Dear Sir,

I read with interest the editorial by Professor Brian Cox in the February 19 edition of the Journal. His plea for a flexible sigmoidoscopy screening program for colorectal cancer in New Zealand is based on a sound analysis of relevant data, but it only tells a part of the story. I write in an attempt to fill in some of the gaps.

Colorectal cancer is such a frustrating disease because it is largely preventable and curable. Every cancer arises in a premalignant lesion and so there is the opportunity to prevent cancer by removal of that lesion. Even if cancer has already developed, it is commonly curable if diagnosed at an early stage. The question for those at risk for the disease is “how best to prevent it or diagnose it early?” The answer is to screen, so that asymptomatic patients with polyps or Stage I or II cancer are discovered and treated. So far, so good. The next question is “how should the screening be done?” and here the answer is contentious. The preferred screening option varies according to the individual risk of the patient and the characteristics of the various tests. In particular, screening tests differ in their availability, their sensitivity and specificity, their tolerability and adverse effects, and their financial implications for the patient and the healthcare system of the country. The implications of an individual approach may be considerably different to that for a population. Thus, the attraction of flexible sigmoidoscopy screening is in the context of screening a population.

There are significant downsides to flexible sigmoidoscopy that are best understood by those who have performed or received the test. These include an unpredictable result from one or two phosphate enemas, especially in patients with sigmoid diverticulosis; the cramping and pain that is common when no sedation or analgesia is given, and an unpredictable depth of insertion that is dictated by the skill of the endoscopist, the tortuosity, fixity and spasticity of the colon, and the tolerance of the patient. In addition, there is the undeniable concern that at best the test examines only half of the colon. While flexible sigmoidoscopy would prevent 88 or 102 cancer deaths a year—depending on the level of participation—colonoscopy would be expected to prevent many more.

Colorectal cancer is no longer a left-sided disease, as shown by brief review of my own unpublished data from colonoscopy screening in average risk patients over the age of 50 years during the last 3 years. Two hundred and eighteen patients out of 427 who were screened had polyps (51%). In 111 patients (51%), the polyps were only proximal to the splenic flexure, and the left colon and rectum were normal. There were left-sided polyps in 107 patients; 55 (25%) had only left-sided polyps and 52 had polyps on both sides of their colon (24%). Thus, flexible sigmoidoscopy would detect lesions in half of the patients at most—the other half would be blissfully unaware of their increased risk. Flexible sigmoidoscopy is not even guaranteed to reach the splenic flexure. In fact, the scope often does not traverse the entire sigmoid as the sigmoid colon is notoriously the most difficult part of the colon to intubate, and in unsedated patients the examiner often has to bail out.

Despite these limitations imposed by polyp
distribution and limited depth of insertion, the assumption that only 5% of patients receiving flexible sigmoidoscopy would need a colonoscopy is an underestimate, depending on the indications for referral used by the program. If the finding of any polyp is an indication for colonoscopy, then about 25% of patients will be referred, as about 25% of patients at average risk have left-sided polyps (55+52/427). Just over half of these polyps will be hyperplastic, but there is still debate about the association between distal hyperplastic polyps and proximal neoplasms, especially sessile serrated adenoma/polyps (SSA/P).4 Discussion of colorectal cancer screening is not complete without consideration of SSA/P. These flat, pale lesions are hard to see, are typically right-sided and account for as many as 18% of colorectal cancers. They are precursors in the promoter methylation route to CIMP high colorectal cancers (CIMP = CpG Island Methylator Phenotype).5 Flexible sigmoidoscopy will detect almost none of these dangerous lesions.

Colonoscopy is not a perfect screening tool either, and there is evidence that colonoscopy screening is not protective against death from right-sided colorectal cancer.6 This raises the issue of the quality of the exam, an issue that applies equally (if not more so) to flexible sigmoidoscopy. However, a recent meta-analysis of studies looking at the effect of colonoscopy on colon cancer incidence and mortality shows an 89% reduction in incidence compared to no colonoscopy (RR: 0.11; 95% CI: 0.08–0.15).7 From a patient point of view, if screening is to be invasive then the test ought to be as comfortable and as thorough as possible, and so in the context of a single patient, colonoscopy is the better choice. However, colonoscopying all the eligible population of New Zealand is clearly not possible, logistically or financially. There are some new alternatives however.

Faecal DNA testing became a commercial test in US last year, based on a paper published in the *New England Journal of Medicine* that showed 92.3% sensitivity for cancer, 69.2% sensitivity for adenomas containing high-grade dysplasia, and 42.4% sensitivity for SSA/P (compared to faecal immunochemical blood testing (FIT)) with a sensitivity of 73.8% for cancer, 46.2% for adenomas with high-grade dysplasia and 5.1% for SSA/P.8 The cost of the test is approximately $600US, and the recommended screening interval is 3 yearly. This program is reimbursed by Medicare and many private payers. Another option may soon be a blood test for a new cancer marker, CA 11-19, which has recently been reported to detect colorectal cancer with 98% sensitivity.9 In the meantime, colorectal surgeons and gastroenterologists are increasingly concerned about the rising incidence of colorectal cancer (and rectal cancer in particular) in young patients who fall outside any of the screening guidelines.10 The newer, non-invasive tests may be a Godsend to clinicians worried about the changing demographics of the disease.

So in the face of conflicting ideas and different emphases in the selection and interpretation of data, what must we do? Given that colonoscopy remains the most sensible and effective tool for colorectal cancer detection and prevention, the strategy must be to use this tool optimally. This means maximising yield, and one way to do this is to stratify patients by risk for colorectal cancer. The importance of a family history of colorectal cancer and polyps cannot be over emphasised. This is a red flag that must be responded to by scheduling a colonoscopy at an appropriate age (10 years prior to the age at diagnosis of the youngest affected relative, or age 50, whichever is younger). A personal history of premalignant polyps should lead to a colonoscopic surveillance program, as should a history of endometrial cancer in a patient or a relative, especially at a young age. Secondly, the symptom of rectal bleeding cannot be ignored or attributed to benign causes. It is an indication for a prompt colonoscopy. In the majority of patients who are at average risk without symptoms, some sort of screening is required. Faecal DNA testing and blood tests for cancer markers are very promising in terms of comfort, safety, high sensitivity and lower cost, but are not yet ready to be rolled out on a population level. Our commitment to FIT has already been shown to be effective in its pilot study and although data for flexible sigmoidoscopy screening show it to be effective also,1 there are problems and issues with both of these compromise
tools. For the individual patient, colonoscopic screening remains the preferred way to clear the colon. To the Minister of Health I would advise patience, and continue with investments already made in the realisation that progress will soon make the issue of colorectal cancer screening much less contentious.

Competing interests:
James Church is a paid speaker for Exact Sciences, the company producing Cologuard faecal DNA test.

Author information:
James Church, Director of the Sandford R. Weiss MD Center for Hereditary Colorectal Neoplasia, Digestive Diseases Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA.

Corresponding author:
James Church, Director of the Sandford R. Weiss MD Center for Hereditary Colorectal Neoplasia, Digestive Diseases Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA.
cyclax@aol.com

URL:

REFERENCES: