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Population Health Colorectal Cancer Screening Strategies in Adults Aged 45 to 49 Years
A Randomized Clinical Trial

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IMPORTANCE Colorectal cancer screening is now recommended at age 45 years for average-risk individuals; however, optimal outreach strategies to screen younger adults are unknown.

OBJECTIVE To determine the most effective population health outreach strategy to promote colorectal cancer screening in adults aged 45 to 49 years.

DESIGN, SETTING, AND PARTICIPANTS Randomized clinical trial with 20 509 participants conducted in a large health system (UCLA Health). Primary care patients aged 45 to 49 years at average risk for colorectal cancer were randomized 1:1:1:1 to 1 of 4 outreach strategies. The trial ran May 2, 2022, to May 13, 2022, with follow-up through November 13, 2022.

INTERVENTIONS Colorectal cancer screening via 1 of 4 strategies: (1) fecal immunochemical test (FIT)–only active choice; (2) colonoscopy-only active choice; (3) dual-modality (FIT or colonoscopy) active choice; and (4) usual care default mailed FIT outreach.

MAIN OUTCOME AND MEASURES Primary outcome was participation in screening (FIT or colonoscopy) at 6 months. Secondary outcome was screening modality completed.

RESULTS Among 20 509 participants (53.9% female, 4.2% Black and 50.8% non-Hispanic White; mean [SD] age, 47.4 [1.5] years), 3816 (18.6%) underwent screening. Participation was significantly lower in each of the 3 active choice groups (FIT only, 841 of 5131 [16.4%; rate difference, −9.8%; 95% CI, −11.3% to −8.2%]; colonoscopy only, 743 of 5127 [14.5%; rate difference, −11.7%; 95% CI, −13.2% to −10.1%]; dual-modality FIT or colonoscopy, 890 of 5125 [17.4%; rate difference, −8.9%; 95% CI, −10.5% to −7.4%]) than in the usual care default mailed FIT group (1342 of 5126 [26.2%]; all $P < .001$). Participants offered dual-modality active choice more likely completed any screening than those offered a single active choice modality (17.4% [dual-modality FIT or colonoscopy] vs 15.4% [FIT only and colonoscopy only combined]; rate difference, −1.8%; 95% CI, −3.0% to −0.1%; $P = .004$]). Among 5125 participants offered a choice between 2 modalities (dual-modality active choice FIT or colonoscopy), colonoscopy was more common than FIT (616 [12.0%] vs 288 [5.6%]; rate difference, −6.4%; 95% CI, −7.5% to −5.3%; $P < .001$). There was notable crossover in the FIT-only groups to colonoscopy (502 of 5131 [9.8%; FIT-only active choice] and 501 of 5126 [9.8%; usual care default mailed FIT]). Crossover from colonoscopy to FIT was modest (137 of 5127 [2.7%; colonoscopy-only active choice]).

CONCLUSIONS AND RELEVANCE In this randomized clinical trial, 3 different active choice interventions had lower colorectal cancer screening completion rates among individuals aged 45 to 49 years compared with usual care.

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n 2021, the US Preventive Services Task Force (USPSTF) revised its colorectal cancer (CRC) screening guidelines, issuing a grade B recommendation to screen average-risk individuals aged 45 to 49 years.[1] USPSTF grade A and B recommendations are mandated for coverage by private insurers under the Patient Protection and Affordable Care Act.[2] This policy update was in response to a nearly 15% increase in CRC incidence among individuals in the United States younger than 50 years during the past 3 decades.[3,4] Colorectal cancer is now the leading cause of cancer-related deaths in men aged 20 to 49 years and the second leading cause in women in the same age group.

Colorectal cancer screening is a cost-effective way to reduce CRC incidence and mortality.[5-8] For adults aged 50 to 75 years, effective strategies to increase screening participation, such as education, reminders, navigation, and mailed outreach, are well established.[9,10] However, health systems lack evidence-based guidance for promoting screening among younger, newly eligible individuals.[11] A recent claims-based study demonstrated that 20 months after the grade B USPSTF recommendations for adults aged 45 to 49 years, screening participation was only 1.51% for this age group.[12] Mailed screening outreach appears feasible for this age group, although it is understudied and untested against alternative outreach strategies.[13,14] To inform population health strategies for promoting screening in this age group, we conducted a randomized clinical trial comparing 4 outreach strategies in a large health system. Findings from this study can inform population health and national efforts to improve screening rates and CRC outcomes in newly eligible adults.

