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Mailed Fecal Immunochemical Test Outreach for Colorectal Cancer Screening: Summary of a Centers for Disease Control-Sponsored Summit

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Abstract

Uptake of colorectal cancer (CRC) screening remains suboptimal. Mailed fecal immunochemical testing (FIT) offers promise for increasing screening rates, but optimal strategies for implementation have not been well synthesized. In June 2019, the Centers for Disease Control and Prevention convened a meeting of subject matter experts and stakeholders to answer key questions regarding mailed FIT implementation in the US. Points of agreement included: 1) Primers such as texts, phone calls, and printed mailings prior to mailed FIT appear to contribute to effectiveness; 2) Invitation letters should be brief, easy to read, and signatory should be tailored based on setting; 3) Instructions for FIT completion should be simple and address challenges that may lead to failed lab processing, such as notation of collection date; 4) Reminders delivered to initial non-completers should be utilized to increase FIT return; 5) Data infrastructure should identify eligible patients and track each step in the outreach process, from primer delivery through abnormal FIT follow up; 6) Protocols and procedures such as navigation should be in place to promote colonoscopy after abnormal FIT; 7) A high-quality, 1 sample FIT should be used; 8) Sustainability requires a program champion and organizational support for the work, including sufficient funding, and external policies (such as quality reporting requirements) to drive commitment to program investment; and 9) Cost effectiveness of mailed FIT has been established. Participants concluded that Mailed FIT is an effective and efficient strategy with great potential for increasing CRC screening in diverse healthcare settings if more widely implemented.

Keywords

Colorectal cancer; CRC; fecal immunochemical test; FIT; mailed outreach; evidence based; colorectal neoplasms

Introduction

Colorectal cancer (CRC) is the 2nd leading cause of cancer death in the United States, accounting for over 52,000 deaths in 2016 (<https://gis.cdc.gov/Cancer/USCS/DataViz.html>). CRC screening can reduce incidence and mortality, but participation nationally is estimated to only be between 67.0 to 68.8%^{1,2} and screening rates have risen more slowly over the past decade. Participation is particularly low among population subgroups such as racial/ethnic minorities, individuals with low socioeconomic position, those without a regular source of care, and the uninsured. Several evidence-based strategies have been demonstrated to improve screening completion, but widespread application has been limited in the United States. Implementation of evidence-based strategies across multiple settings is critical to overcome the observed stagnation in screening trends.

The most effective strategies to improve screening are multi-component and multi-level, addressing barriers at the patient, provider, and health system levels. The fecal immunochemical test (FIT) is an at-home test for blood in the stool recommended by the US Preventive Services Task Force and others to be utilized annually as a strategy for screening to reduce CRC incidence and mortality. Mailed outreach offering a stool-based test such as a FIT-- herein referred to as mailed FIT outreach--is a particularly promising multi-component strategy for improving screening that addresses barriers at all three levels. At minimum, the strategy usually includes a mailed invitation to age-eligible individuals, not up-to-date with CRC screening, to complete and return a FIT through the mail. At the system level, mailed FIT outreach offers screening to every individual who is not up-to-date and is served by the system, and allows for screening independent of the need for an in-person clinic visit, thereby maximizing “reach” within the population, especially important as US healthcare transitions to emphasize telehealth and video visits. As such, mailed FIT represents an implemented policy of outreach to every individual eligible for screening. From the provider perspective, mailed FIT outreach can address the challenge of having limited time available to promote screening. Also, some mailed FIT programs include workflows to reduce burden on providers with respect to ordering and promoting abnormal test follow-up. At the patient level, mailed FIT provides education about the importance of screening, reduces barriers to testing through the convenience of at home testing, offers reminders to complete screening, and may employ navigation to facilitate screening completion and test follow-up (Table 1).

Systematic reviews and meta-analyses have identified numerous observational trials and randomized controlled trials (RCTs) that demonstrate mailed outreach offering a stool test is efficacious and effective. A recent meta-analysis of seven RCTs summarizing data from over 11,000 individuals randomized to either mailed outreach offering a stool test versus usual care (opportunistic clinic-based offers for screening) found mailed outreach resulted in a 28% absolute increase in screening completion (95% CI, 25–30%).³ Indirect comparisons from systematic reviews of strategies for increasing screening completion suggest that mailed outreach offering stool blood tests is associated with a higher likelihood of screening completion compared to other evidence-based strategies such as patient navigation without stool blood test distribution or patient education alone (Table 2).^{4,5}

In addition to the randomized trials that have evaluated mailed FIT outreach efficacy, many other studies have examined the effectiveness of mailed outreach in less controlled environments, or in RCTs employing a waiver of informed consent.³⁻⁵ Most effectiveness studies have shown outcomes similar to efficacy studies, but at least one effectiveness study has shown that replicating interventions is challenging to implement in community clinics⁶. Mailed FIT outreach does appear scalable for reaching large numbers of individuals; one integrated healthcare system in the United States mails over 699,000 invitations annually.⁷

Despite the promise of mailed FIT outreach programs, implementation may be hindered by a lack of knowledge on the part of providers and health systems about the key components of successful programs and the adaptations and resources needed in certain settings or populations for success. To examine implementation of mailed FIT outreach as a possible strategy for improving screening rates, the Centers for Disease Control and Prevention (CDC) and the National Association for Chronic Disease Directors held a meeting including researchers and experts in implementing Mailed FIT outreach programs for a Mailed FIT Summit on June 28, 2019 in Decatur, Georgia. This white paper summarizes information presented at the meeting and discussions that took place therein to answer several key questions about how to optimally implement mailed FIT outreach to increase CRC screening (Table 3).

Methods

The purpose of the meeting was to bring together a group of experts to summarize evidence for mailed FIT outreach, including best practices for implementation, and summarizing the gaps in the research literature. Participants were selected for invitation by LR, MP, and SG through mutual consensus, and based on availability of invited experts. The agenda included review of evidence to support mailed FIT outreach, as well as evidence informing responses to our key questions (Table 3; see Appendix 1 for agenda). Key questions were identified by LR, MP, and SG through mutual consensus. Sources of evidence included published literature and clinical experience. Each agenda item presented, including each key question, was assigned to one or more summit participants prior to the meeting. Participants were instructed to conduct a narrative literature review and evidence synthesis to present at the summit. Evidence reviewed was mainly identified from US programs and studies to ensure their relevance for US health care systems. The international experience with mailed FIT outreach was beyond the scope of our review, and studies outside of the US were only utilized when no US specific data were available, such as for examination of performance of FIT brands/types. A professional facilitator was engaged so that participants could reflect on their review of the literature, their own experiences implementing mailed FIT outreach, and the opinions of other experts in the room.

