoscopy results n.r. • CTC appropriately described • Definition of true match not adequately given **Presentation of results:** • No exclusions reported • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum ? (patient w rectal mass included) • Not standard CTC techniques (IV glucagon and contrast) • Level of CTC reader experience n.r. **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Roettgen et al, 2005 Germany	Not assessable II/III-1 or III-2 (blinding/ no blinding)	**Objective:** to assess CTC accuracy using 3D reconstruction software for the detection of small polyps **Patient enrolment:** Prospective, single centre, dates n.r. **Endpoints:** CTC sensitivity & specificity reported per-polyp for different reconstruction modes for the detection of polyps > 10 mm, 5-9.9 mm, > 5 mm, 3-4.9 mm, < 3 mm, all polyp sizes **Reference standard:** Colonoscopy +/- histopathology **Comparison of CTC detected lesion with reference standard:** n.r.	**n = 48** **Exclusions:** None reported **Male:** 46% **Mean age** (SD): 57 (21) yrs **Other characteristics:** N.r. **Inclusion criteria:** • Abdominal pain • Positive testing of blood in stool • Change of bowel movement • Family history of colorectal carcinoma **Exclusion criteria:** • IBD • Personal history of colorectal carcinoma	**CTC:** *Preparation:* included IV buscopan and IV contrast *Scanning:* Supine and prone positioning Multi-slice (16-detector CT scanner) Other parameters: 0.625 mm collimation; pitch: 1.7; detector rotation time: 0.5 s; 120 kV; 160 mAs; *Imaging:* 1. reconstruction in axial slices; 2. 3D reconstructed virtual colonoscopy; 3. 3D colonic wall dissection *Diagnostic Review:* CTC assessed together by 2 'experienced' radiologists,	**QUALITY NOT ASSESSABLE: FAIR OR LOW QUALITY** (blinding not reported) **Patient selection:** • Eligibility criteria clearly described • Not clear if representative sample **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results n.r. **Test and its interpretation:** • Blinding of CTC to colonoscopy results n.r. • CTC appropriately described • Definition of true match not adequately given **Presentation of results:** • No exclusions reported • 2 × 2 table not reconstructable **APPLICABILITY:** • Relevant patient spectrum • Not standard CTC techniques (contrast material; imaging) • Level of CTC reader experience n.r. **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Van Gelder 2002 Netherlands (no overlap w patients in van Gelder 2004)	II	**Objective:** • To assess CTC accuracy and image quality for the detection of polyps at different dose levels • To study effective CTC doses reported in literature **Patient enrolment:** Prospective, Mar – Nov 2000, single-centre **Endpoints:** CTC sensitivity & specificity for the detection of: polyps ≥ 5 mm, < 5 mm, all polyps, subjective image quality **Reference standard:** Colonoscopy +/- histopathology, videotape recorded **Comparison of CTC detected lesion with reference standard:** • Per-polyp assessment: Same lesion if same size, morphology, segment and anatomic interrelation w haustral folds matched w CC finding • Per-patient assessment: true-positive CTC if at least one true-positive polyp on CTC in the patient	**n = 50** **Exclusions:** None reported **Male:** 56% **Mean age** (range): 59 (20-86) yrs **Other characteristics:** N.r. **Inclusion criteria:** • Previous polyp and/or previous colorectal cancer OR • First- and/or second-degree relative(s) with a polyp and or/ colorectal cancer **Exclusion criteria:** • Pregnancy • Inability to give written informed consent	**CTC:** *Preparation:* included iv buscopan *Scanning:* Supine and prone positioning, Multi-slice CT scanner Other parameters: 2.5 mm collimation; pitch: 1.25; detector rotation time: 0.75 s; 120 kV; 167 mA (100 mAs); reconstruction interval: 1.6 mm *Imaging:* volume-rendered (threshold, -750) 3D cubic projections *Diagnostic Review:* CTC assessment by 1 radiologists (experience: > 50 CTC evaluations)	**FAIR QUALITY** **Patient selection:** • Eligibility criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • No exclusions reported • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Patients received buscopan • CTC reader experience > 50 **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Author, year & setting	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality, applicability and comparison
Vogt et al 2004 Germany	II	**Objective:** to assess CTC accuracy with an ultra-low dose technique for detection of colorectal polyps in patients at average risk with nonspecific abdominal symptoms **Patient enrolment:** Prospective, Sep 2001 – Jul 2002, single centre **Endpoints:** CTC sensitivity reported per-polyp for the detection of: polyps > 10 mm, 5-10 mm, < 5 mm; CTC specificity reported per-patient for all polyps; Radiation dose exposure **Reference standard:** high-resolution videocolonoscopy +/- histopathology **Comparison of CTC detected lesion with reference standard:** same polyp if similar morphology and size and in same or adjacent colon segment	**n = 115** **Exclusions:** None reported **Male:** 57% **Mean age** (range): 58 (41-82) yrs **Other characteristics:** Outpatient clinic **Inclusion criteria:** Referred for colonoscopy for nonspecific abdominal symptoms (chronic constipation/chronic abdominal pain) **Exclusion criteria:** Personal or family history of CRC/polyps	**CTC** *Preparation:* standard *Scanning:* Supine positioning only; Multi-slice CT scanner Other parameters: collimation: 4 × 1 mm; table feed: 8 mm (pitch: 8); 10 mAs (Ultra-low-dose technique); reconstruction: slice width: 1.25 mm, increment: 0.7 mm *Imaging:* noise reduction algorithm; 2D and 3D constructions at the same time *Diagnostic Review:* CTC assessment by 1 radiologist and 1 gastroenterologist (experience: n.r.), by consensus	**FAIR QUALITY** **Patient selection:** • Eligibility criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to CTC results **Test and its interpretation:** • Blinding of CTC to colonoscopy results • CTC appropriately described • Definition of true match given **Presentation of results:** • No exclusions reported • 2 × 2 table not reconstructable **APPLICABILITY:** • Relevant patient spectrum • Not standard CTC techniques (supine positioning only, ultra-low dose technique) **COMPARISON:** • No comparison with colonoscopy • No comparison with DCBE

Table 57 Summary of study characteristics and quality appraisal of accuracy studies of DCBE versus colonoscopy

Author & Year	Level of evidence	Study objective, design and reference standard	Study Population	Index test and comparator	Study quality, applicability
Durdey et al 1987 UK	II	**Objective:** to assess DCBE, DCBE + flexible colonoscopy, colonoscopy as initial investigations of patients with colorectal symptoms and normal findings on rigid sigmoidoscopy. **Patient enrolment:** Prospective, Jul 1985 – Sep 1986, single centre **Endpoints:** Sensitivity and specificity of DCBE, DCBE+FS, and CC for the detection of: colorectal cancer, adenomatous polyps, other abnormalities, complications, patient preference **Reference standard:** Final diagnoses made by clinician supervising the case, based on all investigations, not only those detailed in this study **Comparison of DCBE detected lesion with reference standard:** n.r.	**n = 66** **Exclusions:** 10 of 76 excluded (13%) **Male:** 53% **Median age** (range): 62 yrs (19-88) **Other characteristics:** n.r. **Inclusion criteria:** • Requiring Barium enema; • Symptoms of colonic disease (altered bowel habit (46%), rectal bleeding (39%), left-sided abdominal pain (7%), mucuous discharge (4%), weight loss (4%)) **Exclusion criteria:** Cancer found on initial digital rectal examination and rigid sigmoidoscopy	**DCBE** *Preparation:* standard Performed by one of three experienced radiologists **Colonoscopy** Routine colonoscopy Performed by one of four experienced surgeons	**FAIR QUALITY** **Patient selection:** • Eligibility criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Does not include 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to DCBE results **Test and its interpretation:** • Blinding of DCBE to colonoscopy results (DCBE read prior) • DCBE not appropriately described • Definition of true match not given **Presentation of results:** • Exclusions and reasons reported • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • Level of radiologist experience n.r. **COMPARISON:** • No comparison DCBE with CTC

Author & Year	Level of evidence	Study objective, design and reference standard	Study Population	Index test and comparator	Study quality, applicability
Irvine et al 1988 Canada	II	**Objective:** to assess the accuracy of flexible sigmoidoscopy (FS) + DCBE versus colonoscopy in patients with overt rectal bleeding **Patient enrolment:** Prospective, single centre, Aug 1985 – Dec 1986 **Endpoints:** Sensitivity and specificity of DCBE, FS, FS+BE, colonoscopy for the detection of: colorectal cancer, colorectal adenomatous polyps, Other; Examination completeness, complications **Reference standard:** • Maximum diagnostic data available, any lesion (with the exception of haemorrhoids and anal fissures) was required to be reported on at least three test results or be upheld by histology • Second-look colonoscopy (segmental unblinding) if pathology on DCBE/FS and missed on initial colonoscopy. • Discordant results: repeat DCBE focussed on controversial segment of bowel **Comparison of DCBE detected lesion with ref standard:** n.r.	**n = 71** **Exclusions:** 18 of 89 excluded (20.2%) **Male:** 46% **Mean age** (SD): 53.5 (16.7) yrs **Other characteristics:** • 1/3 referred by family physicians • 2/3 by gastroenterologists/ gastrointestinal surgeons (of eligible subjects (315)) **Inclusion criteria:** • Red blood per rectum ≤ previous 3 months • Hospitalised, had no postural hypotension ≥ 20 mm or transfusion requirement of more than 2 units of packed red blood cells (subset) **Exclusion criteria:** • History of melaena stools alone • Occult bleeding or • Contraindication to either procedure	**DCBE** Preparation: Rapid colonic lavage No sedation **Colonoscopy** Preparation: Rapid colonic lavage preparation IV sedation (meperidine/diazemuls) Completed in standard fashion (no more details reported)	**FAIR QUALITY** **Patient selection:** • Eligibility criteria clearly described • Representative sample – prospective, consecutive **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to DCBE results **Test and its interpretation:** • Blinding of DCBE to colonoscopy results • DCBE not appropriately described • Definition of true match not given **Presentation of results:** • Exclusions and reasons reported • 2 × 2 table reconstructable (for all diagnoses) **APPLICABILITY:** • Relevant patient spectrum **COMPARISON:** • No comparison DCBE with CTC

Author & Year	Level of evidence	Study objective, design and reference standard	Study Population	Index test	Study quality and applicability
Rockey et al 2004 USA	II/III-1 (if consecutive / not consecutive)	**Objective:** to assess the sensitivity of DCBE versus colonoscopy and to identify factors that influence accuracy **Patient enrolment:** Prospective, 2 centres, dates n.r. **Endpoints:** • CTC sensitivity reported per-polyp for the detection of: Polyps > 10 mm, 6-9 mm, ≤ 5 mm • CTC specificity reported per-patient for all polyps, cancer, polyps ≥ 10 mm, ≥ 6 mm • Location of cancers, effect of diverticula, quality of bowel prep **Reference standard:** • Colonoscopy +/- histopathology • If results discrepant, colonoscopy was repeated **Comparison of DCBE detected lesion w Ref standard:** Same lesion if within same colonic segment and if size within 5 mm	**n = 89** **Exclusions:** 21 of 110 excluded (19%) Exclusions due to test failure: 10% (11/110) (ACBEs inadequate because of retained stool (8.2%), caecum not intubated at CC 1.8%), inability to complete the colon prep (?%) **Male:** 57% **Mean age** (SD): 60 yrs (10) **Inclusion criteria:** At least one positive test for faecal occult blood **Exclusion criteria:** • Age < 18 yrs, pregnancy • Active GI bleeding • Iron deficiency anemia	**DCBE** *Preparation:* standard Preliminary x-ray to ensure adequate colon cleansing No sedation DCBE and colonoscopy performed by specialist trainee under supervision	**FAIR QUALITY** **Patient selection:** • Eligibility criteria clearly described • Not sure if representative sample – prospective, consecutive not clear **Reference Standard:** • Reference standard valid • Reference standard includes 2nd-look colonoscopy • Reference standard independent • All patients received reference standard • Blinding of colonoscopy to DCBE results **Test and its interpretation:** • Blinding of DCBE to colonoscopy results • DCBE appropriately described • Definition of true match given **Presentation of results:** • Exclusions and reasons reported • Exclusions due to test failures • 2 × 2 table reconstructable **APPLICABILITY:** • Relevant patient spectrum • DCBE and colonoscopy performed by specialist trainee under supervision **COMPARISON:** • No comparison DCBE with CTC

Table 59   Summary of results of direct comparative studies accuracy of CTC versus DCBE and colonoscopy

Author & Year	Patient characteristics	Comparator & Reference standard	Prevalence	CTC accuracy	DCBE accuracy	Colonoscopy accuracy	Other outcomes
Rockey et al, 2005 USA	n = 614 symptomatic 68% high-risk asymptomatic 32%	**Comparator:** • Initial colonoscopy • DCBE **Reference standard:** Colonoscopy, initial +/- 2nd-look, +/- additional diagnostic tests.	Cancer: 1.5% (9/614)* Lesions ≥ 10 mm: 10.3% (63/614) Lesions 6-9 mm: 18.9% (116/614) All lesions: 88.8% (545/614)	**Sensitivity (95% CI):** • Lesions ≥ 10 mm: 59% (45-71%) CTC vs DCBE, p = 0.11 • Lesions ≥ 6 mm: 55% (47-63%) CTC vs DCBE, p = 0.003 • Lesions 6-9 mm: 51% (41-60%) CTC vs DCBE, p = 0.008 • Lesions ≤ 5 mm: 45% (n.r.) • Colorectal cancer: 78% (40-97%)* (7/9) **Specificity (95% CI):** • Lesions ≥ 10 mm (n = 551): 96% (94-98%) CTC vs DCBE, p < 0.0001 • Lesions ≥ 6 mm (n = 459): 89% (86-92%) CTC vs DCBE, p = 0.0007	**Sensitivity (95% CI):** • Lesions ≥ 10 mm: 48% (35-61%) • Lesions ≥ 6 mm: 41% (33-49%) • Lesions 6-9 mm: 35% (27-45%) • Lesions ≤ 5 mm: 32% (n.r.) • Colorectal cancer: 89% (52-100%)* (8/9) **Specificity (95% CI):*** • Lesions ≥ 10 mm (n = 551): 90% (87-92%) • Lesions ≥ 6 mm (n = 459): 82% (78-85%)	**Sensitivity (95% CI):** • Lesions ≥ 10 mm: 98.4% (91-100%) CTC vs colonoscopy, p < 0.0001 • Lesions ≥ 6 mm: 98.7% (95-100%) CTC vs colonoscopy, p < 0.0001 • Lesions 6-9 mm: 99% (95-100%) CTC vs colonoscopy, p < 0.0001 • Lesions ≤ 5 mm: 99% (n.r.) • Colorectal cancer: 100% (66-100%)* (9/9) **Specificity (95% CI):** • Lesions ≥ 10 mm (n = 551): 99.6% (99-100%) CTC vs colonoscopy, p < 0.0001 • Lesions ≥ 6 mm (n = 459): 99.6% (95% CI: 98-100) CTC vs colonoscopy, p < 0.0001 • For all comparisons of DCBE vs colonoscopy sensitivity for lesion detection, p < 0.0001	**Other colonic disease:** n.r. **Safety:** n.r. **Extracolonic findings:** 57% patients ≥ 1 finding • abdominal aortic aneurysms 12/614 (2%) • cancer 4/614 (1%) **Test failures:** • Inadequate bowel preparation 9/775 (1.2%) • CTC failure 5/623 (0.8%) • Colonoscopy incomplete 4/623 (0.6%) (excluded from analysis) **Other outcomes:** CTC: No statistically significant difference in detection between more/less reader experience
			* assuming one cancer per patient	* 95% CIs calculated from reported data	* 95% CIs calculated from reported data	* 95% CIs calculated from reported data	