Methods

Trial Design

This investigator-initiated, single-center, randomized clinical trial was conducted at UCLA Health, a large, urban, integrated academic health system with more than 420 000 primary care patients and 50 ambulatory primary care clinics across Southern California (NCT05275530). The trial was conducted between May 2, 2022, and May 13, 2022, with follow-up through November 13, 2022. We received University of California, Los Angeles institutional review board approval and were granted a waiver of informed consent, given that offering CRC screening is standard of care at our institution and presents minimal risk to participants. We also conducted meetings with primary care leadership, clinic directors and managers, and other stakeholders to design and execute the study. We focused on screening colonoscopy and the fecal immunochemical test (FIT) because these are the most frequently used screening options in our health system and nationally.[1] The trial reporting followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.[15]

Participants

Participants were individuals aged 45 to 49 years at average risk for CRC (no personal or family history of predisposing conditions), identified through an electronic health record query on April 19, 2022, for patients with an assigned primary care physician at UCLA Health. We excluded individuals with (1) prior CRC screening test use (previously documented fecal occult blood test, FIT, or colonoscopy); (2) inactivated electronic patient portal; (3) documented family history of CRC or personal history of CRC, inflammatory bowel disease, colonic adenomatous polyps, or hereditary CRC syndromes; or (4) undocumented telephone number. We also excluded 1000 individuals randomly selected for an unrelated trial (**Figure 1**).
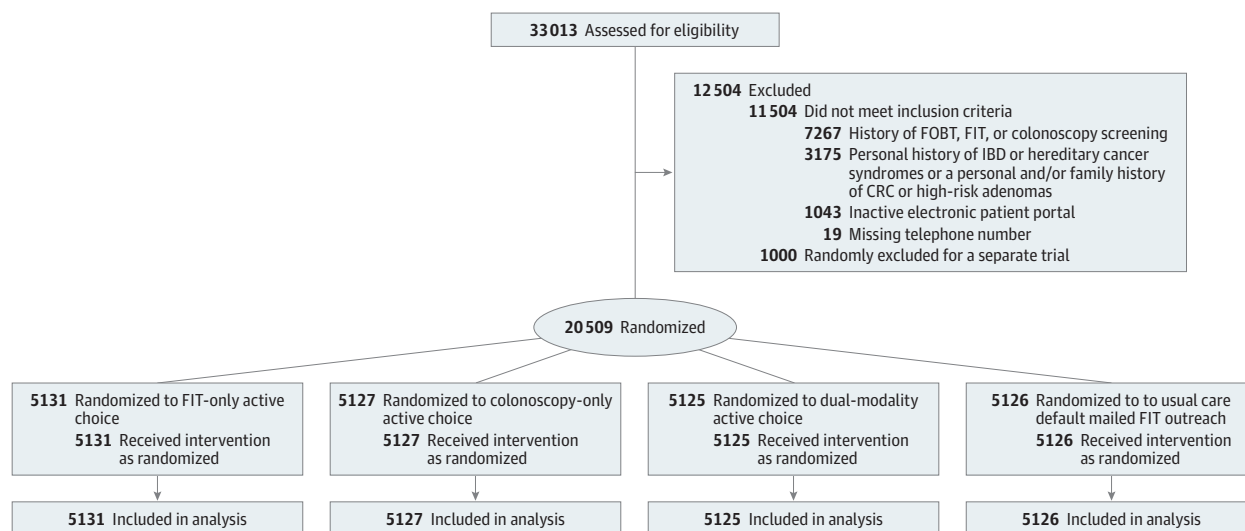
Randomization

Participants were randomly assigned in a 1:1:1:1 ratio by a study statistician using a random number generator to 1 of 4 study groups: (1) FIT-only active choice; (2) colonoscopy-only active choice; (3) dual-modality (FIT or colonoscopy) active choice; and (4) usual care default mailed FIT outreach. Each participant received a screening invitation as an electronic message via the patient portal (detailed below) and 3 text messages (eMethods in Supplement 3). The study team did not directly interact with participants. Participants were not notified about the trial and were likely unaware of their assignment, as were the investigators, excluding the team statistician.

Rationale for Intervention Design

The first objective was to compare 2 general approaches shown to improve patient participation in preventive health behaviors over traditional opt-in approaches. One strategy is default enrollment,[16-18] which, in the context of CRC screening, is defaulting participants into screening by sending them a FIT kit without eliciting their preference for a screening modality or getting screened at all.[19-27] The other strategy is active choice,[18,28-31] or asking patients to explicitly choose to either accept or decline a screening offer.[24,25,32]

Each of these 2 strategies has distinct advantages. Default mailing of FIT kits may reduce effort and cognitive costs, reach patients who otherwise miss opportunities to opt in, and signal to patients the importance of screening.[33-35] Active choice may give patients a sense of agency and engender greater commitment to follow-through with screening.[29,36,37] It is unclear which strategy leads to higher screening rates, especially among newly eligible adults who may require more information on screening options and resist defaults due to unfamiliarity.

Key Points

Question What is the most effective population health strategy to promote colorectal cancer screening among average-risk adults aged 45 to 49 years?

Findings In a randomized clinical trial of 20 509 participants, the 3 strategies requiring active choice through the electronic patient portal were significantly less effective than default unsolicited mailed fecal immunochemical test (FIT) outreach: 16.4%, 14.5%, and 17.4% vs 26.2%.

Meaning Default unsolicited mailed FIT outreach was the most effective population health screening strategy for adults aged 45 to 49 years. Overall screening rates were low, underscoring the need for more effective strategies to engage this age group.