Summaries of the narrative reviews were presented at the Summit using PowerPoint and an extensive discussion was held following each presentation. The discussion was summarized through note taking and provided to summit participants for review. The lead authors (M.P.; G.C.; and S.G.) developed a first draft of the white paper summarizing the original narrative reviews, meeting presentations, discussions, and any agreement reached regarding best practice suggestions for mailed FIT implementation. In the results section of this white

paper, for each key question, we report a brief summary of the published literature, followed by the key points raised in discussion at the Summit meeting, concluding with key conclusions and resources. Agreement on best practices for mailed outreach was based on discussions during the meeting and/or review of the final white paper manuscript. The draft was circulated among all authors for review and editing, and then finalized by the lead authors and submitted for publication.

Results

Section 1: Infrastructure and FIT kit selection

We define data infrastructure for mailed outreach (KQ1; Table 3) as infrastructure required to identify candidate participants, mail invitations, process results, and track results and follow-up. For some programs, infrastructure also should allow for accounting of costs, sharing information with primary care or other providers, and/or tracking invoices and payments for follow-up colonoscopies triggered by abnormal stool blood tests. In this section, we include key considerations for selecting a FIT kit (KQ2; Table 3), recognizing that FIT kits vary in their performance characteristics as well as in ways that may impact patients' willingness or ability to appropriately complete them.

KQ1: Which data, and what data infrastructure are required to support mailed FIT outreach?

We did not identify any published literature on data infrastructure used for mailed FIT outreach, including comparison of different strategies. Summit participants discussed several different models for data tracking. One model, a "stand alone" model, requires creation of a tracking database to capture outcomes of all steps required for mailed outreach. A second model, an 'embedded' model, involves embedding the tracking functions for mailed outreach directly into the electronic health record. For example, a large mailed outreach program led by Moncrief Cancer Institute in Fort Worth, TX initially implemented a stand-alone model to deliver mailed FIT outreach across several practices using different electronic health record systems. In the initial iteration of the program, a customized, relational structured query language (SQL) database was constructed to allow uploading of patients eligible for mailed outreach, generation of mailed outreach interventions (including lists for automated primer calls, invitation letters, reminder letters, and results letters), batch input of FIT results, and tracking of key steps in the screening promotion process. The database also allowed for tracking of results and reimbursement for diagnostic colonoscopies completed in response to abnormal FIT. Other summit participants reported building similar data infrastructure for mailed outreach but noted that often they also required access to the EHR system used as part of usual medical care to verify completion of steps required for outreach. A challenge of "stand alone" models is that specified resources are required for upkeep, to both import and export electronic health record information to conduct program activities (e.g. identifying eligible patients, providing primary care providers with results), and that scaling may be difficult. Summit participants discussed that embedding a mailed FIT data infrastructure within an established EHR system might address some of the previously outlined logistical challenges specific to a stand-alone system.

An Oregon-based study that involved 8 federally qualified health centers relied on embedded electronic health record tools to identify individuals eligible for CRC screening and deliver mailed FIT outreach.⁶ The tools used real-time data to create lists of persons who were eligible for each step of the mailed FIT outreach program (introductory letter mailing, FIT kit mailed, reminder). The tools also generated lists of individuals who had a positive FIT result and were due for a follow-up colonoscopy. The tools queried data from multiple fields in the electronic health record (e.g. problem list, laboratory orders and results), including a preventive health tracking tool, which allowed clinicians to postpone or suspend screening for those determined to be ineligible because of having limited life expectancy, being on hospice, or other clinical reasons. Patients whose preventive care was postponed or suspended were automatically removed from the lists; enabling seamless and real-time integration of the outreach program with clinical care delivery. The embedded lists were used to generate materials for step-specific mailings (e.g. letter, kit labels). A batch ordering function allowed for the single-click placement of FIT laboratory orders for all patients on a given list. Consistent with usual care, results from completed FITs were input directly into the medical record through an established electronic interface. While embedded tools offer some advantages over stand-alone systems, they also require upkeep in the face of changing screening guidelines and rapidly changing technology for healthcare. Another important fact is that the more complex the tools are, the more training is required for their adoption and continued use.

In recent years, a few health insurance plans, including Medicaid and Medicare managed care plans, have begun to deliver mailed FIT outreach as part of their efforts to increase CRC screening participation among enrollees. These programs generally rely on lists generated by the health plan using claims data (some programs have allowed clinics to review these lists to remove patients who have been recently screened or have not yet established care at a given clinic). Nevertheless, these programs generally partner with outside vendors who can complete all aspects of the program, including mailing outreach components, delivering phone calls, and even offering care coordination for patients who need a follow-up colonoscopy. These programs also sometimes contract with centralized laboratories for all their FIT processing and rely on claims data for tracking of completed FITs. Research is lacking on the validity of relying on claims data for participant selection and tracking.⁸ Research is also lacking on rates of inappropriate inclusion of individuals for outreach (e.g. over-screening due to prior receipt of colonoscopy, mis-screening of individuals with a family history of CRC which should trigger colonoscopy), and inappropriate exclusion (e.g. failing to include an eligible individual). Participants did not specifically identify ability of the data infrastructure to facilitate identification of individuals with personal or family history of polyps or CRC as a requirement. While these criteria are desirable to focus mailed outreach on individuals at average risk for CRC, such data are perceived to be inconsistently recorded and may not be easily accessible in many health systems. Some participants included language in their invitation letters specifying patients who believe they are at increased risk for CRC can contact their primary care provider instead of completing mailed FIT. Strategies for improving the capture of colonoscopy information into EHRs is an ongoing and important challenge, especially for non-integrated health care systems.

Best practice suggestions regarding data infrastructure—Summit participants recognized the need for data infrastructure, which, at a minimum, should be able to identify eligible patients for mailed outreach and track key steps in the screening process, i.e., to document mailings sent, FIT results, and FIT result communication to patients and providers. The ideal infrastructure also tracks steps in navigation to colonoscopy for abnormal FIT, allows for repeat invitation for patients with normal results, and accommodate tracking of reimbursement if applicable (i.e., for programs that cover colonoscopy costs). Scalable resources for data infrastructure, whether “stand alone” or “embedded” within electronic health records, could enhance implementation of mailed FIT outreach.

KQ2: What are the key considerations for selecting a FIT for mailed outreach?

FIT kits can vary in terms of test characteristics for neoplasia detection, number of samples required, steps required for sample collection, methods required for processing, threshold for positivity, and scalability for high throughput processing, among other characteristics. These variations may affect program sensitivity for neoplasia, ease of test completion, rates of sample rejection, and ability of a lab to process samples efficiently. The evidence base regarding individual test characteristics for neoplasia detection for a range of FIT kit brands has been reviewed elsewhere in detail, and is beyond the scope of this white paper.^{9,10} Available data suggest some variation in sensitivity and specificity for neoplasia across FIT kit brands, with some available tests having little data to allow for evaluation of diagnostic performance. There is limited evidence concerning which FIT kit characteristics promote successful response to FIT outreach, defined by returning the kit and also having a sample that can be processed.