Table 60   Summary of results of direct comparative studies of accuracy of CTC compared to DCBE

Author & Year	Patient characteristics	Comparator & Reference standard	Prevalence	CTC accuracy	DCBE accuracy	Other outcomes

Johnson et al, 2004
 	
USA
	n = 691
	
	Symptomatic 3%
	
	High-risk asymptomatic 97%
		Comparator:
		DCBE
		
		Reference standard:
		Colonoscopy, flexible sigmoidoscopy, proctoscopy or surgery
			Cancer: 0.87% (6/691)*
			
			Polyps ≥ 10 mm: 4.2% (29/691)
			
			Polyps ≥ 5 mm: 7.5% (52/691)
				Sensitivity (95% CI)*:
				• Lesions ≥ 10 mm:
				  3 reviewers: 56-77%
				  Mean 69% (49-85%)** (40/58)
				  CTC vs DCBE p ≥ 0.06 for 3 reviewers
				• Lesions 5-9 mm:
				  3 reviewers: 38-90%
				  Mean 70% (51-85%)** (42/60)
				  CTC vs DCBE p≥0.21 for 3 reviewers
				
				Specificity (95% CI)
				• Lesions ≥ 10 mm:
				  3 reviewers: 96-99%
				  Mean 97% (95-98%)** (1284/1324)
				  CTC vs DCBE p < 0.05 for 2 reviewers
				• Lesions 5-9 mm:
				  3 reviewers: 90-93%
				  Mean 91% (89-93%)** (1202/1322)
				  CTC vs DCBE p < 0.001 for all 3 reviewers
					Sensitivity (95% CI)*:
					• Lesions ≥ 10 mm:
					  Mean 48% (29-68%)** (28/58)
					• Lesions 5-9 mm:
					  3 reviewers: 44-75%
					  Mean 60% (36/60)
					
					Specificity (95% CI)
					• Lesions ≥ 10 mm:
					  3 reviewers: 99-100%
					  Mean 99% (98-100%)** (1312/1324)
					• Lesions 5-9 mm:
					  3 reviewers: 97-98%
					  Mean 97% (1286/1322)
						Other colonic disease: n.r.
						
						Safety: n.r
						
						Extracolonic findings: n.r.
						
						Test failures:
						• CTC failure n.r.
						• incomplete colonoscopy 10/116 (9%)
						
						(included in analyses)

			* Assuming 1 cancer per patient.	* Sensitivity and specificity reported for three reviewers, each reviewing 2 patients. ** 95% CIs calculated from reported data	* Sensitivity and specificity reported for three reviewers, each reviewing 2 patients. ** 95% CIs calculated from reported data	

Table 61   Summary of results of direct comparative studies of accuracy of CTC compared to colonoscopy

Author, year & setting	Patient characteristics	Comparator & reference standard	Prevalence	CTC accuracy	Colonoscopy accuracy	Other outcomes
Cotton et al, 2004 USA	n = 600 Symptomatic High-risk, asymptomatic	**Comparator:** Initial colonoscopy **Reference standard:** Colonoscopy (initial +/- 2nd-look), +/- additional diagnostic tests	Cancer: 1.3% (8/600)* Lesions ≥ 10 mm: 7.0% (42/600) Lesions 6-9 mm: 9.8% (59/600) Lesions ≤ 5 mm: 11.3% (68/600) All lesions: 51.3% (308/600) * Assuming 1 cancer per patient and no cancers in lesions < 6 mm.	**Sensitivity % (95% CI):** [*fly-through interpretations*] • Lesions ≥ 10 mm: 55% (40-70%) [60% (45-74%)] • Lesions 6-9 mm: 30% (20-40%) [36% (25-46%)] • Lesions ≥ 6 mm: (39% (30-48%) [45% (35-55%)] • Lesions 1-5 mm: 14% (10-18%) [18% (13-22%)] **Specificity (95% CI):** [*fly-through interpretations*] • Lesions ≥ 10 mm: 96% (94-98%) [98 (97-99%)] • Lesions 6-9 mm: 93% (91-95%) [95% (93-97%)] • Lesions ≥ 6 mm: 91% (88-93%) [93% (91-95%)] • Lesions 1-5 mm: 91% (87-94%) [91% (87-94%)]	**Sensitivity (95% CI):** • Lesions ≥ 10 mm: 100% • Lesions 6-9 mm: 99% (96-100%) • Lesions ≥ 6 mm: 99% (97-100%) • Lesions 1-5 mm: 97% (95-99%) **Specificity (95% CI):** • Lesions ≥ 10 mm: 100% • Lesions 6-9 mm: 100% • Lesions ≥ 6 mm: 100% • Lesions 1-5 mm: 100%	**Other colonic disease:** n.r. **Safety:** overall minor adverse events 14/600 (2.3%), not reported by test, includes extracolonic lesions of possible clinical significance (8) and mild bleeding after polypectomy (1) **Extracolonic findings:** findings of possible clinical signifance 1.3% (8/600) **Test failures:** • CTC failure n.r. • incomplete colonoscopy 9/600 (1.5%) (included in analyses) **Other outcomes:** • Did not find that technical issues influenced CTC interpretation • Preference questionnaires (n = 518): 46% preferred CTC, 41% preferred CC, 13% no preference

Author, year & setting	Patient characteristics	Comparator & reference standard	Prevalence	CTC accuracy	Colonoscopy accuracy	Other outcomes
Ginnerup Pedersen et al, 2003 Denmark	n = 148 Symptomatic High-risk asymptomatic Known CRC, preoperative (5%)	**Comparator:** Initial colonoscopy **Reference standard:** colonoscopy (initial +/- 2nd-look)	Cancer: 7.4% (11/148) All lesions ≥ 6 mm: 29.7% (44/148)	**Sensitivity (95% CI)*:** • Cancer: 100% (72-100%)* • Masses ≥ 20 mm: 100% • Polyps ≥ 6 mm: 91% (78-98%)* **Specificity (95% CI):** • Polyps ≥ 6 mm: 97% (92-99%)* * 95% CIs calculated from reported data	**Sensitivity (95% CI)*:** • Cancer: 100% (72-100%)* • Masses ≥ 20 mm: 100% • Polyps ≥ 6 mm: n.r. **Specificity (95% CI):** • Polyps ≥ 6 mm: n.r. * 95% CIs calculated from reported data	**Other colonic disease:** 1 case of diverticulitis detected on CTC **Safety:** • No complications of CTC/colonoscopy • Effective radiation dose: 6 mSv **Extracolonic findings:** n.r. **Test failures:** • CTC failure 5/148 (3%) • CTC poor quality 36/148 (24%) • Incomplete colonoscopy 13/148 (9%) Difference between CTC and colonoscopy test failures, p < 0.01
Hoppe et al, 2004 Switzerland	n = 92 Symptomatic High-risk asymptomatic	**Comparator:** Initial colonoscopy **Reference standard:** Colonoscopy (initial +/- 2nd-look)	Cancer: 9% (8/92)* Polyps ≥ 10 mm: 22% (20/92) All lesions: 53% (49/92) * Assuming 1 cancer per patient	**Sensitivity (95% CI):** • Lesions ≥ 10 mm: 95% (75-99%) • Lesions ≥ 6 mm: 76% (59-89%) **Specificity (95% CI):** • Lesions ≥ 10 mm: 98% (92-100%) • Lesions ≥ 6 mm: 88% (77-95%)	**Sensitivity (**based on per lesion sensitivity for 19 segments undergoing 2nd-look CC): • Lesions ≤ 5 mm: 100% • Lesions ≥ 10 mm: 100%	**Other colonic disease** n.r. **Safety** n.r. **Extracolonic findings** n.r. **Test failures** • CTC failure 2/100 (2%) • Incomplete colonoscopy 6/100 (6%) (excluded from analyses) Two additional lesions were detected in patients w an incomplete colonoscopy

Author, year & setting	Patient characteristics	Comparator & reference standard	Prevalence	CTC accuracy	Colonoscopy accuracy	Other outcomes
Taylor et al, 2003 UK	n = 54 Symptomatic/ not known	**Comparator:** Initial colonoscopy **Reference standard:** Colonoscopy +/- histopathology (+/- 2nd colonoscopy)	Cancer: 11% (6/54) Polyps & cancer > 10 mm: 19% (10/54) Polyps < 10 mm: 35% (19/54) Any polyps: 46% (25/54) Polyps or cancer: 54% (29/54)	**Sensitivity (95% CI):** • Cancer: 83%* (36-99.6%)** • Polyps or cancer > 10 mm: 90% (56-100%)** • Polyps < 10 mm: 47% **Specificity (95% CI):** • Cancer: 100% (93-100%)** • Polyps or cancer > 10 mm: 100% (92-100%)** • Polyps < 10 mm: 84% * CTC sensitivity based on improved reference standard (7 cancers), CTC sensitivity 83% (5/6) based on original colonoscopy alone ** 95% CIs calculated from reported data	**Sensitivity (95% CI):** Cancer: 83% (36-99.6%)* * Calculated from information reported in article text.	**Other colonic disease:** Diverticular disease in 52% (28/54) on CTC and 50% (27/54) on colonoscopy **Safety:** n.r. **Extracolonic findings:** 7.4% (4/54) renal cancer (1), gallstones (1), renal calculus (1), aortic aneurysm (1) **Test failures:** CTC failure n.r. Incomplete colonoscopy 10% (5/49). At least one lesion identified at CTC in patient with incomplete colonoscopy.

Computed tomography colonography

Author, year & setting	Patient characteristics	Comparator & reference standard	Prevalence	CTC accuracy	Colonoscopy accuracy	Other outcomes
Van Gelder et al, 2004 Netherlands	n = 249 Asymptomatic high risk	**Comparator:** Initial colonoscopy +/- histopathology **Reference standard:** Colonoscopy +/- histo-pathology +/- 2nd-look colonoscopy	Cancer: 1.6% (4/249) Polyps ≥ 10 mm: 12% (31/249) Polyps ≥ 6 mm: 18% (45/249) All polyps: 57% (141/249)	**Sensitivity (95% CI):** (1st/2nd reviewer) • Polyps ≥ 10 mm: 84% (67-93%) for both reviewers (95% CI : 66-95% (calculated from reconstruction of 2×2 table using reported data)) • Polyps ≥ 6 mm: 76% (61-86%)/80% (66-89%) mean: 78% (63-89%)* • All polyps: 62% (54-69%/)/62% (54-70%) mean: 88% **Specificity (95% CI):** • Polyps ≥ 10 mm: 92% (87-95%/)/92% (88-95%) mean: 92% (87-95%)* • Polyps ≥ 6 mm: 71% (64-76%)/69% (61-74%) mean: 70% (63-76%)* • Polyps any size: 32% (24-41%/)/30% (22-39%) mean: 31% * Calculated from reported data	**Sensitivity (95% CI):** Polyps ≥ 10 mm: 81% (63-93%)* (25/31) **Specificity (95% CI):** Polyps ≥ 10 mm: 100% (98-100%)* * Calculated from reported data	**Other colonic disease:** n.r. **Safety:** n.r. **Extracolonic findings**: n.r. **Test failures:** • Bowel preparation insufficient 4% (excluded from analyses) • CTC failures: 7% (20/288) • Incomplete colonoscopy 2% (5/288) **Other outcomes:** Interobserver agreement was good (K = 0.70 (0.66-0.74)

Table 62   Summary of results of CTC accuracy with colonoscopy as reference standard

Author & Year	Patient characteristics	Reference standard	Prevalence	CTC accuracy	Other outcomes
Bruzzi et al, 2004 Ireland	n = 82 (72 for per-patient sensitivity & specificity) High-risk asymptomatic	Colonoscopy	Polyps ≥ 10 mm: 2% (2/82) Polyps 6-9 mm: 7% (6/82) Polyps ≤ 5 mm: 33% (27/82) All polyps: 41% (34/82)	**Sensitivity (95% CI):** • Lesions ≥ 10 mm: 100% (16-100%)* • Lesions 6-9 mm: 33% (4-78%)* • Lesions ≤ 5 mm: 32% (17-54%)* **Specificity (95% CI):** • Lesions ≥ 10 mm: 100% (95-100%)* • Lesions 6-9 mm: 95% (87-99%)* • Lesions ≤ 5 mm: 83% (68-92%)* *95% CIs calculated from reported data	**Other colonic disease:** Diverticular disease in 36% (26/82) **Safety:** n.r. **Extracolonic findings:** n.r. **Test failures:** • CTC failure n.r. • Incomplete colonoscopy 12% (10/82) (excluded from analyses)
Cohnen et al, 2004 Germany	n = 137 High-risk asymptomatic (27%)/ Symptomatic (73%)	Colonoscopy	Lesions: 43% (59/137)	**Sensitivity (95% CI):** Overall lesions: 76% (45/59, from Table 1 of publication) (63-86%)* **Specificity (95% CI):** Overall: 76% (59/78, recalculated from data in Table 1 of publication, specificity reported in text of publication = 81% (65-85%)* * 95% CIs calculated from reported data	**Other colonic disease:** n.r. **Safety:** Effective radiation dose: 0.7 mSv men, 1.0 mSv women **Extracolonic findings:** 1% (2/137) ureteric stone (1), abdominal aortic aneurysm (1). (Authors note that CTC technique used not suited to assessment of extracolonic disease) **Test failures:** n.r. (But suboptimal colonic distension 3%)
Gluecker et al, 2002 Switzerland	n = 50 High-risk asymptomatic/ Symptomatic	Colonoscopy	n.r.	**Sensitivity (95% CI):** *Per-patient sensitivity:* n.r. *Per-polyp Sensitivity:* • Overall: 22% (15/67)* • Lesions ≥ 10 mm: 82% • Lesions 5-9 mm: 33% • Lesions < 5 mm: 2.4% (1/41)** **Specificity (95% CI):** Overall lesions: 90% * Calculated from figures in table 1 of publication ** Re-calculated from figures from table 1, differs from sensitivity reported in text (40%)	**Other colonic disease:** n.r. **Safety:** No complications of CTC/CC **Extracolonic findings:** n.r. **Test failures:** • Bowel preparation failure 2% (1/50) excluded from analyses • CTC failure: 8% (4/50) insufficient bowel preparation (included in analysis) • Incomplete colonoscopy: n.r.