Figure 1. Participant Eligibility and Randomization

All randomly assigned participants were considered to have received the intervention as allocated, defined as having been sent the appropriate condition-specific message via the patient portal. Whether each participant viewed the message could not be verified, but all participants received the intervention materials as designed and were included in the intention-to-treat analysis. There were no dropouts or follow-ups based on the design of the study. CRC indicates colorectal cancer; FIT, fecal immunochemical test; FOBT, fecal occult blood test; and IBD, inflammatory bowel disease.

Our second objective was to test within the active choice approach whether it is more effective to prompt patients to consider 1 screening option (eg, FIT or colonoscopy) or offer both.[32] Although giving 2 options may better suit individual preferences, it may also increase decision-making complexity and lead to delays or inaction.[38-40]

Interventions

All screening invitations were sent to eligible patients via the electronic patient portal. Participants randomized to the FIT-only active choice group were sent a message via the portal notifying them that they were now age-eligible for CRC screening and that the FIT kit is an easy and effective screening method. In this message, participants were asked to actively choose by clicking to select an option between being screened with a FIT kit and deferring screening altogether (trial protocol in Supplement 1). Participants who chose the former received a FIT kit at their home address via the US Postal Service within 2 weeks of their selection, with step-by-step instructions and a prepaid mailer to return their completed kit to the UCLA Health central laboratory.

Participants in the colonoscopy-only active choice group received an invitation message in the electronic patient portal stating that a colonoscopy is an effective CRC screening method. Participants were asked to actively choose between screening with a colonoscopy or deferring screening altogether (trial protocol in Supplement 1). If a participant elected colonoscopy, an electronic order for colonoscopy was generated and sent via the electronic health record to the participant's primary care physician, with default communication stating that the patient was due for CRC screening and agreeable to colonoscopy. Once this order was signed by the primary care physician, it was processed through standard mecha-

nisms: participants were contacted by a colonoscopy scheduler to select a procedure date and sent standard information about the procedure and bowel preparation instructions (eMethods in Supplement 3). Participants who declined colonoscopy did not receive further intervention.

In the dual-modality active choice group, participants received information about both FIT and colonoscopy via the portal. They were then asked to actively choose to screen with FIT, screen with colonoscopy, or defer screening altogether (trial protocol in Supplement 1). Participants who selected FIT or colonoscopy received the same workflow as FIT-only active choice and colonoscopy-only active choice participants, respectively, as detailed earlier.

Participants randomized to usual care default mailed FIT outreach received a portal message stating that a FIT kit would be mailed to them (trial protocol in Supplement 1).[41] They were then mailed a FIT kit with step-by-step instructions and a prepaid mailer to return the completed kit. In contrast to FIT-only active choice, kits in usual care default mailed FIT were mailed to patients unsolicited; this was the only difference between FIT-only active choice and usual care default mailed FIT.

Screening invitations sent to all study groups included language about the updated USPSTF recommendations, information about alternative screening strategies (eg, participants in the FIT-only active choice group could still choose colonoscopy if desired), and easy-to-understand infographics explaining each modality (trial protocol in Supplement 1). To maximize accessibility, all communications and infographics were developed using plain language, short sentences, and culturally sensitive phrasing, accommodating individuals from diverse backgrounds and literacy levels. Participant communications incorporated behavioral science insights to enhance engagement such as highlighting physician endorsements,[42-44]

Table 1. Characteristics of the Trial Participants

	All participants	FIT-only active choice	Colonoscopy-only active choice	Dual-modality active choice	Usual care default mailed FIT outreach
Total	20 509	5131	5127	5125	5126
Age, y[a]					
Mean (SD)	47.4 (1.5)	47.4 (1.4)	47.4 (1.5)	47.5 (1.5)	47.4 (1.5)
Median (IQR)	47.4 (46.1-48.7)	47.4 (46.2-48.7)	47.4 (46.1-48.6)	47.4 (46.1-48.8)	47.4 (46.1-48.7)
Sex, No. (%)	n = 20 506				n = 5123
Male	9458 (46.1)	2277 (44.4)	2420 (47.2)	2365 (46.1)	2396 (46.8)
Female	11 048 (53.9)	2854 (55.6)	2707 (52.8)	2760 (53.9)	2727 (53.2)
Race and ethnicity, No. (%)					
Asian[b]	2814 (13.7)	695 (13.5)	707 (13.8)	700 (13.7)	712 (13.9)
Black[b]	865 (4.2)	211 (4.1)	207 (4.0)	231 (4.5)	216 (4.2)
Hispanic or Latino	2757 (13.4)	706 (13.8)	714 (13.9)	658 (12.8)	679 (13.2)
Other race and ethnicity[b,c]	3653 (17.8)	891 (17.4)	925 (18.0)	900 (17.6)	937 (18.3)
White[b]	10 420 (50.8)	2628 (51.2)	2574 (50.2)	2636 (51.4)	2582 (50.4)
SVI score[d]					
Mean (SD)	31.0 (24.8)	31.1 (24.8)	30.9 (24.9)	31.2 (25.1)	30.8 (24.3)
Median (IQR)	24.5 (10.6-45.7)	24.8 (10.5-46.0)	23.9 (10.4-45.8)	24.5 (10.6-45.6)	24.7 (10.9-45.1)
SVI score >50, No. (%)[e]	4448 (21.9) [n = 20 267]	1131 (22.3) [n = 5073]	1097 (21.7) [n = 5064]	1139 (22.5) [n = 5066]	1081 (21.3) [n = 5064]
Primary insurance coverage, No. (%)[f]	n = 19 703	n = 4920	n = 4924	n = 4945	n = 4914
Private	19 171 (97.3)	4787 (97.3)	4808 (97.6)	4801 (97.1)	4775 (97.2)
Public	514 (2.6)	127 (2.6)	114 (2.3)	139 (2.8)	134 (2.7)
Self-pay	18 (0.1)	6 (0.1)	2 (0.04)	5 (0.1)	5 (0.1)
Patient portal usage (No. of login days in prior year)					
Mean (SD)	22.4 (27.5)	22.8 (28.5)	22.1 (26.3)	22.5 (27.7)	22.3 (27.3)
Median (IQR)	13 (4-30)	13 (4-31)	14 (4-30)	13 (4-30)	13 (4-30)
Vaccinated for influenza in prior season, No. (%)	8196 (40.0)	2034 (39.6)	2025 (39.5)	2086 (40.7)	2051 (40.0)

Abbreviations: FIT, fecal immunochemical test; SVI, Social Vulnerability Index.

[a] Age was calculated based on date of birth and study start date, yielding continuous values rather than whole-number years.

[b] Asian, Black, White, and other race and ethnicity categories refer to individuals who were non-Hispanic or Latino. Hispanic or Latino category includes individuals of any race.

[c] Other race and ethnicity included American Indian or Alaska Native (40 [0.2%]), Native Hawaiian or Other Pacific Islander (81 [0.4%]), multiracial (identified as being 2 or more races; 1245 [6.1%]), and unknown race and ethnicity (2287 [11.2%]).

[d] Social Vulnerability Index (SVI) score refers to the potential negative effects on communities caused by external stressors on human health, with a higher value indicating greater vulnerability. It is a single measure ranging from 0 to 100 that includes measures for socioeconomic status (income, poverty, employment, and education), household composition (age, single parenting, and disability), racial and ethnic minority status and language (race, ethnicity, and English-language proficiency), and housing and transportation (housing structure, crowding, and vehicle access).

[e] Percentage of participants with an SVI score greater than 50 among those with nonmissing SVI data. An SVI score of 50 represents the national median in the United States. As a reference, the SVI score in Los Angeles County was estimated to be 86.29 in 2022.[47]

[f] As a reference, an estimated 69.3% of adults aged 45 to 54 years in California had private insurance (with either employer-based insurance or privately purchased coverage) in 2020.[48]

eliciting anticipated regret for forgoing screening,[29] and sending text reminders[45] (eMethods in Supplement 3).

Study Outcomes

The primary outcome was any screening completion, defined as the completion of either FIT (normal or abnormal FIT result) or colonoscopy within 6 months of receiving the initial screening invitation. These study end points were ascertained between November 2, 2022, and November 13, 2022, due to our staggered implementation and were extracted from the electronic health record (eMethods in Supplement 3). The secondary outcome was screening modality (FIT and colonoscopy) completed. We were also interested in the proportion of crossover from one screening modality to another.

Outcome and patient characteristic data, including age, sex (patient reported), race (patient reported; fixed categories), ethnicity (patient reported; fixed categories), Social Vulnerability Index (SVI) score, and up-to-date (prior year) influenza vaccination, were derived from the electronic health record. Data on race and ethnicity were included because both factors are

Table 2. Engagement With Patient Portal and CRC Screening Invitation Message in the Intention-to-Treat Population of 20 509 Participants

	No. (%)					
	Participants who accessed patient portal[a]		Response to the CRC screening message on patient portal[b]			
	Within 1 wk of their intervention date	Anytime during follow-up period	Made active choice	Selected FIT	Selected colonoscopy	Declined screening
FIT-only active choice (n = 5131)	2528 (49.3)	4166 (81.2)	1148 (22.4)	1065 (20.8)	NA	83 (1.6)
Colonoscopy-only active choice (n = 5127)	2603 (50.8)	4124 (80.4)	878 (17.1)	NA	793 (15.5)	85 (1.7)
Dual-modality active choice (n = 5125)	2571 (50.2)	4156 (81.1)	1116 (21.8)	523 (10.2)	550 (10.7)	43 (0.8)
Usual care default mailed FIT (n = 5126)	2534 (49.4)	4168 (81.3)	NA	NA	NA	NA

Abbreviations: CRC, colorectal cancer; FIT, fecal immunochemical test; NA, not applicable.

