Colorectal Cancer Screening in the United States: What Is the Best FIT?

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In the United States, colorectal cancer (CRC) incidence and mortality have declined by roughly 3% per year since 2001 (1). Screening probably explains much of this public health success; however, the optimal method for it remains unclear. Colonoscopy accounts for at least 60% of all CRC screening in the United States, despite its greater expense and risk for complications compared with other options (2). Surprisingly little published evidence supports the predominance of colonoscopy. Unlike for fecal occult blood testing or flexible sigmoidoscopy, no controlled studies have shown that colonoscopy reduces CRC incidence or mortality. Most studies have reported that the cost-effectiveness of other CRC screening methods equals or exceeds that of colonoscopy (3). Recently, the clinical effectiveness of screening colonoscopy itself came under fire, with several studies showing excellent protection against left-sided CRC but far less against right-sided disease (4). Long-awaited trials comparing colonoscopy with stool blood–based screening methods are under way, but informative results will not be available for years.

Review of this evidence has prompted national CRC screening programs in Europe, Asia, and elsewhere to emphasize guaiac-based fecal occult blood testing (gFOBT) and, more recently, fecal immunochemical testing (FIT) as the primary screening methods. For example, the Canadian Task Force on Preventive Health Care recently published statements supporting FIT while specifically recommending against colonoscopy (5).

In light of these controversial aspects of CRC screening, the U.S. Multi-Society Task Force, which comprises the major U.S. gastroenterological professional associations, just released an extensive and timely examination of evidence regarding the use of FIT for CRC screening in average-risk populations (6). This consensus statement summarizes well the advantages of FIT over gFOBT. First, in pooled analyses, the 79% sensitivity (95% CI, 69% to 86%) of FIT comfortably exceeds that of gFOBT (approximately 35%) while maintaining similar specificity: 94% (CI, 92% to 95%). Second, FIT detects advanced adenomas (intermediate precursors to CRC) more consistently than gFOBT. In a recent meta-analysis of randomized, controlled trials, FIT detected twice as many CRCs and advanced adenomas as gFOBT (relative risk, 2.28 [CI, 1.68 to 3.10]). Third, patients prefer FIT to gFOBT, which is a distinct advantage, because continued adherence is one of the greatest challenges in CRC screening. These data provide tremendous clinical support for a switch from gFOBT to FIT in U.S. primary care settings.

This Multi-Society consensus statement also offers useful recommendations regarding implementation of FIT, such as the number of times FIT should be done per screening round (one), the interval between screening rounds (1 year), whether a qualitative or quantitative immunochemical assay for blood is preferred (quantitative), and the cutoff used to define a positive test result (≤20 μg blood per gram of stool). Although the authors acknowledge that the supporting evidence is "weak" because of "low quality," their recommendations are similar to those of other expert panels in Europe.

Given the preference for colonoscopy screening in the United States, strong evidence would be required to shift this norm. Colonoscopy advocates point to its unrivalled ability to identify and remove adenomas, thereby preventing cancer, whereas gFOBT (or FIT) is seen as useful for detecting rather than preventing CRC. However, recent modeling studies show that when adherence to serial completion is high, FIT-based screening yields reductions in CRC incidence similar to those of colonoscopy (7). In addition, preliminary results from controlled head-to-head trials indicate that when participants were offered FIT, they were more likely to choose it over colonoscopy (8). As a result, more cancers (but fewer advanced adenomas) were detected in populations screened with FIT than those screened with colonoscopy. These early results underline that the absolute number of detected CRCs in any screening initiative reflects the balance between test adherence (greater for FIT than colonoscopy) and test sensitivity (greater for colonoscopy than FIT).

At present, colonoscopy and stool testing for blood are the only readily available CRC screening tests in the United States. Primary care clinicians undoubtedly will be concerned about the practical aspects of implementing more broad-based, annual FIT screening. Nationally, there is no infrastructure to support a CRC screening program using any method. Despite the proliferation of electronic health records, large-scale FIT screening efforts will require efficient tracking mechanisms to ensure that the test is offered, the test kits are returned, patients with positive results are followed up with colonoscopy, and those with negative results repeat FIT in 1 year. Additional logistical barriers loom. The U.S. Food and Drug Administration has approved only qualitative FIT reporting in the United States, effectively predetermining the cutoff level that defines a positive test. More sensitive tests (lower cut points) will trigger a larger number of follow-up colonoscopies. The cut point for FIT recommended by the task force balances sensitivity and specificity. However, that cut point may not equal the manufacturer's choice for some FIT products available in the United States. In contrast, quantitative FIT provides flexibility in selecting a positive cutoff. Having a variety

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of cut points allows some FIT programs to take into account access to follow-up colonoscopy.

The Patient Protection and Affordable Care Act mandates that preventive services endorsed by the U.S. Preventive Services Task Force (USPSTF), including CRC screening, be offered at no cost to the patient, thereby reducing a major barrier to screening uptake. All persons with a positive FIT result (about 5% of tests in average-risk settings) need a follow-up colonoscopy; however, this subsequent "diagnostic" test no longer is defined as "screening" in these cases, so patients may be responsible for deductible and other costs. This paradox might push patients and physicians to opt for screening colonoscopy despite its higher cost and risk and, for some patients, its unpleasantness.

The USPSTF advocates a variety of options to complete CRC screening, acknowledging that no one screening method clearly outperforms the others and that the best test is the one the patient completes (4). Research has shown that patients who are offered a choice between gFOBT and colonoscopy are more than twice as likely to complete screening than if they had been offered only colonoscopy (9). Furthermore, a randomized trial showed that compared with usual care, a CRC screening program featuring centralized provision of CRC screening tests linked to the electronic health record led to lower costs and greater screening rates over a 2-year period (10).

For primary care and other clinicians who provide CRC screening services, this authoritative consensus statement offers strong evidence for FIT as an excellent alternative for CRC prevention. For improvements in CRC prevention and early detection to continue, patients must have access to several effective, low- or no-cost screening options. For a variety of reasons, including access, cost, and patient preference, FIT is a worthy component of any average-risk screening program. The use of this test should be promoted as enthusiastically as colonoscopy.

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