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Authors

Cusumano, Vivy T
May, Folasade P

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Making FIT Count: Maximizing Appropriate Use of the Fecal Immunochemical Test for Colorectal Cancer Screening Programs

Vivy T. Cusumano, MD[1] *and Folasade P. May, MD, PhD, MPhil*[1,2,3,4]

[1]Department of Medicine, David Geffen School of Medicine at UCLA, CA, Los Angeles, USA; [2]Vatche and Tamar Manoukian Division of Digestive Diseases, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [3]UCLA Kaiser Permanente Center for Health Equity, UCLA Jonsson Comprehensive Cancer Center, CA, Los Angeles, USA; [4]Department of Medicine, VA Greater Los Angeles Healthcare System, CA, Los Angeles, USA.

Colorectal cancer (CRC) remains one of the most common and deadly malignancies despite advancements in screening, diagnostic capabilities, and treatment. The ability to detect and remove precancerous and cancerous lesions via screening has altered the epidemiology of the disease, decreasing incidence, mortality, and late-stage disease presentation. The fecal immunochemical test (FIT) is a screening test that aims to detect human hemoglobin in the stool. FIT is the most common CRC screening modality worldwide and second most common in the United States. Its use in screening programs has been shown to increase screening uptake and improve CRC outcomes. However, FIT-based screening programs vary widely in quality and effectiveness. In health systems with high-quality FIT screening programs, only superior FIT formats are used, providers order FIT appropriately, annual patient participation is high, and diagnostic follow-up after an abnormal result is achieved in a timely manner. Proper utilization of FIT involves multiple steps beyond provider recommendation of the test. In this commentary, we aim to highlight ongoing challenges in FIT screening and suggest interventions to maximize FIT effectiveness. Through active engagement of patients and providers, health systems can use FIT to help optimize CRC screening rates and improve CRC outcomes.

KEY WORDS: colorectal cancer; screening; fecal immunochemical test; cancer detection; stool-based test.

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INTRODUCTION

In the United States (U.S.), colorectal cancer (CRC) is the 2nd leading cause of cancer-related deaths.[1] Screening, which improves CRC outcomes by detecting precancerous and cancerous lesions early, has contributed substantially to the decline in CRC incidence and mortality over the past several decades.[2–4] Despite the demonstrated benefits of screening, only 65% of age-eligible adults are up to date in the U.S.[5, 6]

There are multiple stool-based and structural modalities for CRC screening.[7, 8] Of these, the fecal immunochemical test (FIT) is the most common CRC screening modality worldwide and the second most common in the U.S.[9] Currently, the Multi-Society Task Force (MSTF) recommends FIT alongside colonoscopy as 1 of 2 first-tier CRC screening tests.[10] FIT is an inexpensive, noninvasive, and convenient test that has resulted in higher screening participation than other modalities in many settings.[7, 10–12] The test characteristics are superior to stool guaiac tests (i.e. FOBT), with increased sensitivity to detect advanced adenomas and colorectal adenocarcinomas and the ability to reduce both CRC incidence and mortality.[9, 10] The question facing patients, providers, and health systems is no longer whether to use FIT but rather how to optimize its use.

Efficient and effective screening programs employ tests that are sensitive and specific while also assuring patient engagement, provider guidance, and health system tracking to optimize screening quality.[10] Persistent issues in FIT screening include variability in available FIT formats, FIT administration and processing, timely diagnostic follow-up after abnormal FIT, and adherence to recurrent screening recommendations.[10] We will review these ongoing challenges and suggest various strategies to maximize the benefits of FIT screening programs for health systems that wish to improve CRC screening and outcomes. Through active engagement from patients, providers, and health systems, FIT screening programs can be more effective in improving CRC screening and outcomes.

Not All FIT Kits Are Created Equal

There is a wide diversity of available FIT formats that vary in the number of stool samples recommended (1 vs. 3), analytic technique (qualitative vs. quantitative), optimal cut-off value for the amount of hemoglobin detected to define an abnormal result, and type of manufacturer devices.[10, 13, 14] One-sample FIT regimens and multiple sample regimens have similar CRC sensitivity in meta-analysis, and organized CRC screening programs vary in the number of FIT samples recommended.[15–17] Qualitative and quantitative FIT kits have similar

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performance; however, quantitative FIT kits allow users to adjust the abnormal cut-off limit to best target sensitivity for advanced neoplasia (e.g., increasing the cut-off value decreases sensitivity and increases specificity for CRC) and take into consideration population-specific factors such as capacity for colonoscopy and cost-effectiveness.[18–21] The MSTF recommends a cut-off value of < 20 gb/g feces based on evidence from meta-analyses that this cut-off offers the best combination of sensitivity, specificity, and diagnostic accuracy for CRC, and is cost effective.[22]