[a] Total number and percentage of study participants in each study group who accessed the electronic patient portal at least once within 7 days of the date they first received the screening invitation (ie, their randomly assigned intervention date) or from their intervention date to the end of the study period (November 13, 2022). The percentages were calculated with the number of participants assigned to each study group as the denominator.

[b] Total number and percentage of study participants in each active choice group who responded to the active choice question in the CRC screening message on the patient portal, as well as who selected a given option during the study period. The percentages were calculated with the number of participants assigned to each study group as the denominator.

independent predictors of participation in CRC screening.[4] The SVI is a single measure ranging from 0 to 100 referring to the potential negative effects on communities caused by external stressors on human health and includes socioeconomic status, household composition, racial and ethnic minority group status, language, and housing and transportation status; a higher score indicates higher social vulnerability.

Statistical Analyses

We evaluated power using a χ^2 test comparing each of the 3 intervention groups with the usual care default FIT group. A sample size of approximately 5100 participants per group provided 80% power to detect a 3.2 percentage point change in screening rates, which conservatively assumed a control group screening rate of 50% (maximum variance) and a 2-sided significance level of .017 (3-fold Bonferroni correction).

We used linear regression models with heteroskedasticity-robust SEs to evaluate primary and secondary outcomes (statistical analysis plan in Supplement 2 and eMethods in Supplement 3) because treatment effect estimates in terms of rate differences are easier to interpret than odds ratios from logistic regressions.[46] The primary model terms were indicators for each of the 3 intervention groups. We adjusted models for patient age, sex, race and ethnicity, SVI score, and prior-year influenza vaccination to maximize estimation efficiency. We imputed the mean SVI for participants with missing location data and included a missing-SVI score indicator in the models. We performed sensitivity analyses using logistic regression and linear regression without covariate adjustment, assessed effect modification by demographic factors using interaction terms (eMethods in Supplement 3), and used the McNemar test to compare uptake of FIT vs colonoscopy in the dual-choice group. Analyses followed the intention-to-treat principle and were performed using SAS version 9.4 (SAS Institute).

To answer the first research question—whether default enrollment or active choice was more effective—we compared the 3 active choice groups with the default group. To answer the second question—whether it was more effective to prompt an active choice about 1 or 2 screening modalities—we used linear contrasts to evaluate the relative performance of dual choice (FIT or colonoscopy) and single choice (FIT only, colonoscopy only, and these 2 groups combined) and took a gatekeeping approach (eMethods in Supplement 3). We used a 2-sided significance level of .017 for the first research question to account for the 3 comparisons and a 2-sided significance level of .05 for all other analyses.

Results

Participants

Among 20 509 participants, mean age at randomization was 47.4 years (SD, 1.5 years), 11 048 (53.9%) were female, 9458 (46.1%) were male, 2814 (13.7%) were Asian, 865 (4.2%) were Black, 2757 (13.4%) were Hispanic or Latino, 3653 (17.8%) were other race and ethnicity (American Indian or Alaska Native [40, 0.2%], Native Hawaiian or Other Pacific Islander [81, 0.4%], multiracial [identified as being 2 or more races; 1245, 6.1%], and unknown race and ethnicity [2287, 11.2%]), 10 420 (50.8%) were White, and mean SVI score was 31.0 (SD, 24.8). Participant demographics and portal use (before and during the study period) were balanced across study groups (**Table 1** and **Table 2**).[47,48]

Primary Outcome: Any Screening Participation

The overall screening rate was 18.6% (3816 participants) (**Figure 2** and eTable 1 in Supplement 3). Screening completion was significantly lower in the active choice groups (FIT only, 841 of 5131 [16.4%; rate difference, −9.8%; 95% CI, −11.3% to −8.2%]; colonoscopy only, 743 of 5127 [14.5%; rate difference, −11.7%; 95% CI, −13.2% to −10.1%]; and dual-modality [FIT or colonoscopy], 890 of 5125 [17.4%; rate difference, −8.9%; 95% CI, −10.5% to −7.4%]) than in the usual care default mailed FIT outreach group (1342 of 5126 [26.2%; all

Figure 2. Colorectal Cancer Screening Participation (Percentages) Overall and by Screening Modality for Each Intervention Group
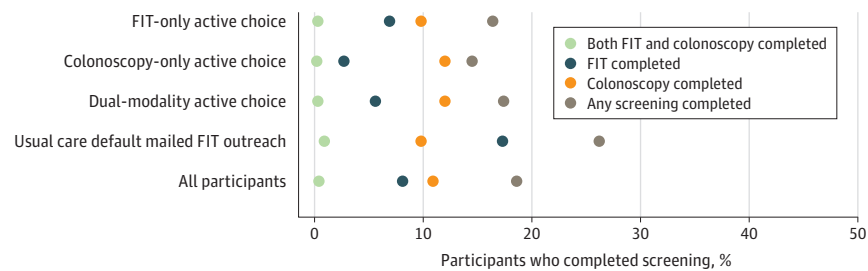
Percentages of participants in each study group (N = 20 509) who completed (1) both FIT and colonoscopy; (2) only FIT; (3) only colonoscopy; and (4) any colorectal cancer screening (primary outcome, defined as completing either FIT or colonoscopy) during the study period. Colonoscopies performed after an abnormal FIT result are not included. The rate of any screening for each group equals the sum of the FIT and colonoscopy completion rates minus the proportion who completed both tests; for example, in the FIT-only group, 16.4% = 6.9% + 9.8% − 0.3%. In the dual-modality group, the sum yielded 17.3%, which differed slightly from the reported 17.4% due to rounding. Exact values plotted in this figure can be found in eTable 1 in Supplement 3. FIT indicates fecal immunochemical test.