Two RCTs in the US have found improved screening participation when a 1 vs 2 sample test was offered. Chubak et al. reported return of any stool blood test after kit mailing within 6 months was 69 vs 64% ($p < 0.005$) for 1 vs 2 sample testing,¹¹ while Mosen et al. reported kit return within 6 months was 43.4 vs 39.6% ($p = 0.012$) for 1 vs 2 sample testing.¹² Data from outside the US suggest that detection of advanced neoplasia and CRC do not appear to differ substantially with 1 versus more than 1 FIT sample.^{13,14} Based on available evidence, a one sample test is generally preferred and is likely more cost effective.¹⁵ Brand of FIT could theoretically impact response to FIT outreach, but few head to head comparisons have been reported. In Europe, participation with OC-Sensor vs. FOB-Gold have been compared in multiple studies, with two studies showing no statistical difference, and a third showing a small statistically significant $< 2.7\%$ reduction in screening participation in patients offered the FOB- Gold (61.8% for OC-Sensor vs. 59.1% for FOB-Gold).^{16–18}

A few practical considerations were discussed at the summit about FIT selection. While insurers are required to cover screening with FIT, some labs may only offer a specific FIT brand. Some FIT kits are batch processed by an automated machine and produce a quantitative result, reflecting the concentration of blood in a patient’s stool. Other FIT kits are hand processed individually and read by a technician and produce a qualitative result (positive or negative). Batch processed FITs that produce a quantitative result may offer advantages, particularly as part of a high volume mailed FIT program, because batch processed FITs can decrease inter- observation variation, can be efficiently processed, and

may allow for an adjustment to the positivity threshold to accommodate a given colonoscopy capacity. However, only one FIT brand marketed in the US can be automated batch processed. In terms of test processing, several Summit participants noted that delays were an important barrier to program effectiveness. Purchase prices for FIT may vary by brand, as well as the purchaser, and therefore influence FIT selection. Traditionally, samples that are received more than 14 days from sample collection have been discarded and repeat sampling is required. Some programs have adopted a policy that modifies this approach: samples whose receipt is delayed are still processed, and those that are positive are treated as true positives, while those that are negative trigger a request for repeat sampling.

Best practice suggestions regarding FIT type—Participants agreed that a high-quality FIT should be used as part of mailed outreach. A FIT that can be batch processed with automation may be preferred for mailed FIT outreach, but the group recognized that there is only one currently marketed test that offers automated reading. Agreement was reached in recommending a strategy of offering a 1-sample over multi-sample kit, given ease of use and potential for higher participation rates, though definitive data to support clear benefit of 1 over 2 sample testing are lacking.

Section 2: Mailed FIT outreach program design and materials

This section includes a summary of published literature and summit participants' discussion about key questions focused on mailed FIT outreach program design and materials (KQs 3–6; Table 3). Most mailed FIT outreach programs have included an advanced notification before the FIT kit is mailed as well as reminders after the kit is mailed. We report literature on these topics as well as on what is known about the content and format of introductory letters and FIT kit instructions.

KQ3: What types of “primers”, or initial patient contacts, are most effective for encouraging response to mailed FIT outreach?

Primers are advanced notifications sent in the form of text messages, live phone calls, automated phone calls, postcards, and/or letters delivered **before** the FIT test mailing. The goal of primers is often multifactorial. A primary goal is to promote FIT return. Primers also can serve to confirm participants' address information, confirm their empanelment with the clinics (as needed), and verify their eligibility for FIT testing (by identifying patients who are up-to-date with screening or who are at higher than average CRC risk), thereby improving the accuracy of the FIT mailing and saving mailing costs.

While most prior mailed FIT programs have delivered advanced notification primers in the form of introductory letters, text messages, or automated phone calls, relatively few programs have reported on their effectiveness. A recent systematic review of advance notifications for mailed FIT programs summarizing data from 4 non-US-based studies showed that advanced notification letters improved uptake, with increases relative to no advanced notification ranging from RR = 1.06 (CI = 1.01–1.11) to RR = 1.22 (CI = 1.08–1.39)^{19–23}. In a similar review that included four studies (1 was US-based) that issued advanced notification automated phone calls or letters (two studies overlapped with the prior

review), Issaka and colleagues showed a median CRC screening completion improvement of 4.1% (IQR 3.6%–6.7%) over usual care.^{4,19,22,24,25}

A limited number of US-based studies have shown positive results for other forms of advanced notifications. In per-protocol analysis, Schlichting and colleagues reported an 85% FIT return rate in a sample of 190 Veterans Administration patients who were sent an introductory letter and live phone call and agreed to be sent a FIT, followed by telephone reminders.²⁶ This compared to a 14% FIT return rate in a similar group only mailed a FIT, with no introductory contacts or reminders. Notably, the programs' introductory phone call reached 73% (1,745/2,392) of the selected patients, of whom 43% (742) agreed to participate in the program, and 190 agreed to be mailed a FIT (of 414 eligible after exclusions) by pressing a number on a touch-tone phone. This study included additional reminders for patients who received advanced notifications; thus, it is impossible to fully attribute the effect to the advanced notification. An automated phone call primer was successfully used as an opt-in approach in two Kaiser Permanente-based studies that mailed FIT kit and delivered reminders, as needed to patients who had opted in. However, in both studies, the usual care comparison groups were not mailed a FIT kit, making it impossible to determine the effect of the automated phone call primer alone.^{24,27}

Best practice suggestions regarding primers—Summit attendees agreed that primers may contribute meaningfully to the success of mailed FIT outreach, and that future research is needed to delineate the specific effect of primers, by assessing the efficacy of various primer modes (e.g. introductory letters, text messaging, phone calls). Primers may motivate test completion equal to or beyond what could be achieved by reminders. Similarly, primers may offset the need for reminders, or act synergistically with them. Thus, a possible study could compare primers to reminders, and their combination, using a factorial design – i.e. study conditions: 1) primer + mailed fit + reminder, 2) primer + mailed FIT, 3) mailed FIT + reminder, and 4) mailed FIT alone.

A key consideration of research on primers that also pertains to reminders (see KQ6) should be the reach of a given delivery mode (i.e. proportion of patients who receive a given component), and reasons patients are not reached (i.e. incorrect addresses or phone numbers or being unavailable by phone or text), as reach is known to vary by mode. It is also important to study the rate at which patients opt out of future contact or reveal that they are ineligible for the program because of a recent screening event, being at higher than average CRC risk, or other reasons. Reporting effectiveness overall and across population subgroups, especially those defined by race/ethnicity, language preference, and socioeconomic position, may be critical for allowing successful tailoring of screening programs. The cost and cost effectiveness of primers, scalability, and variation by prior exposure to screening offers also warrant further study (see KQ9).

KQ4: What letter formats are most effective for increasing response to mailed FIT outreach?