There are currently over 65 FIT formats in circulation globally and 26 unique FIT kits on the market in the U.S., with variable test characteristics.[13, 23–26] The 2016 U.S. Preventive Services Task Force (USPSTF) guidelines recommend the OC FIT-CHEK products (OC-Light and OC-Auto) due to high test performance (sensitivity and specificity).[27, 28] Since this recommendation, however, new evidence has emerged that InSure FIT has higher sensitivity for advanced colorectal neoplasia (26.3%, 95% CI 15.9–40.7) when compared with OC FIT-CHEK (15.1%, 95% CI 6.7–26.1).[29] Health systems must consider FIT format characteristics and local resources when selecting the best FIT kit and assay cut-off value for their patient population.[27]

Patients and Providers Must Know how to Use FIT Appropriately

FIT screening success is determined by appropriate use of the test by providers, patients, and health systems. Providers play a key role in assuring appropriate prescribing of FIT, which should only be performed in the ambulatory setting and with spontaneously passed stools.[21] The use of digital rectal examination to obtain a FIT stool sample is understudied; however, a clinical trial examining the efficacy of digital rectal exam for FIT is underway and may impact recommendations.[30] Patients must be instructed on how to collect the stool sample properly and to return the sample to the laboratory for processing within the timeframe indicated by the FIT manufacturer. The manufacturer for OC-Sensor FIT (Polymedco Inc.), for example, recommends laboratory processing of the sample within 15 days of stool collection to avoid reduced test sensitivity. Two weeks after a sample has been collected, almost a third of abnormal results have the potential to convert to negative.[31] Data also suggest that stool samples exposed to high ambient temperature have reduced sensitivity, which may impact screening outcomes.[32]

Inappropriate use of the test can also occur when patients who are not eligible for CRC screening (i.e due to age, life expectancy) are prescribed a FIT kit. Offering FIT to patients with multiple comorbidities or other factors precluding evaluation with colonoscopy if indicated may have the unintended consequences of worsening quality of care.[22] Mailed FIT interventions that utilize system-level tools to target patients due for screening have been shown to improve FIT completion but should be used with caution as some patients require more personalized decision support.[33] Another common practice that should be discouraged is repeating a FIT when the result is abnormal. Even if the repeat FIT is negative, a patient may have an advanced tubular adenoma or cancerous lesion that requires further evaluation with colonoscopy.[10, 34] Similarly, there are data to support that patients with an abnormal FIT result should be offered a repeat colonoscopy even in the setting of recent prior colonoscopy as poor colonic preparation and missed colonic lesions are common .[10, 35] Providers should receive education about these common shortcomings of FIT administration. Health systems can help minimize inappropriate use of FIT by tracking inappropriate FIT prescribing, FIT processing errors, abnormal results, and repeat FIT orders. By identifying challenges in FIT administration processes, targeted interventions can be implemented to address deficiencies.

Diagnostic Colonoscopy After Abnormal FIT Is Fundamental

Lack of colonoscopic follow-up after abnormal FIT is associated with increased mortality from CRC and late-stage disease at diagnosis.[36–38] However, colonoscopy rates after abnormal FIT are suboptimal across multiple health care systems in the U.S.[39–43] Barriers to colonoscopic follow-up are broad and include patient-, provider-, system-, and health policy-related factors. Patient comorbidity, poor understanding of FIT, anxiety and fear regarding colonoscopy, lack of provider referral for colonoscopy, lack of colonoscopy availability, and scheduling difficulties are associated with low follow-up rates.[39, 40, 43–46] Federally qualified health centers (FQHC) and other closed-health systems without in-house specialty services have the additional challenge of coordinating care with gastroenterologists outside their health system to obtain colonoscopies for patients with abnormal FIT.[24] Current insurance policy also plays a role. Colonoscopies performed after an abnormal FIT are considered diagnostic rather than a covered preventive service, and patients may be required to pay a co-payment.[47]

Interventions to address these barriers and increase colonoscopic follow-up are understudied but have included patient and provider education, mailed and electronic provider and patient reminders, systems to track abnormal FIT results, and patient navigation to increase throughput to colonoscopy.[48] One challenge is that health systems are not currently held accountable for measuring or reporting how often patients with abnormal stool-based screening results undergo colonoscopy. As the screening process is not complete until those with abnormal results undergo diagnostic testing, there should be movement nationally towards requiring health systems to report screening completion rates. Compulsory reporting of colonoscopy follow-up rates, as is done for CRC screening rates through the Healthcare Effectiveness Data and Information Set (HEDIS), will signal to health centers the need for increased attention to abnormal screening results.

Time to Colonoscopy After Abnormal FIT Matters

Until relatively recently, we knew very little about the time interval between an abnormal FIT and diagnostic colonoscopy that is associated with poor outcomes. Prior studies used somewhat arbitrary intervals of 6 or 12 months to define colonoscopy completion endpoints.[49] New data, however, suggest an increased risk for CRC only when colonoscopy is delayed 10 to 12 months or more after abnormal FIT (OR 1.48, 95%CI 1.05–2.08).[38] A microsimulation study to estimate the impact of delays to FIT follow-up in an average-risk population also supports increased mortality and decreased cost-effectiveness of screening when follow-up is delayed beyond 12 months.[50] While the timing of colonoscopy may not be as urgent as previously considered, we must balance this knowledge with what is known about patient behavior around colonoscopy. Patients that have not completed colonoscopy within 6 months of an abnormal FIT are unlikely to ever complete the diagnostic evaluation in the absence of outreach.[51] As we continue to investigate the optimal time to colonoscopy, it is most prudent for health systems to encourage patients and providers to complete colonoscopy as soon as possible and definitely within 10 months.[38]

A Focus on Repeat Screening: Improving Adherence to FIT Screening

Organized FIT screening programs depend on adherence to recurrent FIT to reduce CRC incidence and mortality. FIT sensitivity is highest in the first round of screening (84.5%) and can detect an additional 75% of CRC cases with each subsequent year of testing.[52] The USPSTF recommends an annual approach while the American College of Physicians (ACP) recommends biennial exams; however, randomized controlled trials are underway to compare these two approaches.[7, 8, 53, 54]

While annual FIT is commonly prescribed, adherence is often suboptimal. Studies evaluating adherence over multiple rounds of yearly screening demonstrate less than 50% compliance.[55–58] Adherence appears to improve with implementation of clinical reminders for patients and providers, coupling FIT screening with other annual preventative health screenings like influenza vaccination, and automated orders for screening tests.[59–61] Health systems should assess FIT adherence rates over time to maximize FIT effectiveness and consider strategies to encourage repeat testing among patients and providers when participation is low.

Future Directions in FIT Programs for Improving CRC Outcomes

The introduction of CRC screening in the U.S. accounts for up to 50% of the decline in CRC incidence and mortality over the past four decades.[62, 63] FIT is a staple of many health system screening programs, offering a convenient and inexpensive strategy to increase patient participation in screening and overall CRC screening rates.[64, 65] However, as we have emphasized, screening by FIT is a multistep process and is complicated by several factors, including choice of FIT kit, appropriate FIT kit administration and use, timely diagnostic follow-up after abnormal FIT, and adherence to annual or biennial FIT screening over time.

Inappropriate use of FIT is a clinical challenge that places patients at risk for poor outcomes.[10, 36, 39] Maximizing the effectiveness of FIT screening programs mandates attention from health systems, health professionals, patients, researchers, quality officers, and policy leaders. Health care systems must be mindful of FIT performance characteristics and colonoscopy availability when selecting the appropriate FIT kit for their setting. Furthermore, health care systems must develop mechanisms for measuring and monitoring colonoscopy rates after abnormal FIT. Innovations in informatics technology and EHRs may help automate and optimize how we measure and monitor screening and follow-up rates, which will facilitate the introduction and evaluation of interventions. Researchers and quality improvement leaders can then guide the implementation and evaluation of interventions to achieve quality benchmarks for FIT processes, increase colonoscopic follow-up after abnormal FIT, and improve long-term adherence to FIT. Effective strategies to accomplish these goals, including electronic tracking of patients with abnormal FIT results, provider reminders to order colonoscopy, patient reminders, and patient navigation, should be considered and tailored to the clinical setting.[48, 66] In addition to these efforts, providers and patients must engage in informed shared decision making about appropriate use of FIT to achieve high participation in screening and diagnostic follow-up when needed. Provider education about appropriate and inappropriate use of FIT may help in this capacity.[22, 66] Emphasis must also be placed on policy to improve insurance coverage for and reporting of diagnostic follow-up after abnormal results. With a concerted effort to optimize these critical components of FIT screening, we can make greater strides towards the elimination of CRC and gain progress towards making FIT count.

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Corresponding Author: *Folasade P. May, MD, PhD, MPhil; Department of Medicine, VA Greater Los Angeles Healthcare System, CA, Los Angeles, USA (e-mail: fmay@mednet.ucla.edu).*

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