Table 3. Linear Regression Models of Colorectal Cancer Screening Completion Rates in the Intention-to-Treat Population of 20 509 Participants[a]

Study group	No. of participants (%)	Rate difference (95% CI) (reference = usual care default mailed FIT)	P value
Primary outcome: any screening completed, R^2 = 0.037			
FIT-only active choice	841 of 5131 (16.4)	−0.098 (−0.113 to −0.082)	<.001
Colonoscopy-only active choice	743 of 5127 (14.5)	−0.117 (−0.132 to −0.101)	<.001
Dual-modality active choice	890 of 5125 (17.4)	−0.089 (−0.105 to −0.074)	<.001
Usual care default mailed FIT	1342 of 5126 (26.2)	NA	NA
Secondary outcome: FIT completed, R^2 = 0.046			
FIT-only active choice	352 of 5131 (6.8)	−0.105 (−0.117 to −0.092)	<.001
Colonoscopy-only active choice	137 of 5127 (2.9)	−0.147 (−0.158 to −0.135)	<.001
Dual-modality active choice	288 of 5125 (5.6)	−0.118 (−0.130 to −0.106)	<.001
Usual care default mailed FIT	889 of 5126 (17.3)	NA	NA
Secondary outcome: colonoscopy completed, R^2 = 0.022			
FIT-only active choice	502 of 5131 (9.8)	0.000 (−0.011 to 0.012)	.96
Colonoscopy-only active choice	616 of 5127 (12.0)	0.023 (0.011 to 0.035)	<.001
Dual-modality active choice	616 of 5125 (12.0)	0.022 (0.010 to 0.034)	<.001
Usual care default mailed FIT	501 of 5126 (9.8)	NA	NA

Abbreviations: FIT, fecal immunochemical test; NA, not applicable.

[a] Number and percentages of participants in each study group who completed any screening and modality-specific screening completion for the intention-to-treat population, as well as linear regression models predicting these primary and secondary outcomes. Any screening completion included completion of either a FIT or a colonoscopy during the follow-up period. Models adjusted for patient sex (female, male, and unknown), age, race and ethnicity (American Indian or Alaska Native, Asian, Black, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, multiracial [identified as being 2 or more races], White, and unknown race and ethnicity), neighborhood Social Vulnerability Index (SVI) score, indicator for missing SVI values, and prior-season receipt of the influenza vaccine. Rate differences estimate between-group differences in the probability of screening completion for the intention-to-treat population. For example, the FIT-only active choice group had a 9.8 percentage point lower overall screening completion rate than the usual care default mailed FIT group after adjusting for these covariates. Asian, Black, White, and other race and ethnicity categories refer to individuals who were Non-Hispanic or Latino. Hispanic or Latino category included individuals of any race.

P < .001) (Figure 2 and **Table 3**), with robust results observed in logistic and unadjusted linear regression sensitivity analyses (eTable 2 in Supplement 3). The only observed modifiers of these differences were SVI score and prior-season influenza vaccination status (eTable 3 in Supplement 3).

Among the active choice groups (Table 3), participants offered both FIT and colonoscopy (dual modality FIT or colonoscopy) were more likely to complete screening (any modality) than participants offered only 1 screening modality (FIT only and colonoscopy only combined) (890 of 5125 [17.4%] vs 1584 of 10 258 [15.4%]; rate difference, −1.8%; 95% CI, −3.0% to −0.1%; P = .004). This difference was driven by higher screening in the dual-modality active choice group (17.4%) than the colonoscopy-only active choice group (743 of 5127 [14.5%]; P < .001), but not the FIT-only active choice group (841 of 5131 [16.4%]; P = .25). **Figure 3** illustrates participant pathways through the CRC screening invitation and completion process across study groups.