Author & Year	Patient characteristics	Reference standard	Prevalence	CTC accuracy	Other outcomes
Hara et al, 2001 USA	n = 160 (w multi-slice CTC, total n = 237) Symptomatic/ high-risk asymptomatic	Colonoscopy	Polyps > 10 mm: 5.6% (9/160)	**Sensitivity (95% CI)** Polyps >10 mm: 78% (40-97%)* (2 radiologist consensus on positive test) (by observer sensitivity ranged from 33-71% with weighted mean: 56%) **Specificity (95% CI)** Polyps >10 mm: 93% (87-96%)* (by observer sensitivity ranged from 95-98% with weighted mean: 96%) * 95% CIs calculated from reported data	**Other colonic disease:** n.r. **Safety:** effective radiation dose 2.5 mSv in men, 6.7 mSv in women Test complications n.r. **Extracolonic findings:** n.r. **Test failure:** • CTC suboptimal distension 20% • No mod-severe respiratory artefacts • Incomplete colonoscopy n.r. **Other outcomes:** Polyp detection slightly lower on multi-detector vs single-detector CTC, (not statistically significant)
Iannaccone et al, 2002 Italy	n = 27 Symptomatic/ high risk asymptomatic	Colonoscopy	Polyp/Carcinoma: 56% (15/27) Carcinoma: 33% (9/27)* * Assuming one cancer per patient	**Sensitivity (95% CI)** Cancer: 100% (66-100%)* *Per-patient sensitivity*** • Lesions ≥ 10 mm: 100% • Lesions 6-9 mm: 100% • Lesions ≥ 6 mm: 100% **Specificity (95% CI):** Overall: 100 (82-100%)* * 95% CIs calculated from reported data ** Assumed from per-polyp sensitivities	**Other colonic disease:** n.r. **Safety:** total radiation exposure: 1.7 mSv for men, 2.3 mSv for women **Extracolonic findings:** n.r. (Authors noted that ultra low dose CTC is inadequate for the assessment of extracolonic lesions) **Test failures:** n.r.

Author & Year	Patient characteristics	Reference standard	Prevalence	CTC accuracy	Other outcomes
Johnson et al, 2003 USA (Potential overlap with Johnson et al, 2004)	n = 93 High-risk asymptomatic symptomatic	Colonoscopy +/- histopathology	Cancer: 7.5% (7/93)* Lesions ≥ 10 mm: 47% (44/93) Lesions 5 mm-10 mm: 18% (17/93) Lesions < 5 mm: 16% (15/93) All lesions: 82% (76/93) * Assuming one cancer per patient	**Sensitivity** (Average across reviewers (range)) • Lesions ≥ 10 mm: 75% (50-100%), lower 95% CI 68% • Lesions ≥ 5 mm: 69% (40-100%), lower 95% CI 63% **Specificity:** • Lesions ≥ 10 mm: 73% (38-100%), lower 95% CI 66% • Lesions ≥ 5 mm: 72% (23-100%), lower 95% CI 64%	**Other colonic disease:** n.r. **Safety:** no complications **Extracolonic findings:** n.r. **Test failures:** • CTC inadequate 15% (18/117) (excluded from analysis) • Incomplete colonoscopy n.r**.** **Other outcomes:** • Area under curve (range) • lesions ≥ 10 mm: 80% (58-99%) • lesions ≥ 5 mm 75% (59-90%) • No statistically significant difference observed between display platforms
Laghi et al, 2002 Italy Symptomatic	n = 66	Colonoscopy +/-surgery	Polyp/Carcinoma: 48% (32/66) Carcinoma: 23% (15/66)* * Assuming 1 cancer per patient	**Sensitivity:** • Overall lesions: 94% (95% CI 85-100%) (32/34)* • Cancer: 100% **Specificity:** Overall lesions: 94% (86-100%)	**Other colonic disease:** n.r. **Safety:** no complications of CTC/CC and CTC well tolerated **Extracolonic findings** (only major recorded): in 7.6% (5/66) (lymphadenopathies in 1 pat w non-Hodgin lymphoma & in 4 pat w CRC) **Other outcomes:** • 7.6% (5/66) pat w incomplete CC due to occlusive neoplastic lesions, CTC was able to visualise entire colon; no additional lesions were detected • Analysis of FNs: 6 of 22 missed lesions on CTC due to residual stool (4) or collapsed bowel (2) • Analyses of FPs: 50% due to residual stool (3/6) or hypertrophic haustral folds (3/6)

Author & Year	Patient characteristics	Reference standard	Prevalence	CTC accuracy	Other outcomes
Laghi et al, 2003 Italy	n = 35 High-risk asymptomatic (CRC f/u patients)	Colonoscopy + clinical f/u	Polyp/Carcinoma: 8.6% (3/35) Carcinoma: 2.8% (1/35)* * Assuming 1 cancer per patient	**Sensitivity:*** • Carcinoma: 100% (1/1) • Overall: 100% (3/3) **Specificity:** Overall: 94% (30/32)** * Sensitivity and specificity calculated from information in text ** 2 false positives were < 6 mm	**Other colonic disease:** n.r. **Safety:** No complications of CTC **Extracolonic findings**: 9% (3/35) metastatic disease (liver, lungs). 34 minor findings in 63% patients (22/35). **Test failures:** CTC suboptimal evaluation in 8% of colonic segments, including uninterpretable in 2% of colonic segments. Incomplete colonoscopy 23% (8/35) **Other outcomes:** Patient preferences: CTC 71%, colonoscopy 29%, p < 0.0001 Pain: CTC 16%, colonoscopy 58%, p < 0.0001
Macari et al, 2002 USA	n = 105 High risk asymptomatic/ symptomatic	Colonoscopy	Polyp: 56% (59/105) Cancer: 5.7% (6/105)* * Assuming 1 cancer per patient	**Sensitivity**: Overall: 58% (34/59)* (44-70%)** **Specificity:** Overall: 87% (40/46)*** (74-70%)** * Calculated from Table 1 of paper, assuming any polyp detected on CTC and confirmed on colonoscopy was a true positive per patient, regardless of other potential missed lesions ** 95% CIs calculated from reported data *** Calculated from Table 1 of paper, assuming any polyp in a detected at CTC but not colonoscopy is a false positive	**Other colonic disease:** n.r. **Safety:** Radiation dose: weighted CT dose index: 5.7 mGy/acquisition; 11.4 mGy for supine + prone CTC; effective dose for full CTC: 5.0 mSv for men, 7.8 mSv for women **Extracolonic findings**: n.r. **Test failures:** • CTC failure 0% (visualization of all colonic segments 100%) • Incomplete colonoscopy 2% (2/105)

Author & Year	Patient characteristics	Reference standard	Prevalence	CTC accuracy	Other outcomes
Morrin et al, 2000 USA	n = 81 Symptomatic 93% High-risk asymptomatic 7%	Colonoscopy +/- surgical findings	Cancer: n.r. Polyps/masses ≥ 10 mm: 23% (29/81)* Abnormality (polyps any size, masses): 57% (46/81) Normal colon 43% (35/81) * Assuming no patient has both polyp ≥ 10 mm and colorectal mass ≥ 20 mm	**Sensitivity (95% CI)*:** • Colorectal masses ≥ 20 mm: 100% (78-100%) • Polyps 10-19 mm: 87% (57-98%) • Polyps 5-9 mm: 73% (48-93%) • Polyps < 5 mm: 57% (32-77%) **Specificity (95% CI)*:** • Colorectal masses ≥ 20 mm: 96% (87-99%) • Polyps 10-19 mm: 100% (95-100%) • Polyps 5-9 mm: 96% (87-99%) • Polyps < 5 mm: 92% (82-97%) * 95% CIs calculated from reported data	**Other colonic disease:** n.r. **Safety:** n.r. **Extracolonic findings:** n.r. **Test failures:** • CTC failure 13% (26/200) entire bowel wall not visualised due to fluid or stool. • Incomplete colonoscopy 52% (103/200) **Other outcomes:** Contrast enhancement significantly improved sensitivity in the detection of polyps 5-9 mm, no differences in other-sized polyps, masses
Munikrishnan et al, 2003 UK	n = 80 Symptomatic patients	Colonoscopy	Cancer: 36% (29/80)* Lesions ≥ 10 mm: n.r. Diverticular disease: 20% (16/80) No abnormality: 33% (26/80) * Assuming 1 cancer/patient	**Sensitivity (95% CI)*:** • Cancers: 97% (82-100%) • Polyps ≥ 10 mm: 100% (66-100%) • Polyps 6-9 mm: 80% (36-100%) • Polyps ≤ 5 mm: 36% (12-62%) • All polyps: 74% • Overall colorectal disease (cancer, polyps, diverticulosis, colitis): 82% **Specificity (95% CI)*:** • Cancers: 98% (90-100%) • Polyps ≥ 10 mm: 100% (95-100%) • Polyps 6-9 mm: 99% (93-100%) • Polyps ≤ 5 mm: 97% (89-100%) • All polyps: 96% • Overall colorectal disease: 93% * 95% CIs calculated from reported data	**Other colonic disease:** *Diverticulosis:* • Prevalence 20% (16/80); Sens/Spec: 31%/98% *Colitis:* • Prevalence 4% (3/80); Sens/Spec: 67%/100% **Safety**: no complications Minor adverse events: pain/discomfort: CTC 10%; colonoscopy 44% **Extracolonic findings**: • Not requiring further investigations in 19% (15/80) of patients • Altering management in 13% (10/80): colorectal liver metastases (5), primary HCC (1), ovarian tumours (2), abdominal aortic aneurysms (2) **Test failures:** • CTC failure 5% (4/80) • Incomplete colonoscopy 23% (18/80) (due to poor bowel preparation (7), technical difficulty (4), occlusive CRC (5), sigmoid diverticular strictures (2)

Author & Year	Patient characteristics	Reference standard	Prevalence	CTC accuracy	Other outcomes
Roettgen et al, 2005 Germany	n = 48 Symptomatic High-risk asymptomatic	Colonoscopy	All Polyps: 31% (15/48)	**Sensitivity:** Lesions > 10 mm: 100% (assumed from reported per-polyp sensitivity) **Specificity*:** • All lesions: 94%/94%/100% • Lesions > 5 mm: 50%/50%/100% * Specificities reported for 3 different reconstruction modes: 3D reconstruction "colon dissection"/ endoluminal view "virtual colonoscopy"/axial 2D imaging	**Other colonic disease:** n.r. **Safety:** n.r. **Extracolonic findings**: n.r. **Test failures:** n.r.
Van Gelder, 2002 The Netherlands	n = 50 High-risk asymptomatic	Colonoscopy	All Polyps: 54% (27/50) Polyps ≥ 5 mm: 20% (10/50)	**Sensitivity (100 mAs):** • All polyps: 59% • Polyps ≥ 5 mm: 90% **Specificity:** • All polyps: 26% • Polyps ≥ 5 mm: 55%	**Other colonic disease:** n.r. **Safety:** n.r. **Extracolonic findings**: n.r. **Test failures:** • CTC failures: Image quality decreased with decreasing radiation dose levels • Incomplete colonoscopies 0% **Other outcomes:** Median effective radiation dose of CTC (range) from review of 13 articles: 3.9 mSv (1.7-9.2 mSv)
Vogt et al, 2004 Germany	n = 115 Symptomatic	Colonoscopy	Cancer: 3.5% (4/115)* * Assuming 1 cancer per patient	**Sensitivity:** Lesions > 10 mm: 100% (assumed from per-polyp sensitivity of 100%) **Specificity:** • Overall lesions: 79% • Cancer: 100% • Polyps > 10 mm: 82% • Polyps 5-10 mm: 83% • Polyps < 5 mm: 75% • Lesions ≥ 5 mm: 84%	**Other colonic disease:** n.r. **Safety:** • No complications of CTC/colonoscopy • Radiation dose exposure: effective dose of 0.75 (0.1) mSv for men and 1.25 (0.1) mSv for women (determined by calculating the effective dose based upon the Computed tomography dose index) **Extracolonic findings**: n.r. **Test failures:** • CTC failure (moderate impairment) due to partial colonic collapse 3% (4/115) • Incomplete colonoscopy 3.5% (4/115) due to obstructive neoplasm (1), redundant bowel loops (2), colonic fixation by postoperative bowel adhesions (1)