All published mailed FIT outreach programs included an introductory letter, either sent as a primer (usually 2 or more weeks in advance of the FIT kit) or included with the FIT kit.

These letters usually include a description of why the patient is being mailed a kit, and some address common barriers to screening. Introductory letters vary in degree of personalization in terms of to whom the letter is addressed (e.g. addressed to specific person vs. “Dear Patient”) and by whom the letter is signed (e.g. specific provider vs. ‘care team’). Letters also varied in length, language delivered (English only, English and Spanish and/or others), and amount of education provided on FIT testing, and details about next steps patients should take if they have an abnormal FIT. Letters generally contained branding from patient’s clinical home (clinic letterhead, provider signature), information about out of pocket cost of the test (if any), a telephone contact for questions, and a suggested time frame for response.

Published literature on the relative effectiveness of specific letter content is scarce. Two studies compared tailored and standard message content and showed that letters that were tailored to individual barriers or that used risk or advocacy messages were no more effective than letters using standard content.^{22,28} We found no published US-based studies reporting on differences in patients’ response based on whether letters were signed by the patient’s primary care provider, the medical director, or other clinical representative or care team. While a more personalized approach had the greatest intuitive appeal (letter signed by a person known to the patient), the benefit should be weighed against the possibility of utilizing inaccurate information for matching the primary doctor to the patient, and the added complexity of individualizing letters for automated processes.

Participants discussed the practical challenge of getting patients to “open the envelope.” Discussants noted that a common challenge reported by non-responders’ is that they “don’t remember getting [the kit].” Making the packaging eye-catching, with simple language and pictures, may help increase the likelihood that patients will open, read and respond to the mailing. Similarly, encouraging patients to take the test kit to the bathroom may increase the likelihood that it is completed, but this proposition has not been specifically tested. Participants also discussed the importance of providing invitations in multiple languages, translated effectively and created at as low a literacy level as possible. A single best practice for creating such letters was not identified, though participants described strategies such as eliciting patient and health system leadership feedback on content and clarity.

Best practice suggestions regarding letter formats—Summit attendees agreed that outreach letters should be brief (one page or less), written at a low-literacy level, and include the following elements: branding from patient’s clinical home (clinic letterhead, clinic leader or provider signature), information about out of pocket cost of the test (if any), a telephone contact for questions, and a suggested time frame for response. Letters may include instructions and encouragement for completing the FIT and general information about CRC screening. However, attendees noted that it may be preferable to include separate print and graphical instructions for test completion within the mailed FIT packets, including in multiple languages, especially for populations with literacy and language barriers. Agreement was not reached with respect to who should be the signatory for the letter (e.g. health system or primary care provider).

The group did not believe head-to-head testing of introduction letters was a high research priority relative to other issues, particularly because trials comparing screening invitation letter content have, so far, not identified important differences in screening completion rates. Nevertheless, there was agreement that local context should be considered and that letters be pilot-tested and feedback solicited from target populations where possible.

There was also agreement that an open access repository for templates and examples of screening invitation letters be established, including templates and examples. Several resources for publicly available letters were identified, including through the Kaiser Permanente Center for Health Research (<https://research.kpchr.org/mailedfit>) as well as the National Cancer Institute's Research Tested Intervention Programs (<https://rtips.cancer.gov/rtips/topicPrograms.do?topicId=102265&choice=default>).

KQ5: How can instructions for FIT completion most effectively encourage response to mailed outreach and adequate sample collection?

All published mailed FIT outreach interventions have included instructions for FIT completion. Some have used only the instructions provided by the test manufacturer, while others have included materials specially designed to overcome barriers that may impede FIT completion or lead to improperly collected samples. Research on patient and clinical staff preferences for stool test instructions and the impact of instructions on patients' understanding, adherence, and proper completion of the stool test is scarce.

Coronado and colleagues gathered participant feedback on instructions for common FIT tests.^{29,30} They found that participants generally preferred simple, wordless instructions, reporting they were less intimidating than instructions with words, and helpful as they showed the small amount of stool needed for the test. Participants raised concerns about the collection date field having an open format, which may create confusion for persons from non-US countries of origin, where the notation sequence of day and month differ. Participants had mixed reactions to cartoon-like instructions (as they belied the seriousness of the topic). Concerns raised by participants who were completing their first FIT have included: feeling overwhelmed by the amount of kit paperwork, difficulty reading small print, and confusion about how to use the collection paper and whether they could use toilet paper before collecting the sample. Clinical staff observed issues which might have been addressed by better instructions, such as patients omitting the collection date on the sample collection vial and collecting too much stool. Optimal instructions may also prevent stool leakage, which some programs have reported as a barrier to postal service delivery. These actions led to tests not being processed.

While several research teams have developed pictographic instructions to aid in the proper completion of FITs, quantitative research is lacking on how such pictographic instructions affect individuals' willingness and understanding of how to do the test. Wang and colleagues conducted a study within a larger trial at a San Francisco-based safety-net health system.³¹ The nested study compared the frequency of mishandled FITs among individuals who were sent the manufacture's FIT instructions (OC-Micro, Polymedco), to the frequency of mishandled samples among individuals who were sent (1) low-literacy FIT instruction adapted from Coronado and colleagues,²⁹ (2) a reminder outreach phone call, or (3) the

combination of low literacy instructions and a reminder outreach phone call. Samples were considered mishandled if they were missing a collection date; if the time from collection to laboratory receipt was more than 14 days; or if the stool, buffer or cap was mishandled in a way that prevented the sample from being processed. Overall, of 4,916 FIT samples returned, 971 were mishandled (19.8%), with the predominant reason that the collection date was missing (910 of 971 samples = 94%). The proportion of mishandled samples was highest in the group that received the manufacturer's instructions (usual care: 25.0%), significantly lower in the group that was sent the low literacy instructions (16.5%, *p* value for comparison with usual care <.0001), and lowest in the group that received the combination of the low literacy instruction and a reminder phone call (12.8%, *p* value for comparison with usual care <.0001). Several research teams have developed video instructions in multiple languages, but research is lacking on their comparative effectiveness and use.

