

EDITORIAL

Fecal Immunochemical Tests: The Right Colorectal Cancer Screening Test for the Average-Risk Population?



Colorectal cancer (CRC) screening is cost-effective, and several tests are recommended for reducing the burden of CRC.¹ Policymakers and clinicians need to consider several factors when choosing which test to implement (within organized screening programs) or offer their patients (opportunistic screening). Colonoscopy has long been the test of choice for many clinicians because of its high sensitivity and impact on preventing CRC, despite screening participation rates when offered to the population. Fecal immunochemical tests (FITs) are noninvasive options with high adherence and diagnostic yield when offered within organized screening programs.² Although FIT screening is expected to detect most asymptomatic CRCs in average-risk population and reduce cancer-specific mortality,³ its effectiveness in detecting precancerous lesions and preventing CRC is unclear.⁴ The single-test sensitivity of FIT for advanced adenomas is only about 20%–35%,⁵ and modelling studies have suggested biennial FIT reduces CRC incidence by only about 5%.⁶

In this issue of *Clinical Gastroenterology and Hepatology*, Baldacchini et al⁷ add an important piece of evidence for the effectiveness of FIT screening for reducing the burden of CRC. Their results, evaluating effectiveness of attending multiple rounds of FIT, are especially valuable while we await the results of ongoing randomized trials comparing FIT with colonoscopy (COLONPREV and CONFIRM), which will not be available for another 10 years.^{8,9}

Baldacchini et al⁷ performed a retrospective cohort study in the Italian region of Emilia-Romagna during the period 2005–2016, following 707,751 individuals (342,281 men and 365,470 women) for a median follow-up time of 9.5 years (>5.5 million person-years). They categorized individuals into 2 groups according to their screening history: 380,621 were attenders (responded to both of the first 2 screening invitations), and 327,100 were nonattenders (subjects who did not respond to the first 2 invitations). CRC mortality was reduced by 75% and 54%, respectively, in men and women who attended regularly FIT screening. However, the most novel results were on incidence. Among male attenders, the CRC incidence was 33% lower compared with nonattenders. In women, the effect of attending FIT screening on CRC incidence was lower than in men (21% reduction compared with female nonattenders). Reductions in incidence were higher for rectal cancers and advanced-stage CRCs (stage III and IV combined).

Attending FIT screening resulted in a higher incidence of stage I CRC. The authors concluded that FIT screening was effective in reducing CRC mortality and preventing the incidence of the tumor, confirming the results of previous cohort studies with limited statistical power.⁴

The number of individuals included in the study's cohort further enabled the authors to investigate the impact of FIT stratified by age, sex, stage, and tumor site, as few have been able to do previously. FIT performed less well among older women in particular, possibly because of lower sensitivity for proximal lesions that are more prevalent among older women. Unfortunately, this study adds to previous evidence that CRC screening performs less well for women, particularly elderly women. First, CRC location was seen to be different across men and women, with the latter showing more adenomas located in the proximal colon.¹⁰ FIT sensitivities for advanced adenomas and positive predictive values were also reported to be higher in men compared with women.¹¹ In addition, a meta-analysis of randomized trials assessed the impact of flexible sigmoidoscopy screening stratified by age and sex,¹² and found it to be effective in men of all ages and women younger than age 60, but not in women older than age 60. Taken together, women seem likely to have a lower absolute benefit from CRC screening, given the combination of lower incidence and relative benefit, although the impact on screening recommendations remains hotly debated. Although FIT screening is cost-effective,¹ test results can be assessed differently in men and women because FIT is quantitative test. Decision makers may optimize population health resources using sex-specific FIT cutoff levels.^{13,14} This can lessen the burden of unnecessary colonoscopies in the population.

In men and women, the impact of FIT on CRC incidence demonstrated by Baldacchini et al⁷ is the result of attending FIT screening repeatedly and regularly. FIT can continue to detect additional advanced neoplasia during subsequent screening rounds. This was shown by several works of real-world evidence where FIT is offered within their organized programs.^{2,15,16} Although colonoscopy screening is considered ideal for detecting adenomas (given the high sensitivity of this test), individuals willing to accept FIT screening will repeat 5–10 times the tests (depending on the recommended FIT screening interval) in the 10-year interval between colonoscopies, providing multiple opportunities to detect adenomas. This is highlighted by the results of Baldacchini et al,⁷ where the reduction of CRC incidence is likely to be the direct consequence of detecting and removing adenomas within an organized FIT screening program that is running more than 10 years.¹⁵

Important limitations of this study include the cohort definition, which did not permit to assess the impact of FIT with an intention-to-screen approach, and unmeasured confounding. However, these findings are striking because FIT screening is associated with higher participation rates and requires less endoscopy resources than colonoscopy screening.²

Practicing physicians, particularly gastroenterologists, have long favored colonoscopy over FIT because of its high sensitivity for advanced adenomas and potential to reduce CRC incidence.¹⁷ However, that perspective is overly focused on individual patients seen in consultation and not on the needs of the population. Multiple studies have now demonstrated the impressive impact of mailed FIT to reach the goal of 80% screening rates and decreases in CRC incidence and mortality.¹⁸ This approach works best when supported by organized programs that deliver tests to the entire target population, with a special focus on underserved populations. Evidence is mounting that although one should still offer colonoscopy as an initial screening test for selected individuals, especially those at increased risk of CRC, FIT may be the best test for the average-risk population in a programmatic setting.

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Conflicts of interest

The authors disclose no conflicts.

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