

COLORECTAL CANCER SCREENING

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5. EVALUATION

Screening for colorectal cancer is a multi-stage process, and the effectiveness of a screening programme will ultimately depend on the capacity and quality of the health-care system within which it takes place and on the resources available, as well as on other factors, including participation by the target population in the screening programme.

The following evaluations are based on a comprehensive review of the published scientific evidence. The majority of the randomized controlled trials and observational studies have been conducted: in middle- to high-income settings, where colorectal cancer incidence is generally high; in asymptomatic populations at average risk aged 50–70 years on average; and under conditions in which colorectal cancer screening, including subsequent follow-up and treatment, can be delivered with high quality. Extrapolation of the conclusions of this evaluation to different settings needs to take into account these and other context-related specificities.

The following evaluation statements on the level of evidence for the effects of the different colorectal cancer screening procedures refer to a setting without colorectal cancer screening as a comparator.

5.1 Guaiac faecal occult blood test

There is *sufficient evidence* that screening biennially with the guaiac faecal occult blood test (gFOBT) without rehydration reduces colorectal cancer mortality. This evaluation is supported by two randomized controlled trials, two large cohort studies with up to 11 screening rounds, and one population-based case–control study of both invitation to and attendance at gFOBT screening.

There is *evidence suggesting lack of effect* of screening biennially with gFOBT without rehydration in reducing colorectal cancer incidence. This evaluation is supported by three large randomized controlled trials of screening with gFOBT without rehydration and one Italian cohort study after 11 screening rounds.

There is *sufficient evidence* that the benefits of biennial screening with gFOBT without rehydration outweigh the harms when the screening programme can be delivered with high quality. This evaluation is based on sufficient evidence of reduced colorectal cancer mortality and on a gain in quality-adjusted life years, versus the short-term psychological harms of screening per se or of a positive test result, as well as the potential medical harms of follow-up colonoscopy after a positive test result.

There is *sufficient evidence* that screening annually or biennially with gFOBT of higher sensitivity reduces colorectal cancer mortality. This evaluation is supported by two randomized controlled trials of annual or biennial screening

with gFOBT with rehydration with long follow-up, and a case-control study of biennial screening with gFOBT with rehydration.

There is *limited evidence* that screening annually or biennially with gFOBT of higher sensitivity reduces colorectal cancer incidence. This evaluation is supported by one randomized controlled trial of gFOBT with rehydration conducted in the USA showing similar reductions in colorectal cancer incidence after 11 rounds of annual screening and 6 rounds of biennial screening.

There is *sufficient evidence* that the benefits of annual or biennial screening with gFOBT of higher sensitivity outweigh the harms when the screening programme can be delivered with high quality. This evaluation is based on sufficient evidence of reduced colorectal cancer mortality, limited evidence of reduced colorectal cancer incidence, and a gain in quality-adjusted life years, versus the short-term psychological harms of screening per se or of a positive test result, as well as the medical harms of follow-up colonoscopy after a positive test result.

5.2 Faecal immunochemical test

There is *sufficient evidence* that biennial screening with the faecal immunochemical test (FIT) reduces colorectal cancer mortality. This evaluation is supported by several observational studies of both invitation to and attendance at biennial FIT screening, including three cohort studies, one of which included incidence-based mortality results after four rounds of biennial FIT screening, and one large ecological study after more than three rounds of biennial FIT screening. The evidence from four randomized controlled trials on screening with gFOBT and reduced colorectal cancer mortality, and the increased sensitivity and specificity of FIT compared with gFOBT for the detection of advanced adenomas and colorectal cancer, were also considered.

There is *limited evidence* that biennial screening with FIT reduces colorectal cancer incidence. This evaluation is supported by two cohort studies with up to five rounds of biennial FIT, and one ecological study in areas where biennial screening with FIT had been used for five rounds of screening, all showing a modest reduction in colorectal cancer incidence. The evidence from a randomized controlled trial showing a reduction in colorectal cancer incidence after biennial screening with gFOBT with higher sensitivity, and the increased sensitivity and specificity of FIT compared with gFOBT for the detection of advanced adenomas and colorectal cancer, were also considered.

There is *sufficient evidence* that the benefits of biennial screening with FIT outweigh the harms when the screening programme can be delivered with high quality. This evaluation is based on sufficient evidence of reduced colorectal cancer mortality and limited evidence of reduced colorectal cancer incidence, and a gain in quality-adjusted life years, versus the short-term psychological harms of screening per se or of a positive test result observed with similar screening procedures (such as gFOBT), as well as the potential medical harms of follow-up colonoscopy after a positive test result.