While this research demonstrates that improved instructions can minimize the frequency of mishandled samples, making such instructions a part of FIT packets produced and distributed by manufacturers remains a challenge. Some summit participants suggested that partnerships with FIT manufacturers and laboratories may help support the broad dissemination of FIT instructions that incorporate patient and provider preferences and facilitate proper test completion. Summit participants also discussed that despite best efforts, mishandled FITs due to issues such as missing patient names, collection dates, or delays between sample collection and lab processing (out-of-window) will occur. Clinics whose FITs are processed in outside labs may have little influence over whether the lab will process mishandled FITs. Nevertheless, some participants suggested that kits returned outside the processing window should be processed (rather than discarded). Though delays in processing might impact result in breakdown of hemoglobin and reduced proportion with a positive test, they reasoned that positive tests still likely reflect increased chance of colorectal neoplasia and warrant colonoscopy follow up. With regards to the impact of missing collection dates, data from one large study suggested no difference in positivity rate whether or not the date was recorded at the time of patient collection.³² The decision to use out-of-window test results or those missing collection dates for clinical care should weigh the potential value of abnormal FIT results that are unlikely to be false positive against any false reassurance patients may experience from a possible false negative result. These issues might be addressed by recommending colonoscopy follow up for abnormal FIT results out-of-window or missing a collection date, and repeat FIT for normal FIT results out-of-window or missing a collection date. The issue of best management of mishandled FIT results requires further study.^{33–37}

Best practice suggestions regarding FIT instructions—Participants agreed that instructions should be simple, with strong consideration for wordless instructions. Instructions should address the challenge of adequate stool collection and ensure that participants provide the collection date to avoid failed processing of returned FITs.

Resources for FIT instructions include the Kaiser Permanente Center for Health Research (<https://research.kpchr.org/mailedfit>) as well as the National Cancer Institute's Research

Tested Intervention Programs (<https://rtips.cancer.gov/rtips/topicPrograms.do?topicId=102265&choice=default>).

KQ6: What strategies are most effective for reminding patients to respond to mailed FIT outreach?

Most published mailed FIT program have delivered reminders. Reminders include text messages, live phone calls, automated phone calls, postcards, and/or letters delivered **after** the FIT test mailing with the goal of promoting FIT return. Meta-analyses have provided quantitative estimates of the incremental benefits of reminders after mailed stool tests. Dougherty and colleagues examined US-based trials completed between 1996 and 2017 and found that adding patient reminders (mail, automated or live phone calls) to mailed stool tests led to a 3% point increase in stool testing on average, with larger increases with live phone calls (6 percentage points)⁵. Rat and colleagues and Issaka and colleagues reported similar results.^{4,38}

Reminders of varying intensity have been compared. Green and colleagues compared usual care to mailed stool tests alone, mailed stool tests plus brief medical assistant-delivered phone reminders, or mailed stool tests plus brief phone reminders plus nurse navigation (motivational interviewing addressing barriers and facilitators). They found incremental increases in stool test uptake within 1 year following the reminder delivery. Compared with no reminders, brief phone reminders increased response by 3.8% points. Adding a more intensive phone-based navigation produced an incremental increase of 5.7% points compared with brief reminders (usual care 25.8%, mailed 56.4%, mail plus phone 60.2%, mail plus phone and navigation 65.9%).³⁹ Qualitative interviews revealed that adults preferred that clinic staff making the reminder calls knew their personal history, was knowledgeable about CRC screening, and was able to communicate with their physician.⁴⁰ In a study that partnered with a large federally qualified health center in Washington State, Coronado and colleagues mailed FITs to overdue adults, and randomized those who did not return them within 3 weeks (n = 2010) to one of 7 reminder groups: (1) mailed reminder letter, (2) two automated phone calls, (3) two text messages, (4) a live phone call (up three attempts to reach the patient), (5) a reminder letter and a live call, (6) two automated phone calls and a live call, or (7) two text messages and a live call.⁴¹ They found that 10% of participants completed a FIT before reminders were delivered and an additional 25.5% completed a FIT after reminders were sent, for an estimated overall completion rate of 32.7%. The six-month FIT completion rate was 16.9% among adults assigned text message reminders, and 23.3% and 23.7% in the groups assigned the automated phone call and letter reminders, respectively. Adding a live phone call reminder to mailed or automated approaches produced incremental increases of 10.2% points compared with text messages, 5.6% points compared with automated phone calls, and 3.7% points compared with the reminder letter (27.1% for text plus live call, 28.9% for the automated phone call plus live call, and 27.4% for the letter plus live call). Notably, similarly high completion rates were achieved in the group assigned the live call only -- 31.3%.

Less is known about the impact of different reminder strategies in specific groups such as racial/ethnic subgroups. Walsh et al. offered US Latino and Vietnamese patients language-

concordant mailed stool tests alone versus in addition to theory-based (stages of change) phone counseling delivered by Latino and Vietnamese lay advisors, and found moderate incremental increases in stool test uptake with counseling (UC 7.8%, mail stool test 11.9%, mail plus phone 21.4%).⁴² Among Vietnamese patients, only the mail plus phone counseling group had a significantly higher rate of stool test completion than usual care. In the study by Coronado and colleagues that compared mailed reminders to live phone calls, automated calls, text messages, and various combinations of these interventions, automated and live phone call reminders combined produced the highest FIT completion rates among Spanish-speaking patients.⁴¹ Overall, there are many open questions about the optimal implementation of reminders: who should deliver them, when, how often, and the comparative cost-effectiveness of different approaches. Electronic health records may be able to automatically remind patients not completing tests via text or secure e-mail, which may be a particularly economical method to deliver reminders. Live phone reminders are more difficult and costly to implement; use of vendors that deliver robocalling services for patient reminders might serve to overcome some barriers to implementation.

Best practice suggestions regarding reminders after mailed outreach—The group agreed that reminders (mailed letters or automated or live telephone calls, with or without navigation) lead to small to moderate increases in stool test uptake. Whether reminders work differently in different subgroups warrants further research. The group suggests implementation of at least one type of reminder after mailed outreach among initial non-completers to increase FIT return but recognizes that more research is needed on how to operationalize reminders, and the best and most efficient strategies to implement them. (See KQ9)

Section 3: FIT-positive follow-up

The effectiveness of mailed FIT programs relies on successful completion of colonoscopy after abnormal stool test results, as failure to complete a follow-up is associated with poorer CRC outcomes. In this section, we review guidelines for follow-up colonoscopy completion, and timing of follow-up colonoscopy, we also provide a review of the literature on strategies to improve FIT-positive follow-up rates (KQ 7; Table 3).

KQ7: Which strategies are most effective for ensuring FIT-positive follow-up?

