Faecal occult blood testing (FOBT) as screening for colorectal cancer: the current controversy

Colorectal cancer is the fourth most common form of cancer that occurs worldwide, with an estimated 782,900 new cases diagnosed in 1990 [1]. The disease is not uniformly fatal, although there are large differences in survival according to the stage at which the disease is detected. In advanced colorectal cancer in which curative resection is possible, 5-year survival in Dukes’ B is 45%, dropping to 30% in Dukes’ C [2]. Five year survival in resected Dukes’ A is ~80% and survival following simple resection of an adenomatous pedunculated polyp containing carcinoma in situ (or severe dysplasia) or intramucosal carcinoma is generally close to 100%. Although it has been argued that death from colorectal cancer may be avoidable [3], it is estimated that there are still 394,000 deaths from colorectal cancer annually worldwide [4].

The identification of a well-defined pre-malignant lesion, the adenomatous polyp, together with the good survival associated with early disease, make colorectal cancer an ideal target for screening. In the past quarter of a century, great progress has been made in our ability to screen patients for colorectal cancer or its precursor state, using advances in imaging and diagnostic technology. Winawer [5] noted that Gregor [6] had first employed the faecal occult blood guaiac test cards, that the flexible sigmoidoscope was introduced in the mid-1970s to replace the rigid sigmoidoscope that had been first introduced in 1870 and that colonoscopy has been available since 1970 [7].

Four randomised trials have examined annual or biennial screening with faecal occult blood testing (FOBT), whereas there are only early data available regarding sigmoidoscopy and colonoscopy, and little as yet from randomised trials. There is evidence from these randomised trials to support the use of FOBT [8–10], with a reduction in colorectal cancer mortality of ~16% [95% confidence interval (CI) 7% to 23%] from a meta-analysis [23% (95% CI 11% to 43%) reduction among those screened] [11] and a reduction in incidence reported, but only after 18 years of follow-up [12]. Concerns remain about the high level of false-positive results, the feasibility and the small clinical benefit of such screening. These concerns were recently outlined [13] and it was calculated that 1173 individuals needed to be tested for 10 years to avoid one death from colorectal cancer.

Various organisations have considered recommendations for colorectal cancer screening. A report to the Europe Against Cancer Advisory Committee on Cancer Prevention [14] recommended that ‘FOBT should be seriously considered as a preventive measure’. In an accompanying editorial, Coebergh [15] was not completely convinced by this report, pointing out that the modest effects seen could be due to the more intensive follow-up of controls in some of the trials [16].

Subsequently, some important findings have been reported. Lieberman and Weiss [17] examined the sensitivity of FOBT and sigmoidoscopy for detecting neoplasia. Asymptomatic subjects (2885) provided stool specimens on cards, which underwent rehydration. They then underwent colonoscopy with sigmoidoscopy, defined as examination of the rectum and sigmoid colon during colonoscopy. Of subjects with advanced neoplasia, 23.9% had a positive test for occult blood. Compared with subjects who had a negative test for faecal occult blood, the relative risk of advanced neoplasia in subjects who had a positive test was 3.5 (95% CI 2.8, 4.4). Sigmoidoscopy identified 70% of all subjects with advanced neoplasia. Combined FOBT and sigmoidoscopy identified 75.8% of subjects with advanced neoplasia. The authors concluded that one-time screening with both FOBT (with rehydration) and sigmoidoscopy fails to detect advanced colonic cancer in 24% of subjects with the condition [17].

Detsky [18] considered that there are five important reasons why colonoscopy is not routinely recommended as a screening tool: the standard of evidence, adherence, risk, economics and availability. The issue of standard of evidence is one that requires much attention in epidemiology at the present time. FOBT has been evaluated in randomised trials, whereas colonoscopy has not. Detsky [18] concluded that the higher sensitivity of colonoscopy plus the evidence that early detection improves survival is sufficient to conclude that colonoscopy is more effective than FOBT. In addition, there is support from observational studies.

There are some extremely important issues to address in the area of colorectal cancer screening. Should FOBT now be recommended as a population screening method? Should consideration be given to other screening modalities for colorectal cancer? Since a large proportion of individuals tested for FOBT have positive tests and are referred for colonoscopy, could it prove effective to bypass FOBT and go directly to a screening colonoscopy? Or flexible sigmoidoscopy? This latter strategy is currently being assessed in a large, randomised trial and it is a clear reflection of the tremendous potential for the early detection of colorectal cancer by screening, which is clearly outlined in detail elsewhere [19].

Annals of Oncology has previously addressed such topical issues, notably the issue of prostate-specific antigen testing for prostate cancer [20–25]. To bring all the arguments about colorectal cancer screening with FOBT to the readership, 12
intervention is not the only method available. There are many other screening techniques, such as the faecal occult blood test (FOBT), that can be used to detect colorectal cancer. These methods have their own advantages and disadvantages, and the choice of which to use should be based on careful consideration of the evidence available.

One common thread in all these articles relates to the economics of FOBT. La Vecchia [26] outlines the basic epidemiological data, both from observational studies and randomised trials, and indicates where there are key gaps in knowledge. McArdle [27] notes key issues such as compliance among deprived members of communities and the utility of two pilot studies on-going in the UK at the present to address such issues.

Lowenfels [28] invites the reader to reflect on the question: ‘Why don’t we screen for this potentially preventable cancer?’, emphasising that this is a major practical issue. He lays out the arguments in an epidemiological manner as to why screening is necessary and why FOBT may not be the best test, and weighs the potential benefits of other tests. The other gastroenterologists, Bleiberg [29], Crespi and Lisi [30], and Strul and Arber [31] have a more clinical approach and present good overviews and interpretations of the data available. Strul and Arber also give an interesting glimpse of new stool-based tests that may soon be available for population assessment and use.

Autier [32] and Barry [33] take a broader public health perspective. Arguing that FOBT produces modest changes in mortality rates, Autier concludes that FOBT is less efficient than screening tests for other cancers, such as Pap smear for cervix cancer and mammography for breast cancer [32]. Barry points out that ‘most Americans have not been screened for colorectal cancer by any means’, and the situation is identical throughout the rest of the world [33]. Unfortunately, as Barry emphasises, there is a gap between what the (public health) doctor prescribes and what the patient is willing to do. While this situation persists, and scientific squabbles continue about the best way to screen populations for colorectal cancer, the chance is being missed to prevent a significant number of the 400,000 colorectal cancer deaths that occur each year throughout the world.

I greatly enjoyed reading the expert opinions proposed by the authors of the articles in this issue [26–33], and it is quite important to note both the similarities in the assessments and also the differences in the conclusions that are reached based on the same evidence. Consensus is an interesting, and frequently very useful, process, but sometimes a variety of viewpoints can give depth of insight. It is clear that there is a wide range of opinions about recommendations regarding the introduction of FOBT, or indeed any other test, as a population screening method for colorectal cancer.

This is not the end of the story. Eight opinions out of the hundreds potentially available does not constitute a random sample by any means. *Annals of Oncology* recognises the colorectal cancer screening debate as one of the most current in oncology and public health. To encourage this debate, we invite those interested to reply (in less than 1000 words) to the debate engaged above. These replies will be considered for publication in *Annals of Oncology* using an accelerated review process.

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**References**