Table 63   Summary of results of studies of accuracy of DCBE versus colonoscopy

Author & Year	Patient characteristics	DCBE characteristics	Reference standard	Prevalence	DCBE accuracy	Colonoscopy accuracy	Other outcomes
Irvine et al, 1988 Canada	n = 71 Symptomatic	Standard DCBE No sedation	Maximum diagnostic data available	Polyps: 36.6% (26/71) Cancer: 7% (5/71)	**Per-polyp sensitivity** (not explicit in article)**:** • All lesions (may include diverticular disease & inflammatory bowel disease): 43% • All lesions (in all $\geq$ 5 mm): 50% • Neoplasm: 77% • Cancer: 83% • Adenoma: 32% • Adenoma (in all $\geq$ 5 mm): 58% **Specificity:** All lesions $\geq$ 5 mm: 67%	**Sensitivity:** • All lesions: 67% • All lesions (in all $\geq$ 5 mm): 69% • Neoplasm: 93% • Cancer: 100% • Adenoma: 77% • Adenoma (in all $\geq$ 5 mm): 96% **Specificity:** All lesions $\geq$ 5 mm: 78%	**Other colonic disease:** • DD: 46.5%; Sens (DCBE/CC): 84%/50% • IBD: 8.5%; Sens (DCBE/CC): 33%/83% **Safety:** • FS/DCBE: MI in 1.4% (1/71)after bowel prep • colonoscopy/ Polypectomy: haemorrhage requiring blood transfusion in 1.4% (1/71) **Extracolonic findings**: n.r. **Test failures:** • DCBE failures: incomplete in 1% (1/71) of patients and suboptimal visualisation after DCBE and sigmoidoscopy in 18% of patients • Incomplete colonoscopy: 17% (12/71) and suboptimal visualisation in 30% of patients

Author & Year	Patient characteristics	DCBE characteristics	Reference standard	Prevalence	DCBE accuracy	Colonoscopy accuracy	Other outcomes
Durdey et al, 1987 UK	n = 66 Symptomatic	n.r.	Maximum diagnostic data available	Colonic abnormality: 65% (43/66) Adenomatous polyps: 17% (11/66) Cancer (Dukes A): 3% (2/66)	**Sensitivity:** • All colonic abnormality (cancer, Adenomas, DD, IBD): 56% (40-71%)* • Cancer: 0% (0/2) • Adenomatous polyp: 27% (3/11) **Specificity:** All colonic abnormality: 78% (56-93%)* * 95% CIs calculated from reported data	**Sensitivity:** • All colonic abnormality (Cancer, Adenomas, DD, IBD): 91% (78-97%)* • Cancer: 100% (2/2) • Adenomatous polyp: 91% (10/11) **Specificity:** All colonic abnormality: 91% (72-99%)* * 95% CIs calculated from reported data	**Other colonic disease:** • DD prevalence: 23%; Sens (DCBE/CC): 100%/80% • IBD: prevalence 21%; Sens (DCBE/CC): 36%/100% **Safety:** No complications of DCBE/colonoscopy **Extracolonic findings**: n.r. **Test failures:** • DCBE failures: incomplete 11% (7/66) • Incomplete colonoscopy 25% (16/86) **Other outcomes:** *Patient preference:* 74% preferred colonoscopy *Distress/discomfort:* DCBE 48%, colonoscopy 23%, p = 0.004

Author & Year	Patient characteristics	DCBE characteristics	Reference standard	Prevalence	DCBE Accuracy	Other outcomes
Rockey et al, 2004 USA	n = 89 Symptomatic	Standard DCBE No sedation	Colonoscopy +- histo-pathology (+/- repeat CC)	• Polyps: 33.7% (30/89) • Adenomas ≥ 10 mm: 12.4% (11/89) • Cancer: 5.6% (5/89)* * Assuming 1 cancer per patient	**Sensitivity:** *Per-polyp Sensitivity:* • Overall: 18% (12/66) • Polyps ≥ 10 mm: 27% • Polyps 6-9 mm: 33% • Polyps ≤ 5mm: 8% **Specificity:** *Per-patient specificity:* • Overall: 88% • Polyps > 10 mm: 100% • Polyps ≥ 6 mm: 97%	**Other colonic disease:** • Diverticula (ACBE/CC): 47.2%/ 20.2% • Colitis (ACBE/CC): 2.2%/2.2% • Vascular ectasia (ACBE/CC): 0/ 2.2% **Safety:** n.r. **Extracolonic findings:** n.r. **Test failures:** • DCBE failure: 9% grossly inadequate (9/100) • Incomplete colonoscopy 2% (2/100)

Table 65   Summary of characteristics and results of studies of patient preferences and quality of life associated with testing

Author & Year	Study design	Study Population	Outcomes	Study Quality
Akerkar et al, 2001 USA	**Objective:** To compare CTC versus colonoscopy for: • Patient tolerance • Patient preferences **Patient enrolment:** Prospective, single centre, Feb 1998 – Nov 1999 **Endpoints:** • QoL: symptoms of abdominal pain, discomfort, sense of disrespect • Patient preferences **Tests evaluated:** • *CTC:* helical CT scanner (single-slice?), supine scanning • *Comparator:* colonoscopy under conscious sedation **Design:** CTC 2-3 hrs before colonoscopy **Outcomes assessment:** • 3 assessments: - Immediately after CTC (health professional-administered questionnaire) - At the clinic after both colonoscopy and CTC (health professional-administered questionnaire) - Mailed in from home within 24 hours following both colonoscopy and CTC (self-administered questionnaire) before. • Instruments: - QoL: using 7-point Likert scale adapted from validated and reliable symptom impact questionnaire - Patient preferences: Modified time-trade-off technique: waiting time accepted for preferred test	**n = 295** (267 first assessment) **Exclusions:** 1.7% (11%) of 300 did not complete questionnaire Reasons for noncompletion: n.r. **Male**: 97% **Mean age**: 62.4 yrs **Inclusion criteria:** • CRC screening (35.3%) • Symptoms (hematochezia, positive FOBT, iron deficiency anaemia, personal or family history of colorectal neoplasia) (64.7%) **Other characteristics:** Veterans of Northern California (mainly men > 50 years of age) **Exclusion criteria:** Pregnancy	**Quality of Life:** *For both time points:* • Pain scores higher for CTC than colonoscopy (p < 0.01) • Discomfort scores higher for CTC than colonoscopy (p < 0.01) • Disrespect scores higher for CTC than colonoscopy (p < 0.01) **Patient preference:** • 63.7% of patients preferred colonoscopy to CTC • 91.2% had a strong preference for colonoscopy (scores 1+2 on scale of 1-7 (1 = strongest) • Time trade-off: patients would wait an average of 4.9 weeks/1 week (after 24 hrs assessment) to undergo colonoscopy rather than CTC	**FAIR QUALITY** **Sample** • Consecutive sample • Relevance – 35% screening **Eligibility criteria**: explicit **Data collection methods**: Adequately described **Outcome assessment tool:** • Adequately described • QoL: Adapted from validated instrument **COMPARISON:** Direct comparison of CTC with colonoscopy

Author & Year	Study design	Study Population	Outcomes	Study Quality

Gluecker et al, 2003 USA	**Objective:** To compare CTC versus DCBE and colonoscopy for:
	• Patient tolerance
	• Patient preferences
	Patient enrolment: prospective, single centre, enrolment dates n.r.
	Endpoints:
	• Patient quality of life (tolerance): physical discomfort; inconvenience
	• Patient preference, patient satisfaction
	Tests evaluated:
	• *CTC:* single/multi-slice CT scanner, supine and prone scanning, spasmolytic (glucagon)
	• *Colonoscopy:* standard procedure, sedation
	• *DCBE:* standard procedure, sedation not routinely used, glucagon for pain
	Design: 2 groups:
	• Group 1: CTC prior colonoscopy on same day
	• Group 2: CTC prior DCBE on same day
	Outcomes assessment:
	• 1 assessment by self-administered questionnaire after both procedures, to be returned by mail
	• Instruments:
	  - Questionnaire on QoL/patient preferences, 11 questions, not validated
	  - Patient preference: one question 'which exam did you prefer?'
		Group 1: n = 696, 74% response rate
		Group 2: n = 617, 87% response rate
		Exclusions:
		9% (7) of 78 excluded (8% (6) did not complete questionnaire, 1% (1) did not complete DCBE)
		Male: 63% (group 1); 49% (group 2)
		Median age (range): group 1: 65 yrs (41-84 yrs), group 2: 64 yrs (50-82yrs
		Inclusion criteria:
		• Referred to colonoscopy or DCBE:
		• 50 years of age (except 3 patients) AND
		• 1st degree relative or prior personal history of colorectal neoplasia, or new onset of asymptomatic anaemia
		Exclusion criteria:
		• gastrointestinal symptoms
		• recent overt gastrointestinal bleeding
		• IBD
		• familial adenomatous polyposis
		• bowel resection/polyp removal within the prior 2 months
			Quality of Life:
			CTC versus colonoscopy: no stat sig difference in level of discomfort
			CTC vs DCBE: more discomfort experienced in DCBE vs CTC (p < 0.001)
			Patient preference:
			• 72% preferred CTC, 5% preferred CC (p < 0.001)
			• 97% preferred CTC, 0.4% preferred DCBE (p < 0.001)
				FAIR QUALITY
				Sample:
				• Consecutive sample
				• Relevant population
				Eligibility criteria: explicit
				Data collection methods: Adequately described
				Outcome assessment tool:
				• Adequately described
				• QoL: no validated instrument
				COMPARISON:
				• Direct comparison of CTC with colonoscopy
				• Direct comparison of CTC with DCBE

Author & Year	Study design	Study Population	Outcomes	Study Quality
Ristvedt et al, 2003 USA	**Objective:** To compare bowel preparation, CTC and colonoscopy for: • Patient tolerance • Patient preferences **Patient enrolment:** Prospective, single centre, enrolment July 2000 – May 2001 **Endpoints:** • QoL: Pain/discomfort, embarrassment, difficulty, overall ('unpleasant') • Preferences: Influence of Qol on willingness to perform procedures, preference, strength of preference **Procedures evaluated:** • *CTC:* multirow detector CT scanner, supine and prone scanning • *Comparator:* Routine colonoscopy, sedation **Design:** CTC before colonoscopy **Outcomes assessment:** • 3 assessments: pretest (1), post-CTC (1), post CTC and colonoscopy (1) • First two assessments face-to-face, 3rd telephone interview • Instruments: Questionnaire with 5 response choices	**n = 120** **Exclusions:** None reported **Male:** 44% **Mean age** (SD): 58 (8.2) yrs **Inclusion criteria:** High-risk patients (95%) defined as: • History of prior polyps; family/personal history of CRC (46%/55) • Currently suspected polyps (22%/22) • Rectal bleeding (13%/16) • Positive hemoccult stool (14%/17) • Other reasons for colonoscopy (5%): • IBD, diarrhea, constipation, screening **Exclusion criteria:** N.r.	**Quality of Life:** • Pre-examination subjects expected more pain and embarrassment with colonoscopy than CTC, $p < 0.05$ • Postexamination subjects reported higher pain, embarrassment and difficulty scores with CTC than colonoscopy, $p < 0.001$ • Overall rating 'unpleasant', 95% for both tests • Bowel preparation: more unpleasant than CTC and colonoscopy procedures, $p < 0.001$ **Patient preference:** • 58% of patients preferred CTC, 14% preferred colonoscopy, 28% no preference • Strength of preference: CTC: 65% strong/very strong; colonoscopy: 47% strong/very strong	**FAIR QUALITY** **Sample:** • Consecutive • Relevant **Eligibility criteria:** Explicit **Data collection methods:** Adequately described **Outcome assessment tool:** • Adequately described • QoL: No validated instrument **COMPARISON:** Direct comparison of CTC with colonoscopy

Author & Year	Study design	Study Population	Outcomes	Study Quality
Svensson et al, 2002 Sweden	**Objective:** to prospectively evaluate patient acceptance of CTC compared with CC in patients with or suspected of having colorectal disease **Patient enrolment:** Prospective, single centre, enrolment May 1998 – Sep 1999 **Endpoints:** • QoL: Difficulty, discomfort, embarrassment, pain, • Patient preference **Procedures evaluated:** • *CTC:* single CTC, supine and prone scanning, spasmolytic • *Colonoscopy:* standard procedure, sedatives and analgesics (95%) **Design:** CTC before colonoscopy **Outcomes assessment:** • 3 assessments: after CTC, directly after colonoscopy, 1 day after colonoscopy • self-administered questionnaires • Instruments: Questionnaire, QoL with 4 response choices	**n = 111,** response rate 94-95% for each questionnaire **Exclusions:** None reported **Male:** 59% **Median age (range):** 66 (19-86) yrs **Inclusion criteria:** Referred for colonoscopy: • Symptoms (positive FOBT, rectal bleeding anemia, abdominal pain and/or diverticulitis, diarrhea) (72%) • Suspected malignancy (4.5%) • Previous finding on DCBE (10%) • Colitis or polyp surveillance (13.5%) **Exclusion criteria:** • Acute colitis or enterostomy • Women <50 yrs	**Quality of Life:** • 44% found bowel preparation 'fairly' or 'very difficult' • More patients found colonoscopy 'more difficult overall' than CTC (69% of n = 71 (64%), p = 0.002) • More patients found colonoscopy 'more unpleasant' than CTC (71% of n = 76 (68%), p = 0.0008) • 86% found any procedure 'more embarrassing' • More patients found colonoscopy 'fairly' or 'very painful' than CTC (29% vs 6%, p < 0.00001) • More patients found more discomfort with airfilling at CTC than w instrumentation at colonoscpy (40% vs 21%, p = 0.02) **Patient preference:** • 82% vs 18% preferred CTC vs colonoscopy (of n = 68 expressing preference, p < 0.0001) • More patients would undergo CTC again than colonoscopy (79% vs 70%)	**FAIR QUALITY** **Sample:** • Consecutive • Relevant **Eligibility criteria:** Explicit **Data collection methods:** Adequately described **Outcome assessment tool:** • Adequately described • QoL: No validated instruments **COMPARISON:** Direct comparison of CTC with colonoscopy