There are several steps in completing a follow-up colonoscopy. Individuals with an abnormal stool test result should be informed of their result, a colonoscopy should be scheduled and completed in a timely matter, colonoscopy results should be returned to the individual, and a treatment consultation should be arranged if cancer is found. Most studies of FIT-positive follow-up focus on colonoscopy completion as the primary outcome. Because follow-up colonoscopies are the means of identifying and removing precancerous polyps (for cancer prevention) and for diagnosing early stage cancers (to reduce the risk of CRC mortality), it is essential that programs achieve high rates of follow-up colonoscopy completion. Colonoscopy 6 to 9 months after abnormal FIT may lead to worse CRC outcomes compared to earlier colonoscopy. Data from a cohort of 70,124 Kaiser Permanente members with a positive FIT result show that compared to delays of 30 days or less, delays of 12 months or

more were associated with a 2.25-fold increased risk of any CRC and a 3.22 increased risk for advanced-stage CRC.⁴³

Colonoscopy completion rates following abnormal stool test result vary substantially across health care systems, ranging from 30% to 82% in screening trials.⁴ The US Multi-Society Task Force on Colorectal Cancer recommends an 80% colonoscopy completion rate for those with FIT-positive result.⁴⁴ Some health systems, such as Kaiser Permanente Northern California, have been able to exceed this target (85% in 2016).⁷ However, the rates in many health systems fall well below this target. Evaluations of federally qualified health centers and safety-net systems, for example, report follow-up colonoscopy rates that range from 53–56%^{6,45,46} in one-year follow-up data and 44–52%^{46–48} in 6-month follow-up data. Gaps in colonoscopy completion have been attributed to a combination of patient, provider, and system-level factors.^{45,49–54}

Time to colonoscopy completion is also an important indicator of program quality. While national organizations concerned with CRC have set no specific recommendation for the optimal timing of the follow-up colonoscopy, scientists involved with the Population-based Research to Optimize the Screening Process (PROSPR) consortium recommend that follow-up colonoscopy occur within 90 days and not later than 180 days of an abnormal stool test result.⁵⁵ Available studies report high variation in time to colonoscopy receipt, with median times ranging from 64 [IQR: 40–94] to 184 [IQR: 140–232] days^{45,46,48}.

A recent systematic review of interventions to improve FIT-positive follow-up concluded there was moderate strength of evidence for patient navigation and provider reminders/provider feedback as strategies for increasing colonoscopy completion.⁵⁶ Though patient navigation and provider reminders/feedback show promise, available studies have been limited by small sample sizes and were tested in a limited number of health system settings. Several studies have tested practical system-level interventions, such as automatic referral to a colonoscopy specialist, eliminating need for a pre-procedure visit prior to the colonoscopy appointment, and establishing a registry to track patients with positive results, but overall evidence to support these interventions was judged to be of low strength. Notable limitations cited from this review were: (1) most U.S. studies (10/14) were conducted in the Veterans Affairs (VA) system with more than 90% male patients, few comparable studies in federally qualified health centers and safety-net systems were available for inclusion; and (2) no evaluations of interventions to improve diagnostic colonoscopy uptake specifically in patients receiving mailed FIT (versus fecal occult blood tests). Another meta-analysis was unable to determine overall effectiveness of any intervention to improve FIT-positive follow-up due to the low number of available studies.⁵ While moderate evidence for provider-based and navigator-based interventions for FIT-positive follow-up exist, widespread use of these strategies are limited by the personnel costs associated with one-on-one navigation.

At the summit, a successful usual care program to optimize colonoscopy completion after positive FIT was reviewed. Between 2010 and 2016, Kaiser Permanente Northern California implemented numerous system-level strategies to improve diagnostic colonoscopy completion to accompany ongoing mailed FIT outreach efforts.⁵⁷ Interventions included: (1) hiring additional gastroenterology personnel to expand endoscopy capacity, (2) creating a

central registry and tracking patients with positive FIT results with lists generated 30, 60, and 90 days after an abnormal result, (3) designating an individual responsible for tracking patients with abnormal FIT results, (4) assigning follow-up of abnormal FIT results to the gastroenterology department, (5) standardizing outreach by patient navigators, (6) mailing certified letters to patients unresponsive to navigator telephone calls or secure message prompts, and (3) adopting a quality metric goal to achieve 80% diagnostic colonoscopy completion within 30 days of an abnormal FIT result (consistent with the US Multi-Society Task Force on Colorectal Cancer recommendation) to track the success of the program. Over the 10-year period, these combined interventions improved diagnostic colonoscopy completion within 1 year of an abnormal result from 73% to 85%. A challenge of generalizing this experience is that the use of multiple implementation strategies at once makes it difficult to disaggregate the effects of individual intervention components, which is important for evaluating other outcomes of interest including acceptability, feasibility, and implementation cost. These findings are from an integrated health system, and many of these innovations may be difficult to adapt for a non-integrated care setting, potentially limiting generalizability. Also, results may be difficult to generalize to settings where colonoscopy capacity and access are more limited and to individuals without insurance coverage for the cost of a follow-up colonoscopy.

Best practice suggestions regarding abnormal FIT follow-up—Summit participants agreed that having protocols and procedures in place to ensure completion of diagnostic colonoscopy after an abnormal stool test is critically important. Participants supported patient navigation as a promising strategy, but recognized that navigation, by itself, may be insufficient to promote timely follow-up colonoscopy completion, in the absence of system-level strategies. Some participants expressed enthusiasm for multi-component strategies, which have shown success in at least one large integrated healthcare system⁵⁷ but more data are needed to understand the effectiveness and feasibility of these strategies in other settings. An important overarching consideration is whether colonoscopy capacity in a given setting is sufficient meet the demand for services.

Section 4. Program sustainability/cost

Because stool testing is recommended annually, we reviewed the literature and discussed the ability to continue high-quality mailed outreach beyond initial invitation (KQ's 8 and 9; Table 3). Our discussion recognized that sustainability requires resources to support all aspects of a mailed outreach program, from personnel managing invitations to materials and data infrastructure required. Another aspect of sustainability is the cost and cost-effectiveness of mailed FIT outreach programs.

KQ8: What strategies can be used to ensure sustainability of mailed FIT outreach?

There are several examples of sustained mailed FIT screening programs in the US, including Kaiser Permanente Northern California^{7,58}, and certain safety net health systems⁵⁹. These programs have demonstrated consistent response rates over multiple years of screening. The exact factors responsible for sustainability have not been tested in RCTs.

Participants at the summit identified several common features of sustainable programs. First and foremost, a reliable funding mechanism for population management and FIT mailing is essential. Integrated systems like Kaiser Permanente and the VA system are well-placed to develop such programs as they bear the financial risk for the downstream costs of care. Other value-based payment models like capitation or pay for performance incentives can also provide funding. Traditional fee-for-service reimbursement does not currently provide enough funding (through individual test charges and reimbursement) to cover the costs and needs of a high-quality mailed FIT program. Dedicated programmatic funding, such as the grant-based Cancer Prevention and Research Institute (CPRIT) program in Texas, has been used successfully for program start-up and growth. The Centers for Disease Control's Colorectal Cancer Screening Program has provided funding for practice facilitation and screening services that support mailed FIT outreach in a variety of clinics throughout the United States.^{60,61} Notably, long term sustainability of CPRIT and Centers for Disease Control programs are subject to availability of funds and policy directives, suggesting more robust solutions are needed to ensure sustainability of programs sponsored by these entities.