The Working Group is aware that there is a large variety of qualitative and quantitative FIT tests available, with wide ranges of sensitivity and specificity. The balance of benefits and harms will depend on the cut-off level for positivity.

5.3 Flexible sigmoidoscopy

There is *sufficient evidence* that a single screening with flexible sigmoidoscopy reduces colorectal cancer mortality. This evaluation is supported by four randomized controlled trials and corroborated by several observational studies in screening settings. No conclusion can be drawn about the added benefit of subsequent

screenings with flexible sigmoidoscopy on colorectal cancer mortality.

There is *sufficient evidence* that a single screening with flexible sigmoidoscopy reduces colorectal cancer incidence. This evaluation is supported by four randomized controlled trials and corroborated by several case-control studies in screening settings. No conclusion can be drawn about the added benefit of subsequent screenings with flexible sigmoidoscopy on colorectal cancer incidence.

There is *sufficient evidence* that the benefits of a single screening with flexible sigmoidoscopy outweigh the harms when the screening programme can be delivered with high quality. This evaluation is based on sufficient evidence of reduced colorectal cancer incidence and mortality and on a gain in quality-adjusted life years, versus the short-term psychological harms of screening per se or of a positive test result, the infrequent procedural harms of sigmoidoscopy, and the medical harms of follow-up colonoscopy after a positive test result.

5.4 Colonoscopy

There is *sufficient evidence* that a single screening with colonoscopy reduces colorectal cancer mortality. No conclusion can be drawn about the added benefit of subsequent screenings with colonoscopy on colorectal cancer mortality.

There is *sufficient evidence* that a single screening with colonoscopy reduces colorectal cancer incidence. No conclusion can be drawn about the added benefit of subsequent screenings with colonoscopy on colorectal cancer incidence.

These evaluations are supported by the evidence from randomized controlled trials on screening with flexible sigmoidoscopy: given the close similarity between the two procedures, a properly done full colonoscopy, by definition, includes a sigmoidoscopy, and therefore it is inferred that colonoscopy will be at least as good as flexible sigmoidoscopy at detecting advanced

adenomas and colorectal cancer. In addition, three observational studies and a meta-analysis of observational studies reported a reduced colorectal cancer incidence or mortality, and chance, bias, and confounding can be ruled out with reasonable confidence.

There is *sufficient evidence* that the benefits of a single screening with colonoscopy outweigh the harms when the screening programme can be delivered with high quality. In reaching this evaluation, the Working Group considered the evidence of reduced colorectal cancer incidence and mortality and a gain in quality-adjusted life years, versus harms such as bleeding and perforations, as well as the psychological harms of screening per se or of a positive test result.

A minority of the Working Group members considered that the evidence was *limited* because of the variability and the related limited accuracy of the effect estimates, the associated harms of colonoscopy, and the inherent limitations in extrapolating from data of screening with flexible sigmoidoscopy.

5.5 Computed tomography colonography

There is *limited evidence* that a single screening with computed tomography (CT) colonography reduces colorectal cancer incidence and mortality. No conclusion can be drawn about the added benefit of subsequent screening with CT colonography on colorectal cancer incidence and mortality.

In reaching this evaluation, the Working Group considered that: CT colonography has a very high sensitivity and high specificity, in particular a high sensitivity for the detection of advanced neoplasia (i.e. large adenomas and cancerous lesions), which has been shown to be associated with increased risk of developing colorectal cancer; CT colonography is comparable to a stool-based test in that a positive result

requires referral for colonoscopy; however, there are currently no randomized controlled trials or observational studies on the effect of CT colonography on colorectal cancer incidence or mortality in a screening setting.

A minority of the Working Group members considered that the evidence was *inadequate*, because of: the lack of randomized controlled trials or observational studies with incidence and mortality as end-points; the wide extrapolation needed from the known detection rates of lesions to an expected reduction in colorectal cancer incidence and mortality in a screening setting; the lack of studies with repeated CT colonography screening; and the fact that only detection rates and test performance in terms of sensitivity and specificity were available.

There is *inadequate evidence* that the benefits of a single screening with CT colonography outweigh the harms. This evaluation is based on the lack of direct evidence for a beneficial effect of screening with CT colonography in reducing colorectal cancer incidence or mortality, versus the harms of ionizing radiation, the uncertain harms and benefits of extracolonic findings, and the uncertainty when quantitative data of beneficial and adverse effects are lacking.