Secondary Outcome: Screening Modalities

Participants offered dual-modality active choice (5125 participants) were more likely to complete screening with colonoscopy

Figure 3. Colorectal Cancer Screening Pathways by Outreach Strategy and Patient Engagement
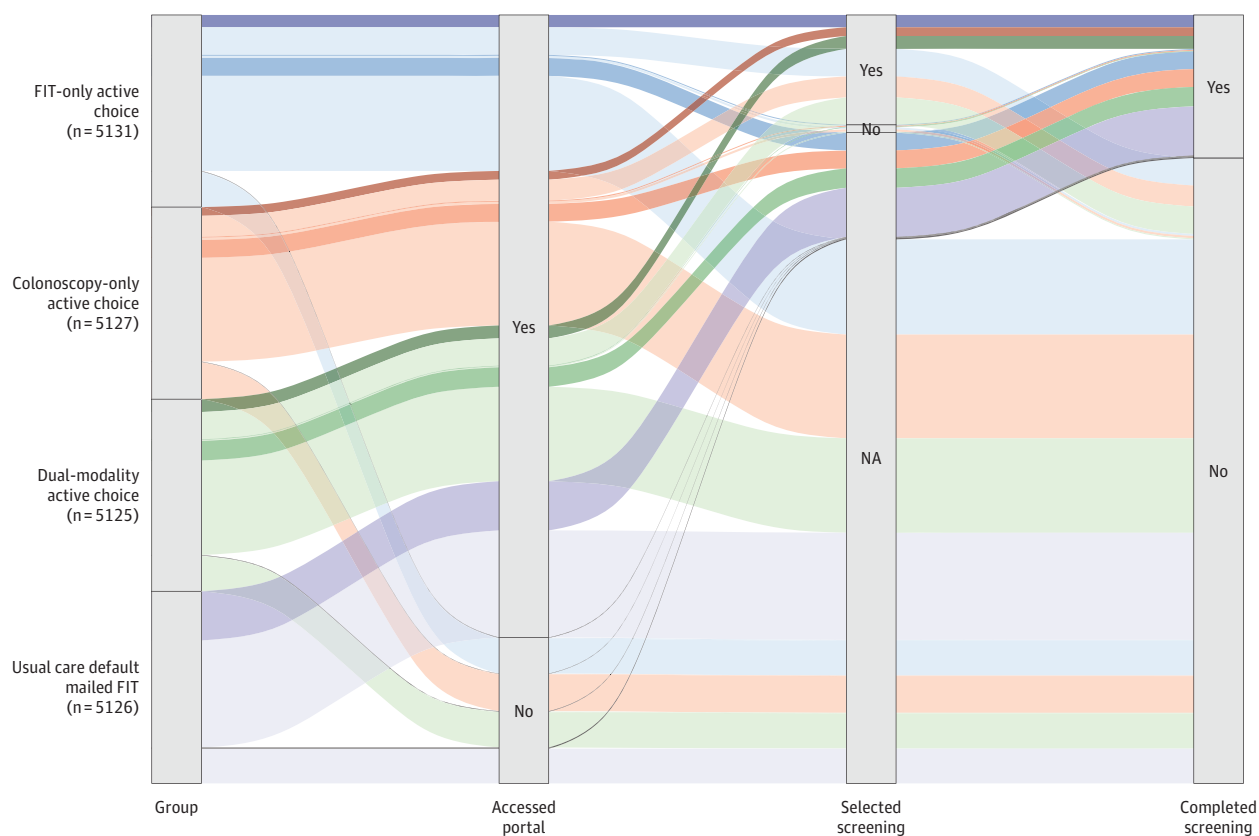
This alluvial plot illustrates participant pathways through the colorectal cancer screening invitation and completion process across 4 study groups (N = 20 509). Each flow represents the percentage of participants (within each group) progressing through sequential stages: accessing the electronic portal (yes or no), selecting a screening modality (yes, no, or NA), and completing any screening (yes or no). In the "selected screening" stratum, yes indicates participants in the FIT-only, colonoscopy-only, and dual-modality groups who selected a modality in the portal message, no indicates those who actively deferred screening, and NA includes participants in the FIT-only, colonoscopy-only, and dual-modality groups who did not respond to the message and all participants in the usual care default mailed FIT group, who were not asked to select a modality. Flow widths reflect the proportion of participants at each transition, and colors denote study group. Color saturation conveys participant behavior: full saturation indicates participants in the

FIT-only, colonoscopy-only, and dual-modality groups who accessed the portal, selected a modality, and completed screening; medium saturation indicates participants who accessed the portal but did not select a modality and still completed screening in all 4 groups (including all participants in usual care default mailed FIT who completed screening because they were not asked to select a modality); and light saturation indicates all other participants, except that dark gray highlights a small number of participants who completed screening without accessing the portal (n = 11, 9, 14, and 31 in the FIT-only, colonoscopy-only, dual-modality, and usual care default mailed FIT groups, respectively, corresponding to 0.21%, 0.18%, 0.27%, and 0.60%) via in-person care or default mailed FIT. These participants were included to reflect ongoing care delivery and maintain consistency in outcome representation. FIT indicates fecal immunochemical test; NA, not applicable.

than FIT (12.0% vs 5.6%; rate difference, −6.4%; 95% CI, −7.5% to −5.3%; $P < .001$) (Figure 2). In this group, 288 participants (5.6%) completed a FIT, 616 participants (12.0%) completed a colonoscopy, and 14 participants (0.3%) completed both.

