Cost-effectiveness of computerized tomographic colonography versus colonoscopy for colorectal cancer screening

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Computerised tomographic (CT) colonography was compared with colonoscopy for colorectal cancer screening in patients over 50 years of age. For CT colonography, this study considered a primary 2-dimensional approach with 3-D reconstruction for problem-solving. In addition, a segmental unblinding technique was used for CT colonography, whereas both segmental unblinding and back-to-back colonoscopy were used to assess the diagnostic accuracy of colonoscopy. For this, same-day colonoscopy with segmental unblinding was considered to be the "gold" standard.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The base-case population modelled consisted of average-risk individuals over the age of 50 years.

Setting
The setting was primary and secondary care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were taken from several trials and studies published between 1987 and 2005. The costs and resource use data were taken from several sources dating from 1995 to 2005. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from published studies, with some estimates based on authors' assumptions.

Modelling
A decision model was constructed to compare CT colonography and colonoscopy for colorectal cancer screening of average-risk patients over the age of 50 years. A period of 3 years was chosen for the model. This was based on several facts. First, the risk of cancer after a therapeutic colonoscopy and the natural history of unresected large polyps (≥10 mm) were known over this period. Second, an appropriate re-screening interval for CT colonography, although not yet established, was unlikely to be shorter than 3 years. Finally, short-term economic considerations are important for health policy decision-makers.

Outcomes assessed in the review
The outcomes included were:

- the sensitivity and specificity of the screening test;
- the numbers of colonoscopies, perforations and adenomas removed;
- deaths related to perforation and from early-stage cancers arising from missed adenomas; and
- cancer prognosis.

**Study designs and other criteria for inclusion in the review**
The authors reported that they used high-quality prospective studies evaluating the test performance characteristics of CT colonography and colonoscopy for polyps sized 6 - 9 mm and \( \geq 10 \) mm. The search included colonoscopy, computed tomography and cancer as search terms, and was restricted to studies reported in English. In addition, the bibliographies of these papers and selected recent reviews were examined to ensure that important studies were not omitted.

**Sources searched to identify primary studies**
The literature search was performed using PubMed, and covered articles published from 1990 through March 2005.

**Criteria used to ensure the validity of primary studies**
Two independent reviewers performed the literature search. Both reviewers critiqued each abstract, with individual papers pulled for further review if they met the criteria or if the methodology was unclear. For CT colonography, only studies using the segmental unblinding technique were included, whereas for colonoscopy, both segmental unblinding and back-to-back colonoscopy studies were used to assess diagnostic accuracy.

**Methods used to judge relevance and validity, and for extracting data**
Two external-content experts were consulted to ascertain that no other published or unpublished studies were overlooked.

**Number of primary studies included**
The authors reported that at least 35 primary studies were included in the review for different purposes (e.g. prevalence and incidence rates, sensitivity and specificity, adherence to screening and treatment).

**Methods of combining primary studies**
A narrative method was used to combine the studies. For the size-specific sensitivities and specificities and the risk of perforation, a weighted average was used for the base-case estimates. The prevalence of polyps and the proportion that were adenomatous within each size category were averaged from CT colonography studies, where available.

**Investigation of differences between primary studies**
The authors did not explicitly report details of any investigation of differences between the primary studies. However, some of the primary studies were used as best-case and worst-case scenarios for the sensitivity analysis.

**Results of the review**
The prevalence of polyps, including adenomatous and nonadenomatous, was 15.5\% for 6- to 9-mm polyps and 7.6 \% for polyps \( \geq 10 \) mm.
The probability of a polyp being adenomatous was 61% for 6- to 9-mm polyps and 67% for polyps \( \geq 10 \) mm.

The 3-year risk of cancer from a missed adenoma was 0.9 for 6- to 9-mm polyps and 1.5% for polyps \( \geq 10 \) mm.

The sensitivity of CT colonography was 61% for 6- to 9-mm polyps and 71% for polyps \( \geq 10 \) mm, whereas the sensitivity values for colonoscopy were 94% (6 - 9 mm in size) and 96% (\( \geq 10 \) mm in size), respectively. The specificity, considering that a "true negative" was a patient with no polyps \( \geq 5 \) mm in size, was 84% for CT colonography and 100% for colonoscopy.

