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Brief Communication

Investigating FIT kit completion for CRC screening in younger adults in rural areas

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Abstract
Rural regions have higher incidence rates of colorectal cancer (CRC) than urban regions, while screening is lower in rural residents than in urban residents. Rural residents experience barriers to CRC screening due to a lack of access to healthcare, perceived lack of privacy, and other cultural factors. The fecal immunochemical tests (FITs) may provide an inexpensive and convenient alternative for those lacking access to a colonoscopy or sigmoidoscopy. In a clinical trial, we investigated factors that influenced the return of a FIT kit for CRC screening among 1,230 rural residents in a midwestern U.S. state. Participants were selected from two cancer screening databases maintained by the state health department. Participants returning and not returning the FIT kit were compared for differences by age category (45–54, 55–64, 65–74), gender (female vs. male), race (non-white vs. white), and ethnicity (Hispanic vs. not Hispanic) using chi-square tests and logistic regression. Cox proportional hazard models and Kaplan–Meier curves were used to assess differences in FIT kit return time by age and gender. The youngest age group was significantly less likely to return the FIT kit and were slower at returning it when they did. In models adjusted for age category, females were significantly more likely to return the FIT kit than males and returned the FIT kit sooner than males. The results suggest that efforts are needed to reach those 45 to 55, especially males, who are not likely to see the need for CRC screening.

Keywords Rural regions · Colorectal cancer (CRC) · Screening · Fecal Immunochemical test (FIT) kit

1 Introduction

Rural colorectal cancer (CRC) incidence rates (43.9 per 100,000) are higher than in urban populations (40.1 per 100,000), both for early onset CRC and average age onset of CRC [1]; however, CRC screening rates are lower in rural areas compared to urban areas [2]. It is important to increase screening rates because the survival probability is at least 90% if CRC is diagnosed

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before it has spread outside of the colon or rectum, but only 40% of CRCs are diagnosed at a localized stage [3]. Low CRC screening rates in rural areas may be because compared to urban residents, rural residents have additional barriers to CRC screening such as lack of access to healthcare facilities and a lack of specialists, requiring them to drive long distances [4, 5]. If they are agricultural operators, they may not have time to undergo screening and may lack adequate health insurance [6, 7]. There is also the issue of a lack of privacy and lack of attention to prevention in rural communities [6, 7]. Options such as the fecal immunochemical tests (FITs) may provide an inexpensive and convenient alternative for those lacking access to a colonoscopy or sigmoidoscopy. In this study, we investigate, via a clinical trial, what factors influence completion of FIT kit for CRC screening among rural residents in a midwestern U.S. state.

Randomized controlled trials have examined whether mailing FIT kits to rural residents can increase screening rates in rural communities. A study of 169 Medicare and Medicaid enrollees living in rural communities who were mailed a FIT kit and given one year to return the kit found that 36 (21.3%) returned the kit within three months and 26 (15%) used another method to screen for CRC [8]. In contrast, in a study of 345 participants from eight economically distressed counties in rural Kentucky, 82% returned a mailed FIT kit. This high response rate may be attributed to the fact that participants were compensated for their time [9]. They also responded to a survey asking for demographic information and included a four-item cancer fatalism scale. Further, in this study, low-income individuals (< $15,000 per year) and those with normal body mass index were more likely to return the FIT kit than those with a higher income or who were overweight or obese.

We previously conducted a randomized clinical trial in a rural midwestern state where FIT kits were mailed out with and without an informational flyer. We found no difference in the response rate between those who received the flyer and those who did not, and the intervention was not cost effective. The distribution of the return dates suggested a group of early responders and a group of late responders. We were interested in how the early responders compared to the later responders**.** Few studies have addressed the issue of early and late responders in the collection of biological samples. In the health survey literature, late responders are thought to be more demographically similar to non-responders than to early responders [10–13]. Late responders tend to be male, younger, and less healthy than early responders, and these characteristics are also seen in non-responders [11, 14]. However, we do not know whether this same pattern holds when biological samples are being collected [15]. This study is the first to try to examine the time to return of FIT kits based on demographic factors. The response rate can be a function of how many reminders are mailed out and the persistence of those sending out kits. Understanding the delay in returning the FIT kit can help with planning and provide information about the number of potential non-responders.

In this report, we focus on comparing the group who returned the FIT kit and asked the following research questions: (1) Did FIT kit return differ by age, gender, or both; (2) Did the time to return of the FIT kit differ by age, gender, or both; and (3) did FIT kit return differ by race or ethnic group. We hypothesized that return rates would be lower in younger participants (age 45–54) and that younger individuals would take more time to return the kit. This is because although the recommended age for initiation of CRC screening has been lowered from age 50 to age 45 by the US Preventive Services Task Force in 2021 due to increasing cancer rates in those less than 50 years of age, [16] younger individuals may not be motivated to be screened due to feeling as if they are too young to develop CRC [6]. We further hypothesized that females would be more likely to return the FIT kits than males based on research that has found that rural women may be more inclined to CRC screening than rural men [6]; we also hypothesized that females would also return them more promptly than males. We did not expect to see differences in return or time to return by race or ethnicity. The factors examined apply to urban populations and are not unique to rural communities. Differences in screening rates in rural compared to urban communities have not been fully assessed. Whether access to care is the primary reason for the differences seen in urban and rural screening rates, or there exist other barriers, is unclear.

