Flexible use of flexible sigmoidoscopy

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With two screening test modalities of proven benefit, colorectal cancer screening has a problem that those working on early detection of cancer at other sites would love to have. It is not so much a question of which is better, but how should we combine the two technologies for optimum effect.

In bowel screening, the two basic modalities are faecal testing and visualization. Both come in a variety of forms: guaiac testing, immunohistochemical testing, and genetic testing of faecal samples: flexible sigmoidoscopy, colonoscopy and CT imaging for visualization. These methods have been recently reviewed by a working party convened by IARC.[1]

In this edition of the journal, Steele et al. report on a randomized controlled trial of the offer of guaiac faecal occult blood test (FOBT) alone or in conjunction with flexible sigmoidoscopy (FS) in people aged 60 in Scotland.[2] Compared with previous studies of FS, this trial had very low uptake: 17.8% overall, ranging from 7.4% among the most deprived women to 28.6% among the least deprived men.

Reasons for the very low uptake are unclear, but the fact that individuals invited in this trial had already been invited for biennial FOBT since the age of 50 may have something to do with it, and should be investigated further. Nevertheless, it is encouraging that 14% of those screened by FS had missed their previous invitation to FOBT screening, and 9% had not been screened before. Thus, some people who are not interested in FOBT screening may agree to FS. Despite this, there is little evidence of a decoy effect of offering FS in increasing uptake of FOBT; the uptake of any screening was 58.6% in the intervention arm and 59.3% in the control arm, but that could be because those in the intervention arm were not explicitly given a choice – they were invited for FS, and were only invited for FOBT if they did not accept the FS.

The greater detection of adenomas by FS is clear. Despite only 17.8% of invited individuals being screened by FS, overall 1.8% of individuals in the intervention arm had an adenoma removed compared with 0.3% in the control arm. Undoubtedly many of those additional 1.5% will thereby have had cancer prevented.[3] Indeed, in the UK Flexible Sigmoidoscopy Trial, incidence of distal colorectal cancer 2–6 years after screening was almost zero,[4] and distal incidence rates were still much lower 15–16 years after screening than in unscreened individuals.[5]

A model that assumed equal (60%) uptake of FS and FOBT estimated that whereas biennial FOBT from age 60 to 69 would reduce colorectal cancer incidence and mortality by 4% and 14%, respectively, FS at age 60 followed by biennial FOBT to age 69 would reduce incidence by 23% and mortality by 33%.[6] Even though the uptake was extremely low in this trial, it should be clear that the added benefit of FS at age 60 in those who were so screened is substantial.

Faecal immunochemical testing (FIT) replaced guaiac FOBT in Scotland from November 2017, and in England from summer 2019. Unlike the old FOBT, FIT is quantitative, and when used at a low threshold has high sensitivity, both for occult cancers and for adenomas. The question then is: how can we integrate both FIT and FS to substantially reduce colorectal cancer incidence and mortality in an acceptable and affordable screening programme? In the Scottish trial, everyone with a negative FS was offered FOBT, and 81% completed the test. Of those having an FOBT following a negative FS, 0.06% had cancer detected (compared with 0.28% following FS, and 0.12% following FOBT in the control arm), and 0.12% had an adenoma (compared with 8.66% following FS, and 0.52% following FOBT in controls). Thus, the value of FOBT in those with a recent negative FS is questionable.

The excellent sensitivity of FIT at a low threshold suggests that those with a high-level positive (e.g. 100 µg Hb/g faeces – 80 µg is used in Scotland, 120 µg in England) might be referred to colonoscopy, and those with a low-level positive (20–99 µg) to FS. Based on the English pilot of FIT, referring those with 20–99 µg on FIT to FS would result in 5.5% of screened individuals being offered FS, potentially increasing the cancer detection rate (compared with only offering colonoscopy to those with 100 µg or greater) by 50%, and the adenoma rate by 150%.[7] Compared with guaiac FOBT, using a threshold of 20 µg would potentially more than double cancer detection, and increase adenoma detection rate by up to five times. It is also of interest that the uptake of colonoscopy in those with at least 20 µg on FIT was over 85%. Using an even lower threshold for referral to FS should increase the adenoma detection rate still further. With 60% of the population accepting FIT, and 85% uptake of triage endoscopy, reducing the threshold such that 20% of those tested by FIT would be offered FS would result in just 10% of those invited for screening having FS.

FS is an extremely effective method of screening the distal bowel in those who are willing to be tested, in that it not only detects cancers early, thereby reducing

mortality, but it also detects advanced adenomas, thereby preventing cancer incidence. The challenge is how to incorporate FS in population screening in an acceptable and affordable manner.

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