Author & Year	Study design	Study Population	Outcomes	Study Quality

Taylor et al, 2005
 	
UK
	Objective: To compare CTC versus DCBE for:
	• Patient preference
	• Patient tolerance
	• Patient satisfaction
	Patient enrolment: July 2002 – December 2003
	Endpoints:
	• QoL: perceived pain; satisfaction, worry, physical discomfort, tolerance (f/u),
	• Patient acceptance/preference
	Tests evaluated:
	• *CTC:* multi-slice CT scanner, supine and prone scanning, spasmolytic
	• *DCBE:* standard procedure, spasmolytic
	Design: CTC before DCBE on same day
	Outcomes assessment:
	• During (perceived pain) and after each procedure, 1 follow-up assessment
	• Perceived pain measured during procedures + questionnaire + visual analogue scale (self-administered)
	• Instruments:
	  - Perceived pain: handheld counting device
	  - QoL: 25 items with 7-point Likert scale, representing 3 components, previously validated, + visual analogue scale, Tolerance assessed with a one week follow-up questionnaire
	  - Patient preferences: questions on 'would you have it again', preference and acceptance assessed with a one week follow-up questionnaire
		n = 78, response rate 93% (71/78)
		Exclusions: 9% (7) of 78 excluded (8% (6) did not complete questionnaire, 1% (1) did not complete DCBE)
		Male: 44%
		Median age (range): 70 (61-87) yrs;
		Inclusion criteria: Referred to DCBE due to symptoms of colorectal cancer (change in bowel habit, iron deficiency anemia, palpable abdominal mass)
		Exclusion criteria: N.r.
			Quality of Life: *CTC vs DCBE*:
			• More satisfied with CTC than DCBE (p = 0.03)
			• No stat sig difference in worry
			• Less physical discomfort for CTC than DCBE (p = 0.03)
			• Significantly less pain registered during CTC than during DCBE (proportion clicking at least once: 38% vs 19%, p = 0.007)
			• More tolerated CTC (100%) than DCBE (83%) well/fairly well (p = 0.002)
			Patient preference:
			• 83% would have CTC again vs 36% would have DCBE again (p < 0.001)
			• 100% (of n = 52) preferred CTC as future test over DCBE (p < 0.001)
			• 98% (of n = 45) preferred CTC as most acceptable over DCBE (p < 0.001)
				HIGH QUALITY
				Sample:
				• Consecutive sample
				• Relevant population
				Eligibility criteria: Explicit
				Data collection methods: Adequately described
				Outcome assessment tool:
				• Adequately described
				• QoL: validated instrument
				COMPARISON: Direct comparison of CTC with DCBE

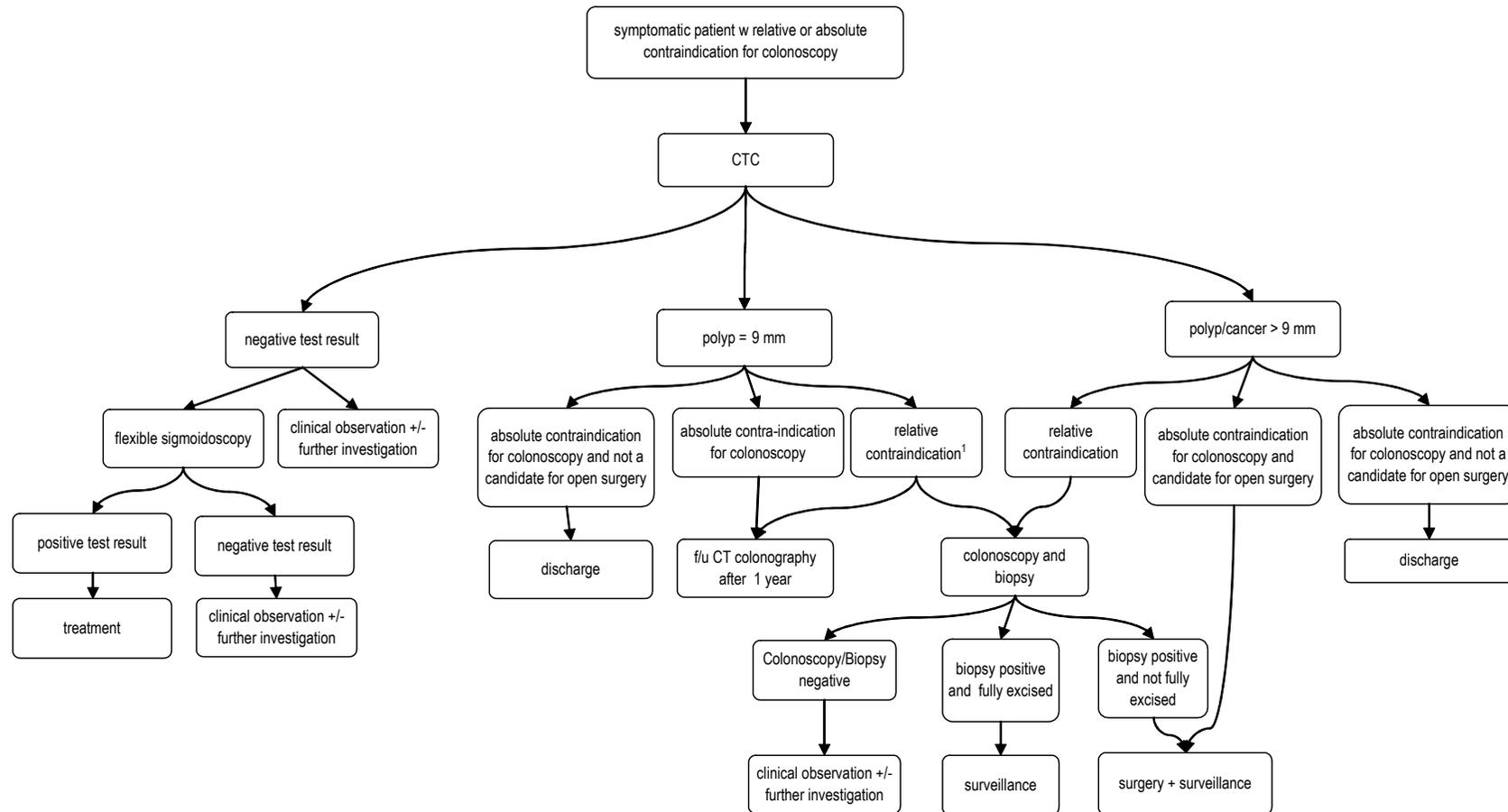| Author & Year	Study design	Study Population	Outcomes	Study Quality

Taylor et al, 2003b UK	**Objective:** to compare CTC versus colonoscopy, DCBE or flexible sigmoidoscopy (FS) for:
	• Patient preference
	• Patient satisfaction
	• Patient tolerance/quality of life
	Patient enrolment: Prospective, multi-centre, enrolment April 2001 – April 2002
	Endpoints:
	• QoL: satisfaction, worry, physical discomfort, tolerance (f/u),
	• Patient preferences
	Tests evaluated:
	• *CTC:* multi-slice CT scanner, supine and prone scanning, Buscopan in 74% (125/168)
	• *Colonoscopy:* standard procedure; IV sedation, analgesia and spasmolytic routinely
	• *FS:* standard procedure, no sedation, spasmolytic
	• *DCBE:* standard procedure
	Design: group 1: CTC before Endoscopy (colonoscopy or FS); group 2: DCBE (indirect comparison with CTC)
	Outcomes assessment:
	• 1 assessment after each CTC/Endoscopy/DCBE, 1 follow-up assessment (CTC and endoscopy)
	• Questionnaire + visual analogue scale (self-administered)
	• Instruments:
	  - QoL: Main assessment: 25 items w 7-point Likert scale, representing 3 components, previously validated + visual analogue scale; F/u assessment (group 2 only): 1 question on tolerance
	  - Patient preferences: questions on 'would you have it again', preference and acceptance (f/u)
		Group 1: n = 168, 86% response rate (144/168) male 50%, median age 65yrs
		Group 2: n = 140, 90% response rate (14/140) male 55%, median age 62yrs
		Inclusion criteria:
		Group1: CTC and colonoscopy /flexible sigmoidoscopy
		• High risk (f/u of polyps, family history, f/u of IBD) (19%)
		• Symptoms (rectal bleeding, change in bowel habit, iron deficiency anaemia, palpable abdominal mass, polyps seen on DCBE) (64.7%)
		Group 2: DCBE:
		• High risk (family history) (1.4%)
		• Symptoms (rectal bleeding, change in bowel habit, iron deficiency anemia, palpable abdominal mass) (98.6%)
		Exclusion criteria: n.r.
			Quality of Life:
			CTC vs colonoscopy:
			• Less satisfied with CTC than colonoscopy
			• No difference for 'worry'
			• Less physical discomfort for CTC than colonoscopy (p = 0.002)
			• More patients tolerated CTC than colonoscopy (f/u) (p = 0.005)
			CTC vs DCBE:
			• More satisfied with CTC than DCBE (p < 0.001)
			• Less worried with CTC than DCBE (p < 0.001)
			• More physical discomfort for DCBE than CTC (p = 0.005)
			Patient preference:
			• More prefer to have CTC over colonoscopy in the future (73% (40/55) vs 27% (15/55) of 61% expressing preference, p = 0.001)
			• More found CTC more acceptable than colonoscopy (70% vs 30%, of 67% finding one test more acceptable, (p = 0.003)
			• Sex, age, history of endoscopic intervention had no effect on outcomes
				HIGH QUALITY
				Sample:
				• Consecutive sample
				• Relevant population
				Eligibility criteria: Explicit
				Data collection methods: Adequately described
				Outcome assessment tool:
				• Adequately described
				• QoL: validated instrument
				COMPARISON:
				• Direct comparison of CTC with colonoscopy
				• Indirect comparison with DCBE

Author & Year	Study design	Study Population	Outcomes	Study Quality

Taylor et al, 2003c
 	
UK
 	
Duplicate of group 1 from Taylor et al 2003b
	Objective: to compare CTC versus colonoscopy or flexible sigmoidoscopy (FS) for:
	• cardiovascular effects
	• perceived pain
	Patient enrolment: Prospective, multi-centre, enrolment April 2001 – April 2002
	Endpoints:
	• Physical observations: pulse, blood pressure, oxygen saturation, Holter ECG
	• QoL: Perceived pain
	Tests evaluated:
	• *CTC:* 4-detector CT scanner, supine and prone scanning, group randomised to spasmolytic or not
	• *Comparator:* Standard flexible sigmoidoscopy
	• Colonoscopy: standard, with sedative and analgesic (11% declined), nasal oxygen
	Design: CTC before colonoscopy
	
	Outcomes assessment: QoL: perceived pain measured during procedures by using a handheld counting device
		n = 144
		Exclusions:
		None reported
		Male: 49%
		Mean age (range): 62 (34-84) yrs
		Inclusion criteria:
		• Referred for FS from rectal bleeding clinic (28%)
		• Referred for colonoscopy for:
		  - Symptoms (48%/ rectal bleeding, change in bowel habits, iron-deficiency anaemia)
		  - Asymptomatic (21%/ f/u of polyp or IBD/family history of CRC)
		  - Existence of palpable abdominal mass, polyp present at DCBE (3%)
		Exclusion criteria: n.r.
			Quality of Life:
			• Patients registered more pain or discomfort more often during CC than during CTC (RR = 1.89, p = 0.03)
			• No stat sig difference re pain or discomfort during FS and during CTC
			Patient preference: n.r.
				HIGH QUALITY
				
				Sample:
				• Consecutive
				• Relevant
				Eligibility criteria: Explicit
				Data collection methods:
				
				• Adequately described
				Outcome assessment tool:
				• Adequately described
				• QoL: pain measured with counting device
				COMPARISON: Direct comparison of CTC with colonoscopy

Author & Year	Study design	Study Population	Outcomes	Study Quality
Thomeer et al, 2002 Belgium	**Objective:** to compare CTC versus colonoscopy for: • Patient preference • Patient tolerance/quality of life **Patient enrolment:** Prospective single centre Jan 2000 – Jan 2001 **Endpoints:** • QoL: Discomfort • Patient preferences **Procedures evaluated:** • *Bowel cleansing:* electrolyte solution/polyethylene glycol • *CTC:* multidetector CTC, supine and prone scanning, bowel relaxant IV • *Comparator:* colonoscopy: standard, with sedation **Design:** CTC before colonoscopy **Outcomes assessment:** • 1 assessment 2-3 hrs after CTC and colonoscopy • Self-administered questionnaire • Instruments: QoL: Questionnaire with 10-point scale	**n = 124** **Exclusions:** None reported **Male:** 55% **Mean age** (range): 64 (34-89) yrs **Inclusion criteria:** • Age 20-80 years, ability to give informed consent AND • Indication for colonoscopy: • Primary colorectal screening (16%) (assumed average risk) • Secondary colorectal screening (45%/ f/u polyposis coli/f/u colorectal tumour) • Symptoms (30%/ anal bleeding or melena, abdominal pain, chainge in stool habit, weight loss, anemia) • Tumor search, other reasons (9%) **Exclusion criteria:** • IBD • pregnancy	**Quality of Life:** • Higher degree of discomfort for colonoscopy than CTC (3.5 vs 3, no stat significance given) • Bowel preparation most uncomfortable of procedures (p < 0.05) **Patient preference:** 71% preferred CTC, 24% colonoscopy, 5% no preference, if asked for preference if f/u is needed	**FAIR QUALITY** **Sample:** • Consecutive • Relevant **Eligibility criteria:** Explicit **Data collection methods:** Adequately described **Outcome assessment tool:** • Adequately described • QoL: No validated instrument **COMPARISON:** Direct comparison of CTC with colonoscopy

Author & Year	Study design	Study Population	Outcomes	Study Quality

Van Gelder et al 2004
 	
The Nether-lands
	Objective: to compare CTC versus colonoscopy for short- and midterm patients
	Patient enrolment: Prospective 2 centre study, enrolment Oct 2000 – Sep 2002
	Endpoints:
	• QoL: Pain, embarrassment, discomfort
	• Patient preferences
	Procedures evaluated:
	• *CTC:* multidetector CTC, supine and prone scanning, IV spasmolytic
	• *Comparator:* colonoscopy: standard procedure, w sedative in 25%, w sedatives and analgesics (49%)
	Design: CTC approx. 1 h before colonoscopy
	Outcomes assessment:
	• 5 assessments: 2 weeks before exams, 3 on day (before/after CTC, after colonoscopy), 5 weeks after
	• self-administered questionnaires
	• Instruments:
	  - QoL: Questionnaire with 5-point Likert scale
	  - Preference: Questionnaire with 7-point certainty scale
		n = 249
		Exclusions:
		14% (39) of 288 excluded (1% (1) no show, 4% (12) bowel prep failure, 7% (20) CTC failure, 2% (5) colonoscopy failure
		Male: 59%
		Mean age (SD): 56 (13) yrs
		Inclusion criteria:
		• Indication for colonoscopy:
		• High-risk asymptomatic (personal or familial history of colorectal cancer or polyps)
		Exclusion criteria:
		• Had colorectal polyps or cancer at recent examination
		• Colostomy after colorectal surgery
		• <18 y, no informed consent
			Quality of Life:
			• More experienced 'severe pain' during colonoscopy than during CTC directly (34% vs 3%) and 5 weeks after (p < 0.001)
			• More discomfort for colonoscopy than CTC directly and 5 weeks after (p < 0.001)
			• Similar level of embarrassment for CTC as for colonoscopy directly and 5 weeks after
			Patient preference:
			• More patients preferred CTC over colonoscopy directly after (71% vs 19%, p < 0.001) and 5 weeks after colonoscopy (61% vs 31%, p < 0.001)
			• Painful and embarrassing CTC determinant of preference for colonoscopy
			• Painful colonoscopy determinant of preference for CTC
			• Detection of a polyp on colonoscopy determinant of preference for colonoscopy
				FAIR QUALITY
				Sample:
				• Consecutive
				• Relevant
				Eligibility criteria: Explicit
				Data collection methods: Adequately described
				Outcome assessment tool:
				• Adequately described
				• QoL: No validated instrument
				COMPARISON: Direct comparison of CTC with colonoscopy