Regarding screening modality crossover, in both the FIT-only active choice group and usual care default mailed FIT outreach group, 9.8% of participants (502 of 5131 and 501 of 5126, respectively) completed a colonoscopy despite being assigned to consider FIT. In the colonoscopy-only active choice group, the crossover to FIT was only 2.7% (137 of 5127) (Figure 2). The eFigure in Supplement 3 further illustrates the relationship between the modality selected by participants on the patient portal and their completed modality across study groups.

Among individuals with an abnormal FIT result, 73% (49 of 67) received follow-up colonoscopy within 6 months (eTable 4 in Supplement 3).

Discussion

This randomized trial involving 20 509 adults newly eligible for CRC screening found that requiring people to make an active choice—accepting or rejecting a screening modality (FIT only and colonoscopy only) or selecting FIT, colonoscopy, or neither (dual-modality FIT or colonoscopy)—led to lower screening participation than mailing an unsolicited FIT kit by default. Additionally, providing a choice between 2 screening

modalities yielded higher participation than offering an active choice around a single modality. In the dual-choice group, colonoscopy was selected more often than FIT. When FIT was the only screening option explicitly offered, 9.8% of participants in FIT-only and usual care default mailed FIT groups completed a colonoscopy instead of FIT. This study highlights that health systems can effectively engage adults aged 45 to 49 years with mailed FIT outreach, a practice already adopted by health systems for adults aged 50 years and older.

There is limited research on how to increase CRC screening participation among adults aged 45 to 49 years. Although default FIT mailing is effective in older cohorts,[19-21,23-25,27] to our knowledge this study is the first to demonstrate its effectiveness in a younger cohort less likely to be aware of screening recommendations. Mailed home-based screening tests avoid barriers associated with screening colonoscopy, including attending a clinic visit and completing an invasive procedure. In this study, screening participation in the active choice groups was approximately 10 percentage points lower than in the default mailed FIT group even when the active choice offered home-based FIT as an option, which may have occurred partly because active choice required participants to log in and affirmatively respond to the portal message. However, approximately 50% of participants accessed the portal within 1 week (Table 2), and the screening completion results remained consistent within this subsample (eTable 2 in Supplement 3). Other explanations include that mailing a FIT may reduce cognitive burden[33,35] and signal importance or urgency,[34,49] factors that may influence younger adults who do not yet recognize their risk for CRC.

Nonetheless, active choice may offer other benefits not captured here, such as greater understanding of screening options and increased decision-making confidence. Future research should compare active choice with default enrollment over time, especially with added patient navigation, to assess effects on repeat screening uptake.[50]

This study has numerous strengths. First, default mailed FIT outreach and active choice were simultaneously evaluated, 2 approaches that have outperformed traditional opt-in approaches in encouraging participation in preventive health.[16-18,28-31] Although prior research has explored interventions in which patients could choose among screening options,[24,25] they did not require an explicit affirmative choice to accept or decline screening. Within the active choice framework, we further contribute by evaluating how offering 1 or 2 screening modalities influences uptake.[32] Second, more than 20 000 individuals newly eligible for CRC screening were randomized, a cohort size rarely achieved in

US-based randomized CRC screening studies and, to our knowledge, unprecedented for this age group. These are critical steps toward identifying effective approaches to engage adults aged 45 to 49 years in screening. Third, the study population was racially and ethnically diverse, which is important, given the diversity in this age group in the United States.[51] Fourth, we demonstrated that population health interventions using automation can rapidly drive participation in preventive health services, with more than 3800 individuals completing CRC screening within just 6 months while reducing the amount of work primary care physicians are faced with when addressing numerous health measures.

Limitations

This single-center study has several limitations. First, it included only individuals at average risk for CRC, and the mean SVI score indicated low to medium vulnerability (mean, 31.0; SD, 24.8), which may limit generalizability.[47] Second, the effectiveness of active choice interventions depends on the availability of an electronic health record system capable of supporting automation and patient engagement within an electronic portal. Active use of the patient portal is high among UCLA Health's primary care patients (>80%), aligning with broader trends as health systems adopt this method of patient communication. Third, some colonoscopies performed outside the UCLA health system were missed (eMethods in Supplement 3),[52] and a 6-month follow-up period may favor FIT completion over colonoscopy, given barriers to colonoscopy, including wait times and need for time off work and an escort. Fourth, screening participation rates may have underestimated the true potential of the interventions implemented due to the lingering effect of the COVID-19 pandemic on colonoscopy scheduling at the time.[53] Fifth, although each mailed FIT kit was only $8, cost-effectiveness was not assessed. Sixth, replicating this study may not be feasible with a waiver of consent in some settings.

Conclusions

Although the USPSTF now recommends CRC screening for adults aged 45 to 49 years, evidence-based guidance on how to achieve screening for the millions of US residents in this age group was lacking. This study offers robust evidence for how to engage this age group in CRC screening. Future research should explore further optimization and tailoring of mailed FIT outreach to enhance screening participation across diverse populations and in other health care settings.

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