The risk of bleeding was 0.03% after diagnostic colonoscopy and 0.5% after polypectomy.

The risk of perforation was 0.09% after diagnostic colonoscopy and 0.24% after polypectomy.

The risk of death from perforation was 4.9%.

All cancers discovered after 3 years would have a 5-year survival of 90%.

**Methods used to derive estimates of effectiveness**

This analysis was based on published data and authors' assumptions.

**Estimates of effectiveness and key assumptions**

The authors considered clinically significant polyps to be those larger than 5 mm. When identified with CT colonography, they were assumed to lead to prompt referral for colonoscopy, and polypectomy if confirmed. The authors assumed that polyps 5 mm or less in size would not require further testing: their malignant potential is low, especially in the short term. In addition, the authors assumed a baseline prevalence of colorectal cancer of 0 and no difference in screening adherence at baseline.

**Measure of benefits used in the economic analysis**

The measures of benefits used were the deaths avoided from perforations, additional deaths from missed adenomas and life-years gained (LYG). The health benefits were discounted at a rate of 3% per year.

**Direct costs**

The direct health care costs of colonoscopy (including therapeutic use and treatment of bleeding and perforation) and CT colonography were tabulated for local estimations. They included detailed procedural costs for diagnostic and therapeutic colonoscopy (including physician and nursing charges), costs for medical and surgical supplies, medications and cleaning, and amortised costs for overheads. The costs of complications were taken from medical records, and only complications resulting from colonoscopy confirmed by chart review were included in the analysis.

Since CT colonography is not currently part of any provincial fee schedule in Canada, the cost of it was estimated using the Provincial Common Procedure List Catalogue to calculate the cost of diagnostic imaging tests. An additional cost was estimated to cover a radiologist's interpretation fee, support staff, supplies and equipment maintenance. It excluded capital expenditures and thus assumed that the extra CT scans could be done by means of existing capital infrastructure. Moreover, the CT cost did not include the anticipated higher radiologist's interpretation fee, given the extra time required to interpret a CT colonography study. The authors added an additional fee to account for the cost of extracolonic findings.

The lifetime cost of early-stage colorectal cancer was taken from the literature. Discounting was carried out at a rate of 3%. The quantities and the costs were not analysed separately. The estimations of the quantities and the costs were modelled. The price year was not reported.

**Statistical analysis of costs**
The costs were treated deterministically and no statistical tests were carried out.

**Indirect Costs**
Productivity losses were estimated and reported, but they were not used in the base-case analysis, only in the sensitivity analysis. They were estimated using average hourly earnings from the Canadian Socioeconomic Information Management System. The authors estimated the indirect costs for patients and escorts for colonoscopy, and for patients for CT colonography. Discounting was carried out at a rate of 3%. The price year was not reported.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
To assess the robustness of their conclusions, the authors subjected each of the variables modelled to sensitivity analyses. Plausible ranges, taken from published literature, were used. In particular, the authors modelled a wide range of increased screening adherence for CT colonography over colonoscopy. Variations in the test performance of CT colonography, as reported in medical literature, were used for presenting best- and worst-case scenario analyses. The estimated risk of cancer from missed adenomas and the risk of colonoscopy-associated perforation and death were also tested.

**Estimated benefits used in the economic analysis**
The numbers of deaths per 100,000 people screened for colon cancer were as follows:

- for the colonoscopy strategy, 6.03 perforation-related deaths, 0.64 cancer-related deaths from missed adenomas, and 6.67 total deaths;
- for the CT colonography strategy, 2.25 perforation-related deaths, 4.75 cancer-related deaths from missed adenomas, and 7.00 total deaths.

**Cost results**
The total costs were Can$61.5 million for the colonoscopy strategy and Can$63.8 million for the CT colonography strategy, both per 100,000 people screened for colon cancer.

**Synthesis of costs and benefits**
According to the base-case estimates, a strategy of CT colonography for colorectal cancer screening would cost Can$2.27 million more than colonoscopy per 100,000 patients screened, and would result in 0.33 extra deaths per 100,000 patients screened. As such, colonoscopy was both less expensive and more effective (i.e. dominant).