Appendix E   Clinical flowcharts

Figure 9   Clinical flowchart of symptomatic patients not eligible for colonoscopy – CTC path

symptomatic patient w relative or absolute contraindication for colonoscopy

CTC

negative test result

polyp = 9 mm

polyp/cancer > 9 mm

flexible sigmoidoscopy

clinical observation +/- further investigation

positive test result

negative test result

treatment

clinical observation +/- further instigation

absolute contraindication for colonoscopy and not a candidate for open surgery

absolute contra-indication for colonoscopy

relative contraindication[1]

relative contraindication

absolute contraindication for colonoscopy and candidate for open surgery

absolute contraindication for colonoscopy and not a candidate for open surgery

discharge

f/u CT colonography after 1 year

colonoscopy and biopsy

discharge

Colonoscopy/Biopsy negative

biopsy positive and fully excised

biopsy positive and not fully excised

clinical observation +/- further investigation

surveillance

surgery + surveillance

1 Pathway for patient with relative contraindication to colonoscopy will depend on clinical judgement eg. size 6-9 mm, high risk patient
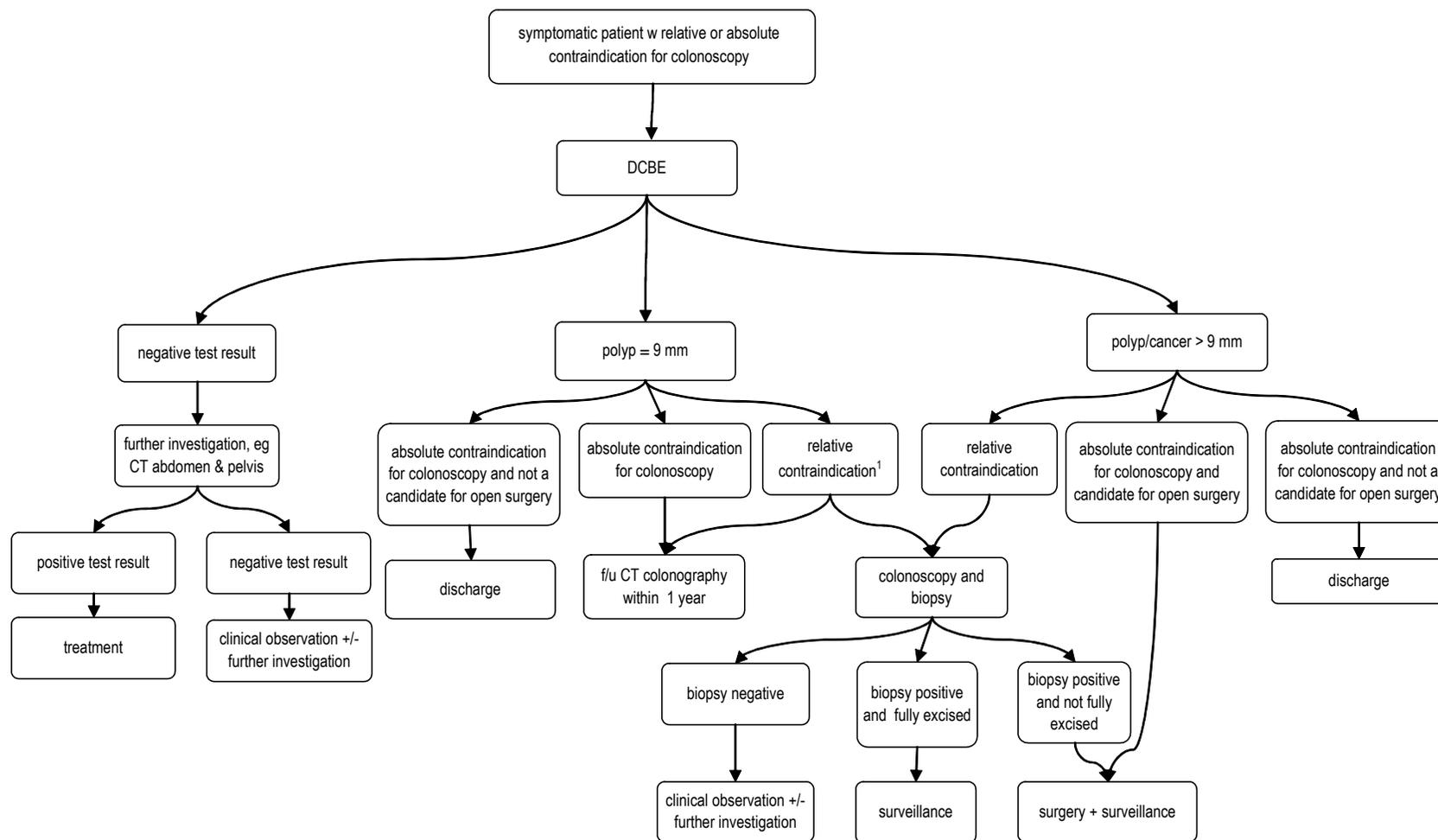
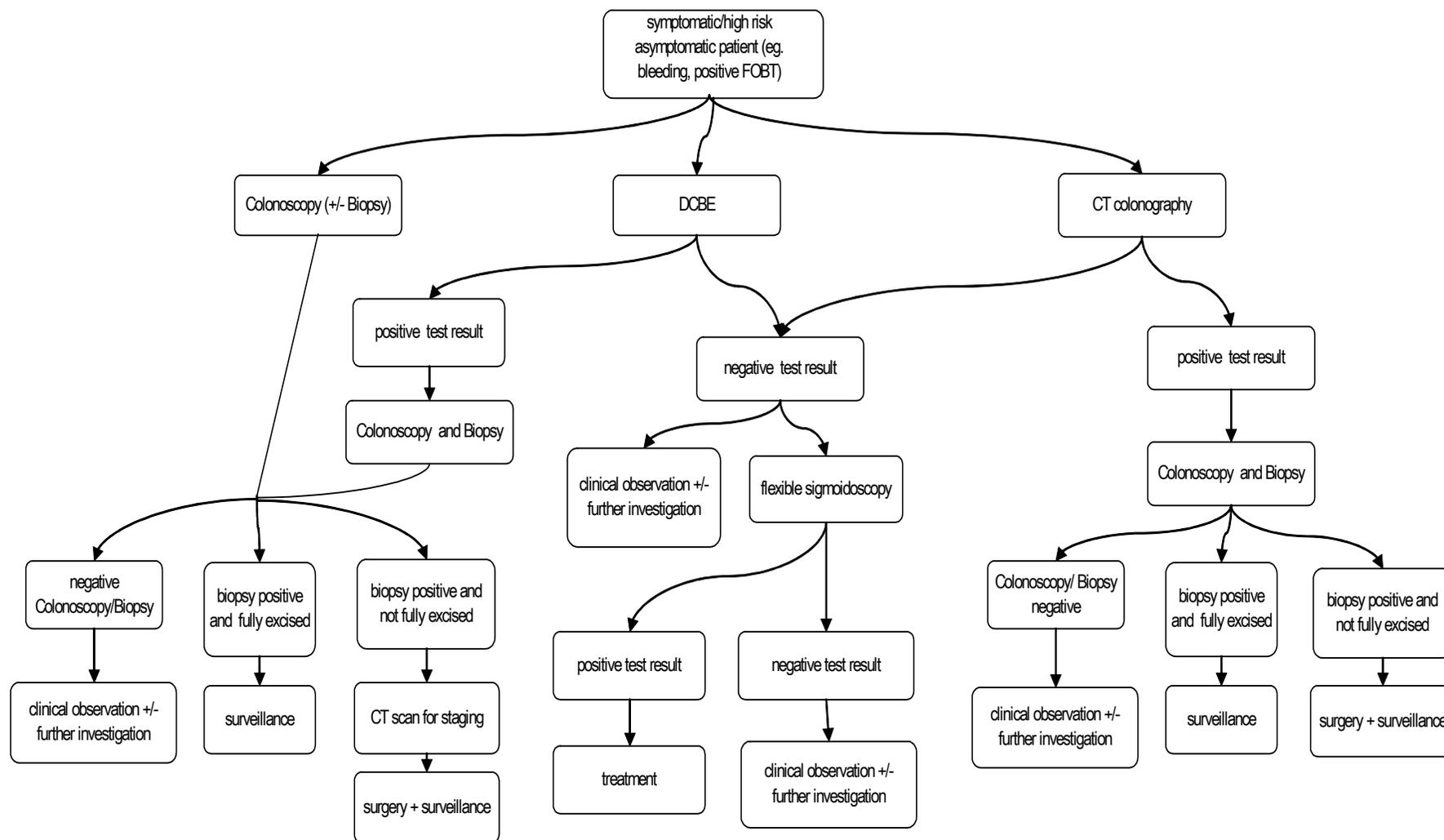**Figure 10   Clinical flowchart of symptomatic patients not eligible for colonoscopy – DCBE path**

1 Pathway for patient with relative contraindication to colonoscopy will depend on clinical judgement eg. size 6-9 mm, high risk patient

Figure 11   Clinical flowchart of symptomatic patients eligible for colonoscopy

Appendix F   DCBE search strategy

Electronic databases of published research (Table 66) were searched for original research papers, including systematic reviews. The search strategies shown in Tables 67 to 70 were used to identify papers in the databases described in Table 47.

Table 66 Electronic databases searched

Database	Period covered
Medline	1994 – June 2005
EMBASE	1994 – June 2005
Premedline	As at June 24 2005
Current Contents	June 24 2005 (previous 6 months)
The Cochrane Library Controlled Clinical Trials Registry	Issue 2, 2005

Table 67 Medline search strategy

Number	Search Strategy
1	*Barium Sulfate/du
2	exp enema/
3	1 and 2
4	exp Colonic Diseases/di
5	exp colonic polyps/di
6	4 or 5
7	3 and 6

Table 68 EMBASE search strategy

Number	Search History
1	exp Barium Enema/
2	exp Colon Disease/di
3	1 and 2
4	trial.mp.
5	3 and 4

Table 69 Premedline search strategy

Number	Search History
1	((barium adj enema) or DCBE or ACBE).mp

Table 70 Current Contents & the Cochrane Library controlled Clinical Trials Registry search strategy

Number	Search History
1	((barium adj enema) or DCBE or ACBE).mp
2	colo*.mp
3	1 and 2
4	(trial* or stud*).mp
5	3 and 4

The search strategy retrieved a total of 328 nonduplicate citations. These were evaluated by two reviewers to determine whether they met the eligibility criteria outlined in Table 71.

Table 71 Study exclusion criteria

1. Not an appropriate clinical study

Reports excluded were those describing animal, laboratory or scientific studies, technical reports or case reports. Nonsystematic narrative reviews, letters and conference abstracts were also excluded in this category.

Case series where the use or reporting of a reference standard was based on the DCBE result (positive/negative) were excluded. Case-control studies where patients were selected for inclusion in the study based on their known disease status were excluded. Retrospective case referent studies (reporting on subjects all known to have the condition of interest) were excluded.

2. Wrong patient group

Studies were to include symptomatic patients being investigated for colorectal abnormalities. Studies with < 10 symptomatic patients undergoing DCBE were excluded.

3. Wrong diagnostic test

Studies were to perform DCBE.

4. Wrong reference standard

Studies were to use colonoscopy or surgical findings as the reference standard.

5. Wrong outcomes

Studies had to report on at least one of the following:

- diagnostic accuracy with sufficient data to calculate sensitivity and/or specificity
- changes in clinical management
- patient outcomes (morbidity, mortality, adverse events, quality of life)

6. Not in English

Due to time constraints, only studies published in English were eligible for inclusion.

Two of the identified studies were already included in the search for CTC studies. Based on the eligibility criteria, 322 citations were excluded from the review. The reasons for exclusion are listed in Table 72.

Table 72 Reasons for exclusion

Reason for exclusion	Frequency	%[1]
1. Not an appropriate clinical study	135	41%
2. Wrong patient group	33	10%
3. Wrong diagnostic test	46	14%
4. Wrong reference standard	90	28%
5. Wrong outcomes	8	3%
6. Not in English	10	3%
Total	322	99%

1 Percentage of frequency is calculated as a percentage of the total 326 citations identified.

As only four studies were included in this search for DCBE studies, the search strategy was extended and two further searches were undertaken to identify systematic reviews and primary studies published after the systematic review by de Zwart et al (2001) identified in the original DCBE search. Both searches covered the years 2000 to 2005. The search for systematic reviews combined the text word colo$.mp with the title word barium enema.ti and was restricted to 'review articles'; this search retrieved 21 studies, none of which were systematic reviews and not considered in this review. The search for primary studies used the very sensitive search strategy for studies of diagnosis developed by Haynes & Wilczynski (2004) and identified 285 studies, of which none met criteria for inclusion in the current review.

Abbreviations

AIHW	Australian Institute of Health and Welfare
CI	Confidence interval
CRC	Colorectal cancer
CT	Computed tomography
CTC	Computed tomography colonography
DCBE	Double contrast barium enema
DHA	Department of Health and Ageing
HIC	Health Insurance Commission
MBS	Medicare Benefits Schedule

References

Akerkar, G. A., Yee, J., Hung, R., McQuaid, K. 2001, 'Patient experience and preferences toward colon cancer screening: a comparison of virtual colonoscopy and conventional colonoscopy', *Gastrointestinal Endoscopy*, 54 (3), 310-315.