In addition, organizational alignment is essential. Leadership engagement and promotion of CRC screening is necessary to ensure adequate resources and consistent staffing for a mailed FIT program. It is also important to have dedicated staff focused on the program. An external measure such as the Healthcare Effectiveness Data and Information Set (HEDIS), Medicare stars rating system, or the Universal Data Set (UDS) of quality metrics for federally qualified health centers may be strong motivators for senior healthcare system or insurer leadership engagement. For managed care Medicaid programs, implementing the reporting of a population CRC screening measure may also help motivate managed care programs to support mailed outreach. Some states, including Oregon and Kentucky, have adopted incentives for Medicaid health plans meeting established performance and improvement targets.^{62,63}

Successfully sustained mailed FIT programs should employ an organized, well-defined and well-documented screening approach. Organized screening has explicit policies and standard workflows for how the screening should be performed and who is in the target population. Organized screening also has an oversight process with a management team responsible for implementation, a clinical team to deliver care, a quality assurance structure, and tracking cancer incidence, complications of screening, and positive FIT follow-up. Leveraging dedicated quality improvement teams may enhance implementation, as these teams may be best positioned to manage data and reporting challenges, and to deliver feedback to clinicians. Compared with opportunistic screening, which is based on a convenience sample of patients seen recently in the office, organized screening focuses much greater attention on the entire eligible population and the quality of the screening process, including follow-up of participants.⁶⁴

Best practice suggestions regarding sustainability and effectiveness—

Participants agreed that key challenges to ensuring sustainability and effectiveness include ensuring funding and maintaining leadership support. In light of data suggesting that mailed FIT is both effective and cost effective (see below) private health plans may be motivated to implement and sustain mailed FIT to reach benchmarks set by HEDIS and the Medicare

Stars program. Beyond private health plans, Medicaid managed care programs may benefit from tracking, monitoring, and reporting HEDIS CRC screening metrics to more consistently implement mailed FIT.

KQ9: What is the cost effectiveness (cost per additional person screened) for mailed FIT outreach?

Several studies have examined the cost effectiveness of mailed FIT outreach programs compared to usual visit-based care in terms of cost per additional patient screened. A micro-costing study from a FIT mailed outreach program by the Washington State Health Department including a FIT kit, reminder letter, and two automated reminder telephone calls reported a cost per returned FIT of \$39.81.⁶⁰ Most of the expenses were related to intervention implementation including mailing the FIT kits, tracking results, and arranging follow-up as needed; however, one-third of costs were due to intervention development including patient identification and staff training. A micro-costing and long-term modeling study from a San Francisco safety net health system reported a cost of \$23 per patient for outreach delivery, and a cost of \$112 per patient screened for a program including an informational postcard, FIT kit, and reminder telephone calls.⁶⁵

Another modeling study evaluated the cost-effectiveness of extending a FIT outreach strategy on a national level.⁶⁶ The authors reported that this strategy would provide CRC screening to approximately 9.4 million people, preventing 3100 CRC-related deaths, at a cost of \$277.9 million. Overall, the cost per person screened would be \$32.38, which was consistent across several one-way sensitivity analyses.

Quality adjusted life years (QALYs) gained as a result of mailed outreach have also been modeled. In the aforementioned study from a San Francisco safety net health system, projecting over a longer timeframe and incorporating downstream effects on cancer incidence and mortality, the authors estimated mailed FIT outreach would provide a mean of 19.62 QALYs at a mean cost of \$2960, compared to 19.61 QALYs for \$2816 for usual care. Overall, FIT outreach was estimated to have an incremental cost-effectiveness ratio (ICER) of \$9200 per QALY versus usual care, which is well below the traditional cost-effectiveness threshold of \$50,000 to \$100,000 per QALY gained. FIT outreach remained cost effective (at an ICER of \$37,400) even if outreach costs were increased to \$50 per patient, and threshold analysis revealed that FIT outreach would dominate usual care, i.e. provide increased QALYs at lower costs, if the cost per patient was reduced to \$14.

Summit participants raised a few issues with interpreting the current cost-effectiveness literature. First, most data used in the models was based on the effect on one-time screening, even though cost-effectiveness of outreach strategies may vary over time due to differential response to FIT outreach.⁶⁷ With the exception of the San Francisco study noted above, most studies used cost per returned FIT as a surrogate of success; however, this is only one step in the CRC screening program continuum.⁶⁸ Several studies have demonstrated only moderate levels of adherence to subsequent yearly tests after a negative index FIT, and to colonoscopy after any abnormal FIT, raising the possibility that different, potentially more expensive interventions may be required to maintain adherence.^{46,68,69} Further, most cost-effectiveness studies have leveraged data from clinical trials and large programs, but it is

unclear how well these data translate to real-world effectiveness given differences in patient populations and team expertise.⁷⁰ A practical issue raised with respect to cost was whether mailed outreach should continue to be offered to initial non-responders to a first round of invitation, particularly in resource limited settings.

Other participants raised the question of whether cost per adenoma or CRC detected would be a more informative intermediate metric than cost per patient screened, given the crucial role of adherence to colonoscopy after positive FIT, and the need for high-quality colonoscopy.

Best practice suggestions regarding cost-effectiveness of mailed FIT

outreach—Participants agreed that available data support mailed FIT outreach as a highly cost-effective strategy for improving CRC screening participation, with high projected potential to impact CRC incidence and mortality. Given that CRC screening itself is highly cost-effective, there is a strong rationale for pursuing mailed FIT programs in the context of limited available resources.

Future cost-effectiveness research on this topic might explore the cost and incremental cost-effectiveness of different mailed FIT components (i.e. primers and reminders). Moreover, given that most programs report a higher overall cost per person screened than is reimbursable though FIT laboratory processing, future research might help derive a sustainable reimbursement rate.

Discussion

Mailed FIT outreach is a research-tested intervention that addresses barriers to CRC screening at multiple levels, and has been shown to substantially improve rates of CRC screening in multiple settings. Despite consistently proven effectiveness, widespread implementation may be hindered by a lack of knowledge on the part of providers, health systems, and policy makers about how to successfully implement such programs. In addition, providers and policymakers may not be aware of the magnitude of effectiveness and cost-effectiveness of mailed FIT as a key prevention strategy, or only prioritize mailed FIT implementation if CRC screening reporting is required and improvement in screening incentivized. As part of the 2019 Mailed FIT Summit, we reviewed evidence to support mailed outreach as an intervention, and outlined and addressed several key questions relevant to any entity considering mailed FIT implementation to help address these barriers to implementation.

Infrastructure and FIT kit selection

Agreement was reached by Summit participants that the minimum data infrastructure required for mailed FIT programs should be able to identify eligible patients and track each step in the outreach process, from primer delivery through abnormal FIT follow up. Such infrastructure can be stand-alone, embedded within an EHR system, and even rely on outside vendors for delivering program components and tracking steps in the process. Ongoing improvements in data linkages between primary and specialty care sites can improve the capture of colonoscopy information in primary care, and real-time EHR tools can allow

integration between the mailed outreach program and clinical care delivery. At a minimum, programs should have some means of querying their own records to limit outreach to those who appear not up to date with screening.