The results from the sensitivity analyses were sensitive to variations in the test performance of CT colonography. In the best-case scenario (sensitivity 94%, specificity 80%), the incremental cost of CT colonography was $220,000 per LYG. In the worst-case scenario (sensitivity 55%, specificity 91%), the cost-savings of $4.51 million for CT colonography yielded an incremental cost of colonoscopy of $106,000 per LYG.

The results were also sensitive to the estimated risk of cancer from missed adenomas and the risk of colonoscopy-associated perforation and death. Colonoscopy was no longer dominant when the cancer risk of a missed adenoma 6 - 9 mm in size was decreased to 0; CT colonography then had an incremental cost per LYG of Can$42,900. When the risk of perforation from colonoscopy was increased to 0.2%, CT colonography became an attractive alternative, with a cost per LYG of Can$2,130. Increasing the risk of death from colonoscopic perforation to 14% generated a cost per LYG of $18,200 for CT colonography. There would appear to be some discrepancies between the values reported in the table and in the text.
Including an estimate of the indirect costs also influenced the results, with CT colonography saving Can$6.15 million, but at a cost of 0.33 extra deaths.

Further, increasing the absolute colorectal cancer screening adherence with CT colonography to a level 50% higher than colonoscopy, in absolute terms, resulted in the CT strategy having fewer deaths, but at an incremental cost per LYG of over Can$700,000.

Authors’ conclusions
Computerised tomographic (CT) colonography does not appear to have been cost-effective for primary colorectal cancer screening in Canada. Although perforation-related mortality could be reduced, this was counterbalanced by excess cancer-related deaths from missed adenomas. Even if the test performance characteristics of CT colonography could eventually rival those of colonoscopy, the current cost of a screening strategy involving CT colonography far exceeded what most would consider good value for health care money. CT colonography has a potential role in centres where the risks of colonoscopy are high, or in patient populations with high operative mortality.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. The authors considered same-day colonoscopy with segmental unblinding to be the "gold" standard. The segmental unblinding technique involved the reinsertion of the colonoscope into colon segments determined to be polyp-free by colonoscopy but shown to contain a lesion by CT colonography. It minimised information bias through misclassification (i.e. false-negative results on colonoscopy recorded incorrectly as false-positive CT results). The authors did not analyse other currently available screening strategies. You should decide if these strategies represented widely used technologies in your own setting.

Validity of estimate of measure of effectiveness
The authors conducted a systematic review of the literature. They also made some assumptions that were justified with reference to the medical literature. The methodology used to select and review the literature was reported in detail. Estimates were appropriately investigated by sensitivity analysis, with the selected ranges justified on the basis of the medical literature.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the effectiveness analysis. The reader is thus referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The authors reported that the costs were estimated from the perspective of a health care purchaser. All the relevant cost categories appear to have been included. All cost estimates were derived from published sources. Discounting was appropriately applied as the study time horizon was longer than 2 years, and all costs were discounted at the same rate (3% per year). The prices were taken from published sources but the resource use quantities were not reported separately, thus limiting extrapolation to other settings. The costs were treated deterministically and no sensitivity analysis of the resource quantities or prices was conducted (except for the inclusion of indirect cost estimates). The price year was not reported, which will make future reflation exercises difficult.

Other issues
The authors compared some of their effectiveness findings with those from other studies. However, they did not compare their findings with those from other economic evaluations on the same topic, even though such economic evaluations exist. The issue of generalisability to other settings was addressed. The authors’ conclusions reflected the scope of the analysis. The authors reported and addressed some limitations of their study. First, the short study horizon and the short-term cost of adopting CT colonography. Second, the assumption that all cancers arising from missed adenomas would be early stage, and would be identified and promptly treated at the 3-year mark. Third, only polyps
larger than 5 mm were considered clinically significant. Finally, the omission of a measure of quality of life from the model.

Implications of the study
This study showed that only substantial increases in the risk of perforation or the risk of death from perforation resulted in a reasonable incremental cost-effectiveness ratio for CT colonography. Therefore, the authors suggested that the choice of screening strategy in a given institution might depend on a balance between the availability and local quality of CT colonography and the experience and complication rates of available endoscopists and surgeons. Given that the results of this analysis appear to have been sensitive to the inclusion of indirect cost estimates, further research is needed to determine the actual indirect costs associated with colorectal cancer screening.

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