American Joint Committee on Cancer (AJCC). 2002, *Cancer Staging Manual,* 6th edition. New York, NY: Springer, 113-124.

Armstrong, K., O'Connell, D.L., Leong, D., Spigelman, A.D., Armstrong, B.K. 2004, *The New South Wales colorectal cancer care survey- Part 1 surgical management.* The Cancer Council NSW.

Australian Bureau of Statistics. 2005, *Life tables, New South Wales, 2002-2004*, cat.no. 3302.1.55.001; Available at: http://www.abs.gov./Ausstats/abs@.nsf/ [accessed on 7 December 2005]

Australian Institute of Health and Welfare (AIHW). 2005, *Interactive national hospital morbidity data (data cubes).* Available at: http://www.aihw.gov.au/hospitals/datacubes/index.cfm [accessed on 10 August 2005]

Bell, J., Coates, M., Day, P., Armstrong, B. 1996, *Colorectal cancer in NSW in 1972 to 1993.* Cancer Council, NSW Health Department.

Bolin, T.D., Korman, M.G., Stanton, R., Talley, N., Newstead, G.L., Donnelly, N., Hall, W., Ho, M.T., Lapsley, H. 1999, 'Positive cost effectiveness of early diagnosis of colorectal cancer', *Colorectal disease,* 1 (2), 113-122.

Bond, J.H. 1993, 'Polyp guideline: diagnosis, treatment, and surveillance for patients with nonfamilial colorectal polyps', The Practice Parameters Committee of the American College of Gastroenterology, *Annals of Internal Medicine,* 119 (8), 836-843.

Bossuyt, P., Irwig, L.M., Glasziou, P. 2003, *Diagnostic test appraisal form*, Screening and Test Evaluation Program, School of Public Health, University of Sydney. Available at: http://www.health.usyd.edu.au/step/about/appraisal/ [Accessed on 15 June 2005]

Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee. 2005, *Australia's Bowel Cancer Screening Pilot and Beyond. Final evaluation report*, Department of Health and Ageing, October. Available at: http://www.cancerscreening.gov.au/bowel/bcaust/pilot.htm [Accessed on 15 November 2005].

Bowles, C.J., Leicester, R., Romaya, C., Swarbrick, E., Williams, C.B., Epstein, O.A. 2004, 'Prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow?' *Gut,* 53 (2), 277-283.

Brown, A.L., Skehan, S.J., Greaney, T., Rawlinson, J., Somers, S., Stevenson, G.W. 2001, 'Value of double-contrast barium enema performed immediately after incomplete colonoscopy.' *American Journal of Roentgenology,* 176 (4), 943-945.

Bruzzi, J.F., Moss, A.C., Brennan, D.D., MacMathuna, P., Fenlon, H.M. 2004, 'Colonic surveillance by CT colonography using axial images only', *European Radiology*, 14 (5), 763-767.

Bucher, H.C., Guyatt, G. H., Griffith, L. E., Walter, S. D. 1997, 'The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials', *Journal of Clinical Epidemiology*, 50 (6), 683-691.

Canadian Coordinating Office for Health Technology Assessment (CCOHTA). *Pre-Assessment Virtual Colonoscopy* [Internet]. Available at http://www.ccohta.ca [Accessed on 6 June 2005].

Centre for Devices and Radiological Health 2005. *Whole body scanning using computed tomography: What are the radiation risks from CT?* US Food and Drug Administration. Available at: http://www.fda.gov/cdrh/ct/risks.html. Last updated 05/04/2005 [Accessed on 8 Novemnber 2005].

Citarda, F., Tomaselli, G., Capocaccia, R., Barcherini, S., Crespi, M., Italian Multicentre Study Group. 2001, 'Efficacy in standard clinical practice of colonoscopic polypectomy in reducing colorectal cancer incidence', *Gut,* 48 (6), 812-815.

Coady-Fariborzian, L., Angel, L.P., Procaccino, J.A. 2004. 'Perforated colon secondary to virtual colonoscopy: report of a case', *Diseases of the Colon & Rectum*, 47 (7), 1247-1249.

Cohnen, M., Vogt, C., Beck, A., Andersen, K., Heinen, W., vom Dahl, S., Aurich, V., Haeussinger, D., Moedder, U. 2004, 'Feasibility of MDCT Colonography in ultra-low-dose technique in the detection of colorectal lesions: comparison with high-resolution video colonoscopy', *American Journal of Roentgenology*, 183 (5), 1355-1359.

Cotton, P. B., Durkalski, V. L., Pineau, B. C., Palesch, Y. Y., Mauldin, P. D., Hoffman, B., Vining, D. J., Small, W. C., Affronti, J., Rex, D., Kopecky, K. K., Ackerman, S., Burdick, J. S., Brewington, C., Turner, M. A., Zfass, A., Wright, A. R., Iyer, R. B., Lynch, P., Sivak, M. V., Butler, H. 2004, 'Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia', *JAMA,* 291 (14), 1713-1719.

de Zwart, I. M., Griffioen, G., Shaw, M. P., Lamers, C. B., de Roos, A. 2001, 'Barium enema and endoscopy for the detection of colorectal neoplasia: sensitivity, specificity, complications and its determinant', *Clinical Radiology*, 56 (5), 401-409.

Department of Health and Ageing (2006). *National hospital cost data collection, cost weights for AR-DRG Version 4.2, Round 7 (2002-03).* Australian Government - Department of Health and Ageing [On-line]. Available at: http://www.health.gov.au/internet/wcms/publishing.nsf/content/health-casemix-costing-fc_r7.htm [Accessed on 10 August 2005].

Department of Health and Ageing. *HealthWiz Database.* Data provided by the Medicare Benefits Branch 2005.

Department of Health and Ageing. *National Bowel Cancer Screening Program.* Available at http://www.cancerscreening.gov.au/bowel/bcaust/program.htm [Accessed on 2 November 2005].

Durdey, P., Weston, P. M., Williams, N. S. 1987, 'Colonoscopy or barium enema as initial investigation of colonic disease', *Lancet*, 2 (8558), 549-551.

Gedebou, T.M., Wong, R.A., Rappaport, W.D., Jaffe, P., Kahsai, D., Hunter, G.C. 1996, 'Clinical presentation and management of iatrogenic colon perforations,' *American Journal of Surgery,* 172 (5), 454-457.

Ginnerup Pedersen, B., Christiansen, T.E.M., Bjerregaard, N.C., Ljungmann, K., Laurberg, S. 2003, 'Colonoscopy and multidetector-array computed-tomographic colonography: detection rates and feasibility', *Endoscopy*, 35 (9), 736-742.

Gluecker, T. M., Johnson, C. D., Harmsen, W. S., Offord, K. P., Harris, A. M., Wilson, L. A., Ahlquist, D. A. 2003, 'Colorectal cancer screening with CT colonography, colonoscopy, and double-contrast barium enema examination: prospective assessment of patient perceptions and preferences', *Radiology*, 227 (2), 378-384.

Gluecker, T., Dorta, G., Keller, W., Jornod, P., Meuli, R., Schnyder, P. 2002, 'Performance of multidetector computed tomography colonography compared with conventional colonoscopy', *Gut*, 51 (2), 207-211.

Halligan, S., Altman, D. G., Taylor, S. A., Mallett, S., Deeks, J. J., Bartram, C. I., Atkin, W. 2005, 'CT colonography in the detection of colorectal polyps and cancer: systematic review, meta-analysis, and proposed minimum data set for study level reporting', *Radiology*, 237 (3), 893-904.

Hara, A. K., Johnson, C. D., MacCarty, R. L., Welch, T. J., Mccollough, C. H., Harmsen, W. S. 2001, 'CT colonography: single- versus multi-detector row imaging', *Radiology*, 219 (2), 461-465.

Hardcastle, J. D., Chamberlain, J. O., Robinson, M. H., Moss, S. M., Amar, S. S., Balfour, James, P. D., Mangham, C. M. 1996, 'Randomised controlled trial of faecal-occult-blood screening for colorectal cancer', *Lancet,* 348 (9040), 1472-1477.

Haynes, R. B. & Wilczynski, N. L. 2004, 'Optimal search strategies for retrieving scientifically strong studies of diagnosis from Medline: analytical survey', *BMJ,* 328 (7447), 1040.

Health Insurance Commission (HIC) 2005. *Medicare Benefits Schedule (MBS) Item Statistics Reports*. Available at: http://www.hic.gov.au/statistics/dyn_mbs/forms/ mbs_tab4.shtml [accessed on 10 August 2005]

Health Technology Advisory Committee, 2002. *Computed Tomographic Colonography (Virtual Colonoscopy)* [Internet], Minnesota Department of Health. Available at: http://www.health.state.mn.us/htac/colon.htm [Accessed on 6 June 2005].

Hoppe, H., Netzer, P., Spreng, A., Quattropani, C., Mattich, J., Dinkel, H. P. 2004, 'Prospective comparison of contrast enhanced CT colonography and conventional colonoscopy for detection of colorectal neoplasms in a single institutional study using second-look colonoscopy with discrepant results', *American Journal of Gastroenterology*, 99 (10), 1924-1935.

Howard, K., Salkeld, G. 2005, 'Measuring patient preferences for virtual and conventional colonoscopy as a diagnostic test in colorectal disease', 5[th] World Congress of the International Health Economics Association, July 10-13, Barcelona, 2005.

Iannaccone, R., Bria, E., Carbone, I., Trasatti, L., Piacentini, F., Lauro, S., Vecchione, A., Passariello, R. 2003, 'Contrast-enhanced computed tomographic colonography in the follow-up of colorectal cancer patients: a feasibility study', *European Radiology*, 13 (4), 883-889.

Iannaccone, R., Carbone, I., Catalano, C., Panebianco, V., Di Giulio, E., Schillaci, A., Passariello, R. 2002, 'Computed tomographic colonography (virtual colonoscopy): blinded prospective comparison with conventional colonoscopy for the detection of colorectal neoplasia', *Endoscopy*, 34 (6), 441-446.

Iannaccone, R., Laghi, A., Catalano, C., Mangiapane, F., Piacentini, F., Passariello, R. 2003, 'Feasibility of ultra-low-dose multislice CT colonography for the detection of colorectal lesions: preliminary experience', *European Radiology*, 13 (6), 1297-1302.

Institute for Clinical Systems Improvement, 2004. *Computed Tomographic Colonography for Detection of Colorectal Polyps and Neoplasms. Technology Assessment Report* [Internet]. Available at: http://www.icsi.org/index.asp [Accessed on 6 June 2005].

Interventional Procedures Advisory Committee (IPAC), 2004. *Interventional procedures consultation document - Computed tomographic colonography (virtual colonoscopy)* [Internet]. National Institute for Clinical Excellence. Available at: http://www.nice.org.uk/page.aspx?o=233209 [Accessed on 6 June 2005].

Irvine, E. J., O'Connor, J., Frost, R. A., Shorvon, P., Somers, S., Stevenson, G. W., Hunt, R. H. 1988, 'Prospective comparison of double contrast barium enema plus flexible sigmoidoscopy v colonoscopy in rectal bleeding: barium enema v colonoscopy in rectal bleeding', *Gut*, 29 (9), 1188-1193.

Irwig L, Macaskill P, Glasziou P & Fahey M, 1995, 'Meta-analytic methods for diagnostic test accuracy', *Journal of Clinical Epidemiology*, 48 (1), 119-130.

Jaeschke, R., Guyatt, G., Sackett, D.L., 1994, 'Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid?' Evidence-Based Medicine Working Group, *JAMA*, 271 (5), 389-391.

Johnson, C. D., MacCarty, R. L., Welch, T. J., Wilson, L. A., Harmsen, W. S., Ilstrup, D. M., Ahlquist, D. A. 2004, 'Comparison of the relative sensitivity of CT colonography and double-contrast barium enema for screen detection of colorectal polyps', *Clinical Gastroenterology & Hepatology*, 2 (4), 314-321.

Johnson, C. D., Toledano, A. Y., Herman, B. A., Dachman, A. H., McFarland, E. G., Barish, M. A., Brink, J. A., Ernst, R. D., Fletcher, J. G., Halvorsen, R. A. J., Hara, A. K., Hopper, K. D., Koehler, R. E., Lu, D. S., Macari, M., MacCarty, R. L., Miller, F. H., Morrin, M., Paulson, E. K., Yee, J., Zalis, M., American College of Radiology Imaging Network 2003, 'Computerized tomographic colonography: performance evaluation in a retrospective multicenter setting', *Gastroenterology*, 125 (3), 688-695.

Koukari A. 2005, *The National Bowel Screening Pilot,* Screening and Test Evaluation Program seminar, School of Public Health, The University of Sydney, 24 August 2005.

Ladabaum, U., Song, K., Fendrick, A.M. 2004, 'Colorectal neoplasia screening with virtual colonoscopy: when, at what cost, and with what national impact?' *Clinical Gastroenterology & Hepatology*, 2 (7), 554-563.

Laghi, A., Iannaccone, R., Bria, E., Carbone, I., Trasatti, L., Piacentini, F., Laro, S., Vecchione, A., Passariello, R. 2003, 'Contrast-enhanced computed tomographic colonography in the follow-up of colorectal cancer patients: a feasibility study', *Eur Radiol*, 13(4), 883-889.

Laghi, A., Iannaccone, R., Carbone, I., Catalano, C., Panebianco, V., Di Giulio, E., Schillaci, A., Passariello, R. 2002, 'Computed tomographic colonography (virtual colonoscopy): blinded prospective comparison with conventional colonoscopy for the detection of colorectal neoplasia', *Endoscopy*, 34 (6), 441-446.

Lieberman, D. A., Weiss, D. G., Bond, J. H., Ahnen, D. J., Garewal, H., Chejfec, G., Harford, W. V., Provenzale, D., Sontag, S., Schnell, T., Durbin, T. E., Nelson, D. B., Ewing, S. L., Triadafilopoulos, G., Ramirez, F. C., Lee, J. G., Collins, J. F., Fennerty, B., Johnston, T. K., Corless, C. L., McQuaid, K. R., Sampliner, R. E., Morales, T. G., Fass, R., Smith, R., Maheshwari, Y. 2000, 'Use of colonoscopy to screen asymptomatic adults for colorectal carcinoma', N *Engl J Med*, 343 (3), 162-168.

Loeve, F., Brown, M. L., Boer, R., van Ballegooijen, M., van Oortmarssen, G. J., Habbema, J. D. 2004, 'Endoscopic colorectal cancer screening: a cost-saving analysis', *Journal of the National Cancer Institute,* 92 (7), 557-563.

Macari, M., Bini, E. J., Xue, X., Milano, A., Katz, S. S., Resnick, D., Chandarana, H., Krinsky, G., Klingenbeck, K., Marshall, C. H., Megibow, A. J. 2002, 'Colorectal neoplasms: prospective comparison of thin-section low-dose multi-detector row CT colonography and conventional colonoscopy for detection', *Radiology*, 224 (2), 383-392.

McGrath, J.S., Ponich, T.P., Gregor, J.C. 2002, 'Screening for colorectal cancer: the cost to find an advanced adenoma', *American Journal of Gastroenterology*, 97 (11), 2902-2907.

McLeish, J. A., Thursfield, V. J., Giles, G. G. 2002. 'Survival from colorectal cancer in Victoria: 10-year follow up of the 1987 management survey,' *ANZ Journal of Surgery*, 72 (5), 352-356.

Medical Advisory Secretariat, 2003. *Computed Tomographic Colonography [Virtual Colonoscopy] Health Technology Literature Review*, Ministry of Health and Long-Term Care, Ontario, Canada.

Morrin, M. M., Farrell, R. J., Kruskal, J. B., Reynolds, K., McGee, J. B., Raptopoulos, V. 2000, 'Utility of intravenously administered contrast material at CT colonography', *Radiology*, 217 (3), 765-771.

Moses, L. E., Shapiro, D., Littenberg, B. 1993, 'Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations', *Statistics in Medicine,* 12 (14), 1293-1316.

MSAC (Medical Services Advisory Committee) 2002. *Horizon Scanning 001: Virtual Colonoscopy*. Department of Health and Ageing, Canberra.

MSAC (Medical Services Advisory Committee) 2004. *Faecal occult blood testing for population health screening, MSAC reference 18*. Available at: www.health.gov.au/msac [Accessed on 2 November 2005] Commonwealth of Australia.

MSAC (Medical Services Advisory Committee (MSAC), 2005, *Medical Services Advisory Committee Diagnostic Test Guidelines*. Available at: www.health.gov.au/msac [Accessed on 2 November 2005] Commonwealth of Australia.

Mulhall, B. P., Veerappan, G. R., Jackson, J. L. 2005, 'Meta-analysis: computed tomographic colonography', *Annals of Internal Medicine*, 142 (8), 635-650.

Munikrishnan, V., Gillams, A. R., Lees, W. R., Vaizey, C. J., Boulos, P. B. 2003, 'Prospective study comparing multislice CT colonography with colonoscopy in the detection of colorectal cancer and polyps', *Diseases of the Colon & Rectum*, 46 (10), 1384-1390.

National Health and Medical Research Council (NHMRC), 1999, *A guide to the development, implementation and evaluation of clinical practice guidelines,* National Health and Medical Research Council, Canberra.

National Health and Medical Research Council (NHMRC), 2000, *How to use the evidence: assessment and application of scientific evidence,* National Health and Medical Research Council, Canberra.

National Health and Medical Research Council (NHMRC), 2005, *Additional levels of evidence and grades for recommendations for developers of guidelines*. Available at: http://www.nhmrc.gov.au/advice/pdf/levels_grades05.pdf [Acessed on 11 August 2005].

Nelson DB, McQuaid KR, Bond JR, Lieberman, D. A., Weiss, D. G., Johnston, T. K. 2002. 'Procedural success and complications of large-scale screening colonoscopy', *Gastrointest Endosc*; 55, 307–14.

O'Connell, J.B., Maggard, M.A., Ko, C.Y. 2004. 'Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging', *Journal of the National Cancer Institute,* 96(19), 1420-1425.

O'Leary, B.A., Olynyk, J.K., Neville, A.M., Platell, C.F. 2004. 'Cost-effectiveness of colorectal cancer screening: comparison of community-based flexible sigmoidoscopy with fecal occult blood testing and colonoscopy' *Journal of Gastroenterology &hepatology*, 19 (1), 38-47.

Pederson, G. B., Moller Christiansen, T. E., Viborg, M. F., Christensen, H., Laurberg, S. 2002, 'Bowel cleansing methods prior to CT colonography'. *Acta Radiol*; 43 (3), 306-311.

Provenzale D. 2002, 'Cost-effectiveness of screening the average-risk population for colorectal cancer', *Gastrointestinal Endoscopy Clinics of North America*, 12 (1), 93-109.

Rex, D.K., Cutler, C.S., Lemmel, G.T., Rahmani, E.Y., Clark, D.W., Helper, D.J., Lehman, G. A., Mark, D. G. 1997, 'Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies', *Gastroenterology*, 112 (1), 24-28.

Ristvedt, S. L., McFarland, E. G., Weinstock, L. B., Thyssen, E. P. 2003, 'Patient preferences for CT colonography, conventional colonoscopy, and bowel preparation', *American Journal of Gastroenterology*, 98 (3), 578-585.

Rockey, D. C., Koch, J., Yee, J., McQuaid, K. R., Halvorsen, R. A. 2004, 'Prospective comparison of air-contrast barium enema and colonoscopy in patients with fecal occult blood: a pilot study', *Gastrointestinal Endoscopy*, 60 (6), 953-958.

Rockey, D. C., Paulson, E., Niedzwiecki, D., Davis, W., Bosworth, H. B., Sanders, L., Yee, J., Henderson, J., Hatten, P., Burdick, S., Sanyal, A., Rubin, D. T., Sterling, M., Akerkar, G., Bhutani, M. S., Binmoeller, K., Garvie, J., Bini, E. J., McQuaid, K., Foster, W. L., Thompson, W. M., Dachman, A., Halvorsen, R. 2005, 'Analysis of air contrast barium enema, computed tomographic colonography, and colonoscopy: prospective comparison', *Lancet*, 365 (9456), 305-311.

Rottgen, R., Fischbach, F., Plotkin, M., Herzog, H., Freund, T., Schroder, R. J., Felix, R. 2005, 'Colon dissection: a new three-dimensional reconstruction tool for computed tomography colonography', *Acta Radiologica*, 46 (3), 222-226.

Rural Doctors Association of Australia. 2005, *Submission to the Senate Inquiry into services and treatment options for persons with cancer*, March 2005. Available at: http://www.aph.gov.au/Senate/committee/clac_ctte/cancer/submissions/sub41_pdf [Accessed on 3 Nov 2005].

Shureiqi, I., Reddy, P., Ruffin, M.T., Brenner, D.E. 2004, 'Prevention and Screening Principles Relevant to Gastrointestinal Malignancies', In: Abbruzzese JL, Evans DB, Willet CG, Fenoglio-Preiser C. (editors) Gastrointestinal Oncology. New York: Oxford University Press; 9-36.

Sonnenberg, A., Delco, F. Bauerfeind, P. 1999. 'Is virtual colonoscopy a cost-effective option to screen for colorectal cancer?' *American Journal of Gastroenterology*, 94 (8), 2268-2274.

Sosna., J., Bar-Meir, E., Amitai, M., Bar-Ziv, J. 2004. 'Assessment of the risk of perforation at CT Colonography' (abstract). Presented at Radiologic Society of North America, Chicago, IL.

Sosna, J., Morrin, M. M., Kruskal, J. B., Lavin, P. T., Rosen, M. P., Raptopoulos, V. 2003, 'CT colonography of colorectal polyps: a metaanalysis', *American Journal of Roentgenology*, 181 (6), 1593-1598.

Surveillance, Epidemiology, and End Results (SEER) Program, 2005, *SEER*Stat Database: Incidence - SEER 9 Regs Public-Use, Nov 2004 Sub (1973-2002)*, US National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2006, based on the November 2005 submission. Available at: www.seer.cancer.gov [Accessed on 3 Nov 2005].

Svensson, M. H., Svensson, E., Lasson, A., Hellstrom, M. 2002, 'Patient acceptance of CT colonography and conventional colonoscopy: prospective comparative study in patients with or suspected of having colorectal disease', *Radiology*, 222 (2), 337-345.

Talley, N.J., Martin, C.J. 1996, *Clinical Gastroenterology*. Sydney: MacLennan & Petty.

Taylor, S.A., Halligan, S., Burling, D., Bassett, P., Bartram, C. I. 2005, 'Intra-individual comparison of patient acceptability of multidetector-row CT colonography and double-contrast barium enema', *Clinical Radiology*, 60 (2), 207-214.

Taylor, S. A., Halligan, S., O'Donnell, C., Morley, S., Mistry, H., Saunders, B. P., Vance, M., Bassett, P., Windsor, A., Stern, Y., Bethel, H., Atkin, W., Bartram, C. I. 2003, 'Cardiovascular effects at multi-detector row CT colonography compared with those at conventional endoscopy of the colon', *Radiology*, 229 (3), 782-790.

Taylor, S. A., Halligan, S., Saunders, B. P., Bassett, P., Vance, M., Bartram, C. I. 2003, 'Acceptance by patients of multidetector CT colonography compared with barium enema examinations, flexible sigmoidoscopy, and colonoscopy', *American Journal of Roentgenology*, 181 (4), 913-921.

Taylor, S. A., Halligan, S., Saunders, B. P., Morley, S., Riesewyk, C., Atkin, W., Bartram, C. I. 2003, 'Use of multidetector-row CT colonography for detection of colorectal neoplasia in patients referred via the Department of Health "2-Week-wait" initiative', *Clinical Radiology*, 58 (11), 855-861.

Technology Evaluation Centre, Blue Cross and Blue Shield Association, 2004. *CT Colonography ("Virtual Colonography") for Colon Cancer Screening', Assessment Program, 19 (6)* Available at: http://www.bcbs.com/tec/vol19/19_06.html [Accessed on 6 June 2005].

The American Society for Gastrointestinal Endoscopy, Standards of Practice Committee. 2005, 'ASGE guideline: guideline on the use of endoscopy in the management of constipation', *Gastrointestinal Endoscopy*, 62 (2), 199-200.

Thomeer, M., Bielen, D., Vanbeckevoort, D., Dymarkowski, S., Gevers, A., Rutgeerts, P., Hiele, M., Van Cutsem, E., Marchal, G. 2002, 'Patient acceptance for CT colonography: what is the real issue?', *European Radiology*, 12 (6), 1410-1415.

Tran, D. Q., Rosen, L., Kim, R., Riether, R. D., Stasik, J. J., Khubchandani, I. T. 2001. 'Actual colonoscopy: what are the risks of perforation?' *American Surgeon*, 67 (9), 845-847.

Valenstein, P.N. 1990. Evaluating diagnostic tests with imperfect standards, *American Journal of Clinical Pathology*, 93 (2), 252-8.

Van Dam, J., Cotton, P., Johnson, D. C., Mcfarland, B.G., Pineau, B.C., Provenzale, D., Ransohoff, D., Rex, D., Rockey, D., Wootton, T. F. 2004, 'AGA future trends report: CT colonography', *Gastroenterology*, 127 (3), 970-984.

van Gelder, R. E., Birnie, E., Florie, J., Schutter, M. P., Bartelsman, J. F., Snel, P., Lameris, J. S., Bonsel, G. J., Stoker, J. 2004, 'CT colonography and colonoscopy: assessment of patient preference in a 5-week follow-up study', *Radiology*, 233 (2), 328-337.

van Gelder, R. E., Nio, C. Y., Florie, J., Bartelsman, J. F., Snel, P., De Jager, S. W., Van Deventer, S. J., Lameris, J. S., Bossuyt, P. M. M., Stoker, J. 2004, 'Computed tomographic colonography compared with colonoscopy in patients at increased risk for colorectal cancer', *Gastroenterology*, 127 (1), 41-48.

van Gelder, R. E., Venema, H. W., Serlie, I. W. O., Nio, C. Y., Determann, R. M., Tipker, C. A., Vos, F. M., Glas, A. S., Bartelsman, J. F. W., Bossuyt, P. M. M., Lameris, J. S., Stoker, J. 2002, 'CT colonography at different radiation dose levels: feasibility of dose reduction', *Radiology*, 224 (1), 25-33.

Vogt, C., Cohnen, M., Beck, A., vom Dahl, S., Aurich, V., Modder, U., Haussinger, D. 2004, 'Detection of colorectal polyps by multislice CT colonography with ultra-low-dose technique: comparison with high-resolution videocolonoscopy', *Gastrointestinal Endoscopy*, 60 (2), 201-209.

Whiting, P., Rutjes, A.W., Reitsma, J.B., Glas, A.S., Bossuyt, P.M., Kleijnen, J. 2004, 'Sources of variation and bias in studies of diagnostic accuracy: a systematic review', *Annals of Internal Medicine*, 140 (3), 189-202.

Whiting, P., Rutjes, A.W., Reitsma, J.B., Bossuyt, P.M., Kleijnen, J. 2003, 'The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic review', *BMC Medical Research Methodology*, 3, 25, Available at: http://www.biomedcentral.com/1471-2288/3/25 [Accessed on 23 May 2006].

Winawer, S., Fletcher, R., Rex, D., Bond, J., Burt, R., Ferrucci, J., Ganiats, T., Levin, T., Woolf, S., Johnson, D., Kirk, L., Litin, S., Simmang, C. 2003, 'Colorectal cancer screening and surveillance: clinical guidelines and rationale - Update based on new evidence', *Gastroenterology,* 124 (2), 544-560.

Winawer, S.J., Zauber, A.G., Ho, M.N., O'Brien, M.J., Gottlieb, L.S., Sternberg, S.S., Waye, J. D., Schapiro, M., Bond, J. H., Panish, J. F., Ackroyd, F., Shike, M., Kurtz, R. C., Hornsby-Lewis, L., Gerdes, H., Stewart, E. T. 1993, 'Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup', *New England Journal of Medicine,* 329 (27), 1977-1981.

Wise, K. N. 2003, 'Solid cancer risks from radiation exposure for the Australian population', *Australasian Physical & Engineering Sciences in Medicine*, 26 (2), 53-62.

Zamora, J., Muriel, A., Abraira, V. 2004, *Meta-DiSc for Windows: Software package for the Meta-analysis of Diagnostic Tests*, XI Cochrane Colloquium, Barcelona 2003, Available at: http://www.hrc.es/investigacion/metadisc.html. [Accessed on 16 September 2004].