EDITORIAL

Colonoscopy as a primary screening method?

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Colorectal cancer (CRC) is a major cause of death worldwide; in England it is the second most common cause of cancer death. In 2010 there were 16,013 deaths from the disease in the UK. It has been estimated that the current faecal occult blood (FOB) screening programme in England could reduce deaths by about 15% by the year 2015, preventing 1800–2400 deaths per year.[1]

Because of the natural history of the adenoma-carcinoma sequence, screening has the potential to reduce both mortality from and the incidence of CRC, depending on the screening method used. The effectiveness of screening both by faecal occult blood testing and by flexible sigmoidoscopy has been demonstrated by randomized controlled trials;[2–4] evidence for the effectiveness of screening by colonoscopy is only available at present from observational studies.[5,6]

In the majority of European countries where population-based screening is undertaken or planned, screening by FOB testing (using either a guaiac or immunochemical test) is the preferred method. 'Once-only' screening using flexible sigmoidoscopy at age 55 is about to be introduced in England in addition to FOB screening from age 60; colonoscopy is used as a screening test in both Germany and Poland, and is the predominant screening method in the United States.

The advantage of endoscopic screening by flexible sigmoidoscopy or colonoscopy is that, in addition to the detection and treatment of cancers at an earlier stage, pre-cancerous adenomas are found and removed, thus leading to a reduction in the incidence of CRC as well as in mortality, and reducing the need for repeat screening. In the UK flexible sigmoidoscopy trial, incidence of CRC was reduced by 23% in the intervention arm at a median of 11 years of follow up, and in the National Polyps study a reduction of 76–90% has been estimated following colonoscopy.[7] Although FOB screening also results in the detection of adenomas, only one trial so far has shown a significant reduction in the incidence of colorectal cancer of 17–20% after 18 years of follow-up; however this may have been due to rehydration of the guaiac test and a consequent high positive/colonoscopy rate.[8]

The disadvantage of colonoscopy, in addition to the resources required, is the rate of serious complications including major bleeding and perforation of the bowel, reported as of the order of 0.0 to 0.3%. By comparison, only those people found positive by FOB testing (approximately 2% of the population) will undergo colonoscopy. Severe complications from flexible sigmoidoscopy have been reported as 0.0 to 0.03%; again approximately 5% may have follow-up colonoscopy with the resulting additional risk.

Two recent papers in the *New England Journal of Medicine* provide further information on the possible impact of screening by colonoscopy. Quintero *et al.* report results on participation, detection of colorectal cancer and adenomas, and complication rates from a randomized trial of one-time colonoscopy versus two-yearly faecal immunochemical testing (FIT) conducted in Spain.[9] The participation rate in subjects randomized to colonoscopy was 24.6% (including 6.1% actually screened by FIT), significantly lower than in those allocated to FIT (34.2%). The increased detection rate of colorectal cancer in people actually screened by colonoscopy of 0.5% versus 0.3% in those screened with FIT was offset by this lower participation, so that in an intention to treat analysis there was no significant difference. However, detection rates of both advanced and non-advanced adenomas were increased in those subjects randomized to colonoscopy screening. Rates of major complications were 0.5% in the colonoscopy group and 0.1% in the FIT group. However these results reflect only the baseline FIT, whereas a population screening programme with two-yearly screening will have higher cumulative rates of both detection and complications.

Colonscopy has the potential to visualise the entire colon, although it has been reported to be less effective at detecting right sided neoplasia, possibly due to incomplete examination. However Quintero *et al.* report a significantly greater difference in the detection of advanced adenomas with colonoscopy as compared with FIT in the proximal compare to the distal colon.

Zauber *et al.* report on results from the US National Polyps Study, providing further cohort study evidence that colonoscopy screening can reduce mortality from colorectal cancer.[10] In patients with adenomas removed at a baseline colonoscopy examination, CRC mortality was reduced by 53% compared with that expected for the general population. Mortality among those with only non-adenomatous polyps removed was similar to that in those with adenomas removed, suggesting that such patients may be at lower risk and require less intensive surveillance. However a lower all cause mortality was observed in the study group, and the study has potential biases due to the inability to adjust for differences in the study population, or to take account of surveillance or other events occurring after the initial colonoscopy. The results cannot therefore be taken as conclusive evidence of effectiveness, and do not provide evidence of the likely benefit of population screening.

Low participation is an acknowledged problem with population-based CRC screening. Results from the first (prevalent) round of the screening programme in the UK show participation with guaiac based FOB testing of 52%.[11] Participation tends to be lower in men than women, at younger ages, in lower socio-economic groups and in some ethnic groups.[12] It is possible that more invasive screening methods may increase such inequalities. Uptake in the UK flexible sigmoidoscopy trial was 71% in those expressing interest and randomized to the intervention arm. Of those approached 53% had expressed interest,

giving a population coverage of 38–39%. It remains to be seen if improved coverage is observed with population-based screening. Virtual colonoscopy/computerized tomography colonography has been shown to have higher participation than colonoscopy and may reduce the rate of complications.

Outcomes from randomized controlled trials of colonoscopy screening, both the Spanish trial and the Northern-European Initiative on Colorectal Cancer (NordICC), are awaited, and will provide more conclusive evidence on the acceptability, effectiveness and complications of such screening. Only when such evidence is available will it be possible to assess the balance of benefits and harms and determine whether colonoscopy may be a cost-effective option for screening.

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