Colon cancer screening

I am a bit perplexed about the cost-effectiveness analysis of CRC screening by Steven Heitman and associates.[1] First, it does not compare CT colonography with a "do nothing" approach nor does it take into consideration the recommendations of the Canadian Task Force on Preventive Health Care.[2] What is the predicted cost-effectiveness, in Canada, of CT colonography as the alternative to doing nothing?

Second, the analysis seemingly presumes that either CT colonography or colonoscopy will be used exclusively. The authors indicate that current population screening rates are less than 20% but that a recent study has shown that up to 28% of the population would be willing to submit to CT colonography. The analysis should have included a population perspective on the benefits and costs of offering CT colonography to patients willing to submit to this strategy who would otherwise refuse screening altogether. Offering several screening methods may be the only way to increase population-wide adherence.

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DOI:10.1503/cmaj.1050215

The article by Steven Heitman and colleagues[1] ignores health human resource realities in Canada. The only logical strategy for people aged 50–74 years at average risk of developing colorectal cancer (CRC) is to start with computerized tomographic (CT) colonography and proceed to full colonoscopy with polypectomy on the same day when polyps greater than 5 or 10 mm in diameter are found.

The Canadian health care system does not have the capacity to offer colonoscopies to everyone aged 50–74 years who is at average risk. Access to gastrointestinal specialty care is limited in many parts of Canada.[2] In 2001, only 3857 colonoscopies were performed per 100 000 Ontarians aged 50–74 years.[3] From 1992 to 2001, only 15.7% of Ontarians aged 50–74 years had at least one colonoscopy; 16.7% underwent double-contrast barium enema.[3]

There are resource planning advantages to a "CT colonography first" strategy. It takes 15 min for an experienced endoscopist to perform a full diagnostic colonoscopy and an additional 5–10 min for a polypectomy. For 100 000 people undergoing CRC screening (27.2% of them will have polyps greater than 5 mm in diameter[1]), the "CT colonoscopy first" strategy will require 3692 endoscopy days. A colonoscopy for the people in this group who are found to have polyps will use only 1417 endoscopy days.

There are 2 questions that need to be addressed with regard to CRC screening programs. The first is whether CT colonography should replace double-contrast barium enema as a screening tool. The second concerns the optimal interval for repeating CT colonography.

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DOI:10.1503/cmaj.1050228

[Four of the authors respond:]

These authors have raised several important issues. Dr. Kiberd suggests that our model should have included comparison to fecal occult blood testing

(FOBT) and to a "do nothing" approach. This approach is not standard care, colonoscopy is felt by many to be the current gold standard screening tool, and colonoscopy has already shown to be cost-effective in comparison to both FOBT and doing nothing. There is also a lack of direct clinical data comparing FOBT, CT colonography, colonoscopy, and a "do nothing" approach.

Dr. Kiberd also notes that our analysis did not consider differences in screening uptake and suggests that "offering several screening methods may be the only way to increase population-wide adherence" with CRC screening. In fact, we did model up to a 50% increase (well above what is likely realistic) in screening adherence using CT colonography in our sensitivity analysis (see Table 4 in the article).[1] Although this resulted in a reduction in net lives lost, it came at an enormous cost. Finally, there is no evidence that we are aware of that increasing the number of options leads to an increase in screening adherence. In fact, there is even some evidence to the contrary.[2]

Dr. Peltekian states that "the only logical strategy" for CRC screening should start with CT colonography followed by colonoscopy in positive cases. From our analysis, we feel that it is rather illogical to switch from a dominant strategy to a dominated (more expensive, less effective) strategy. We are not the only investigators to suggest that CT colonography is an inferior screening test[3-5] and a less efficient use of resources compared to colonoscopy.[6] We agree that access to colonoscopy is limited in Canada and that this important resource deficit needs to be resolved before population-based CRC screening can be implemented. However, these same resource issues also apply to elective radiologic exams. In the most favourable CT colonography study by Pickhardt and colleagues,[7] the mean time spent in the endoscopy suite was 31.5 minutes compared to 14.1 minutes in the CT suite. However, an extra 19.6 minutes was required on average for a radiologist to interpret a CT colonography study. In addition, 15%–30% of patients still require a colonoscopy. It would be an administrative feat to reserve colonoscopy time for the potential positives on CT, so that patients can be done on the same day while still prepped.

Our base-case cost of CT colonography in Alberta almost certainly underestimates the true costs involved. Widespread use of CT colonography for CRC screening would require significant capital expenditure to purchase new CT scanners along with the necessary software. Just as more gastroenterologists would be required to accommodate population-based CRC screening, more radiologists and technicians would need to be trained to perform primary screening using CT colonography. We agree that the appropriate re-screening interval for CT colonography has not been established. However, it is unlikely to be as long as suggested for colonoscopy until further experience is gained. Shorter re-screening intervals are likely to occur in its early stages. All of these factors would undoubtedly increase the cost of a CT colonography-based CRC screening strategy.

Ultimately, it will be up to health policy decision-makers to decide whether or not to provide funding for CT colonography for CRC screening. We believe that resources for CRC screening would be better invested in CRC education and on improving access to our already established screening modalities.

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DOI:10.1503/cmaj.1060024

Conjugate vaccines and polysaccharide response

Purified polysaccharide vaccines work by activation of B cells in a T-independent manner, producing predominantly IgM and little memory B cells.[1] Protein-polysaccharide conjugate vaccines (such as Prevnar/PCV7 which uses 7 prevalent polysaccharides to bind to non-toxic variant of diphtheria toxin, CRM197) allow the protein to present antigen on B cells and CD40/CD40L interaction, while T cells allow antibody class switching from IgM to IgG producing memory cells and longer response. Conjugated vaccines usually use polyribosylribitol phosphate (PRP) conjugated with protein carriers and conjugate vaccines for *Haemophilus influenzae* and *Neisseria meningitidis* (using outer membrane proteins, OMP) have already been developed.[2]

However, conjugate vaccines may not work in high-risk categories like HIV-positive children[3] and asplenics,[2] and the PPV23 vaccine failure comorbid elderly[4] needs to be identified and followed up. IgG subclass measurement for evaluation of vaccine response is vital; anti-IgG1 pneumococcal antibodies in children (both with normal and abnormal immunity) and anti-IgG2 anti-