Moreover, Summit participants agreed that mailed FIT programs should use a FIT with strong performance characteristics, and that a 1 sample FIT has advantages over a 2 or 3 sample FIT. Quantitative FIT offers advantages for mass processing and for adjusting the positivity threshold to accommodate resource constraints.

More research could inform best practices for the accurate selection of patients for a mailed FIT program, as inaccurate patient selection (e.g. mailing to patients who are already up to date with screening) may create inefficiencies and lessen patients' willingness to follow-through on any automated recommendation.

Mailed FIT outreach program design and materials

For specific components of mailed FIT programs, there was agreement that advanced notification primers that are sent prior to mailed FIT appear to contribute to effectiveness and efficiency, though there was limited research on which mode of primer worked best.

Summit participants believed that invitation letters should be brief, written at low-literacy, and the signatory (e.g. primary provider vs. health system) should be tailored based on setting. FIT instructions for FIT completion should be simple and address challenges which may lead to failed processing (e.g. notation of collection date), as limited available data suggest that simple, low-literacy instruction can minimize issues with mis-handled samples. Finally, reminders (e.g. mailed or text) delivered to initial non-completers should be delivered to increase FIT return. Whether direct phone calls should be employed to non-responders depends on program resources as they are more labor intensive.

Summit participants felt that a priority for future research on program components was advanced notification primers. It is unknown, for example, which mode of primer can achieve the greatest effectiveness (e.g. text message, phone call, letters), and whether primers can offset the need for reminders or act synergistically to produce an additive effect. Ongoing research is needed to optimize primers and reminders, to respond to communication trends (e.g. social media, etc.) and to best reach subgroups that are non-responsive to traditional approaches. Research that supports optimization by identifying the key components of a maximally successful program is particularly needed, as are data about cost-effectiveness of different levels and types of primers and reminders.

Follow-up colonoscopy and program sustainability/cost

Summit participants agreed that having protocols and procedures in place to promote colonoscopy completion after abnormal FIT, including with interventions such as patient navigation, was critically important. Data show that about one-half of patients in some settings do not obtain a follow-up colonoscopy after an abnormal FIT result, and that median time to colonoscopy varies dramatically across settings.

More information is needed to address systems- and patient-level barriers to follow-up colonoscopy after an abnormal FIT. Evidence on national and state policies that can drive reporting requirements and incentives for colorectal cancer screening and follow-up would benefit from further research that can inform their effectiveness. Moreover, organizational policies used successfully by large integrated health care systems, such as prioritizing scheduling for abnormal FIT patients over screening colonoscopy patients could be considered for more widespread implementation.

Sustainability of mailed FIT outreach requires leadership commitment, sufficient resources, and likely external forces to drive commitment to investment. Summit participants concluded that the cost-effectiveness of mailed FIT outreach compared with usual care has been established, but that comparative economic analyses of different mailed FIT approaches is needed. Approaches for maximizing adoption and maintenance of mailed FIT programs require further study.

Limitations

We did not specify a key question to address best practices for exclusion of patients from mailed FIT outreach, as the literature in this area is still evolving. Relevant questions of interest include whether criteria for exclusion should include family history of polyps or CRC, participation in hospice or residence at a long term care facility, and how to operationalize exclusions for these scenarios as well as others, such as personal history of CRC, or informed refusal of preventive care. Addressing these issues could avoid misuse of mailed FIT for patients not average risk for CRC, those unlikely to benefit due to limited life expectancy, and those not interested in preventive screening. These topics are complex to address. For example, some may posit that FIT completion by a person with a family history of CRC is better than no completion at all, based on available evidence.^{71–73} Our key questions did not address utility of financial incentives for promoting mailed FIT outreach. The literature in this area is evolving, as currently available randomized trials have had mixed results;^{74–77} future research is likely to clarify whether and how financial incentives may augment FIT completion in response to mailed outreach. We did not include a formal key question focused on cost-effectiveness of patient navigation for abnormal FIT follow up; however, evidence regarding cost-effectiveness of patient navigation across the cancer continuum for multiple cancers has been recently summarized.⁷⁸

Conclusions

Meeting participants felt that mailed FIT outreach represents a promising method to improve CRC screening. Mailed FIT programs help address the ongoing need for greater promotion of evidence-based strategies to increase participation in CRC screening.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Multi-level rationale for mailed FIT outreach*

Level	Evidence-based component
System	<ul style="list-style-type: none"> Establishes policy of outreach to every individual Offers screening independent of need to attend clinic visit
Provider	<ul style="list-style-type: none"> Recognizes provider may have limited time to promote screening Reminds provider to facilitate abnormal test follow-up
Individual	<ul style="list-style-type: none"> Delivers small media education regarding importance of screening Reminds individual to complete screening Navigates screening completion and test follow-up Reduces barriers through convenience of at-home testing

* see Introduction for rationale on how the evidence-based components/constructs fit into each level

Table 2.

Efficacy of colorectal cancer screening interventions, including mailed FIT outreach

Strategy	Colorectal cancer screening completion vs. usual care	
	RR (95% CI)	Percentage Point Difference
Mailed outreach	2.28 (1.74–2.97)	22%
Visit-based FIT distribution (e.g. FluFIT)	2.16 (1.72–2.70)	16%
Patient navigation without fecal test distribution (e.g. offering colonoscopy or choice)	1.62 (1.32–1.98)	10–11%
Patient education alone	1.20 (1.06–1.36)	4%
Patient reminders alone	1.20 (1.02–1.41)	3%

Source: Dougherty MK et al. JAMA Int Med 2018; Issaka RB et al. Prev Med 2018

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Table 3.

Key Questions Regarding Mailed FIT Outreach

Infrastructure and FIT kit selection
<ul style="list-style-type: none"> • KQ1. Which data and what data infrastructure are required to support mailed FIT outreach?
<ul style="list-style-type: none"> • KQ2. What are the key considerations for selecting a FIT for mailed outreach?
Mailed FIT outreach program design and materials
<ul style="list-style-type: none"> • KQ3. What types of “primers,” or initial patient contacts, are most effective for encouraging response to mailed FIT outreach?
<ul style="list-style-type: none"> • KQ4. What letter formats and mailing strategies are most effective for increasing response to mailed FIT outreach?
<ul style="list-style-type: none"> • KQ5. How can instructions for FIT completion most effectively encourage response to mailed outreach and adequate sample collection?
<ul style="list-style-type: none"> • KQ6. What strategies are most effective for reminding patients to respond to mailed FIT outreach?
Abnormal FIT follow-up
<ul style="list-style-type: none"> • KQ7. Which strategies are most effective for ensuring abnormal test follow-up?
Program sustainability/cost
<ul style="list-style-type: none"> • KQ8. What is the cost effectiveness (cost per additional person screened) for mailed FIT outreach?
<ul style="list-style-type: none"> • KQ9. What strategies can be used to ensure sustainability and effectiveness of mailed FIT outreach?