2 Methods

This study was designed as a clinical trial using the Consolidated Standards of Reporting Trials (CONSORT) guidelines [17]. The intervention was conducted from July 2022 through December 2022 in collaboration with the state health department. The study was designated as exempt research as a public health project by the Institutional Review Board at the University of Nebraska Medical Center.

2.1 Participants

The 1,230 participants were selected from two separate datasets: the Nebraska Colon Cancer FOBT/FIT registry and the Nebraska's Breast and Cervical Cancer Screening Program. Inclusion criteria included participants aged 45–74 who had never been screened or had not been screened with a home stool kit in the last 10 months. Individuals screened with a colonoscopy within the last 9 years were excluded from the study. Participants were selected from three rural regions, two having the highest colorectal cancer mortality rates in the state and the third having the lowest screening rate in the state.

2.2 Measures

Participant characteristics of interest in this study include gender (male, female), race (non-Hispanic White, non-Hispanic Black, and non-Hispanic other), Hispanic ethnicity (yes or no), and age. Age was categorized into three age groups: 45–54, 55–64, and 65–74. Race was recoded into non-Hispanic White and Non-Hispanic other which included non-Hispanic Black. Since no differences were observed by inclusion of an informational flyer in the FIT kit, geographic zones that participants were selected from, or either of the two databases which functioned as sources of contacts, these variables were not included in this analysis.

2.3 Statistical Analysis

Descriptive statistics were calculated to compare male and female participants by age, age category, race, and ethnicity. The chi-square test of independence was used to test for statistically significant differences in those who returned the FIT kit. The Jonckheere-Terpstra (JT) test for ordered differences was used to assess trends in positive test results over age categories. Univariable and multivariable logistic regression analysis was used to calculate the odds of returning the FIT kit compared to those who did not return the kit conditional on age category, gender, race, and ethnicity. Odds ratios and 95% confidence intervals were calculated to estimate the effect size for those who returned the FIT kit.

To assess factors associated with time to return the FIT kit, we calculated the number of days between when the kit was mailed out and when it was received. We assessed the predictors gender and age category on the length of time to returning the kit using Kaplan Meier Curves and Cox Proportional Hazards models.

3 Results

3.1 Sample

Of a total sample of 1,230 who received the FIT kits, 192 (15.6%) returned them. The mean age of the entire sample was 60.2 (standard deviation (SD) = 7.60). The mean age in 939 (76.3%) females was 59.2 (SD = 7.56) and for 291 males, 63.4 (SD = 6.80). The sample was mostly white (n = 1058, 87.7%). Hispanic participants were 13.2% of the sample (n = 159).

As shown in Table 1, the FIT return rate, percentages of males and females, and percentages of Hispanic participants differed significantly across the three age categories ($p < 0.0001$ for all). Younger age groups showed lower percentage of FIT kit return rates (6.37% and 15.9%), compared with oldest age group (22.6%). Of the 192 who returned the FIT kit, 14.1% (n = 27) tested as abnormal and participants were referred to their physician for further testing. The frequency of abnormal tests did not differ from the frequency of normal tests across age categories ($p = 0.72$) (Table 1).

Among 192 individuals who returned the kit, there were differences in return rates in gender across age groups ($\chi^2 = 9.40$, $p = 0.009$) (Fig. 1). After stratifying by gender, a significant increasing trend across age category was found for males ($p = 0.004$) and females ($p < 0.0001$), with females showing a stronger association than males. Differences by age and gender showed that more females in the 55–64 age category returned the FIT kits than in the older age category. The percentage of men returning the kit was higher than for women in the oldest age category. The return percentage was low for men and women in the youngest age category.

Table 2 shows univariable and multivariable results from the logistic regression model. In univariable models, both older groups showed a much higher odds of returning the FIT kit compared to the youngest group. Neither race nor ethnicity were significantly associated with returning the FIT kit. In the multivariable model, gender became a

Table 1 Demographic characteristics for sample of 1,230 study participants and stratified by age category, 2022–2023

Demographic variable	Age 45–54 n = 314 (25.5%) n (%)	Age 55–64 n = 527 (42.8%) n (%)	Age 65–74 n = 389 (31.6%) n (%)	$\chi 2$ (p-value)
Return FIT kit				
Yes	20 (6.37)	84 (15.9)	88 (22.6)	34.9
No	294 (93.6)	443 (84.1)	301 (77.4)	< 0.0001
Gender				
Male	32 (10.2)	124 (23.5)	135 (34.7)	57.8
Female	282 (89.8)	403 (76.5)	254 (65.3)	< 0.0001
Ethnicity				
Hispanic	64 (20.4)	71 (13.5)	24 (6.17)	31.4
Not Hispanic	250 (79.6)	456 (86.5)	365 (93.8)	< 0.0001
Race				
Non-Hispanic White	238 (96.4)	419 (95.7)	344 (97.2)	1.27
Non-Hispanic Other	9 (3.64)	19 (4.34)	10 (2.82)	(0.53)
FIT result	n = 20	n = 84	n = 88	
Normal	16 (80.0)	73 (86.9)	76 (86.4)	0.66*
Abnormal	4 (20.0)	11 (13.1)	12 (13.6)	(0.72)

*JT test for ordered differences

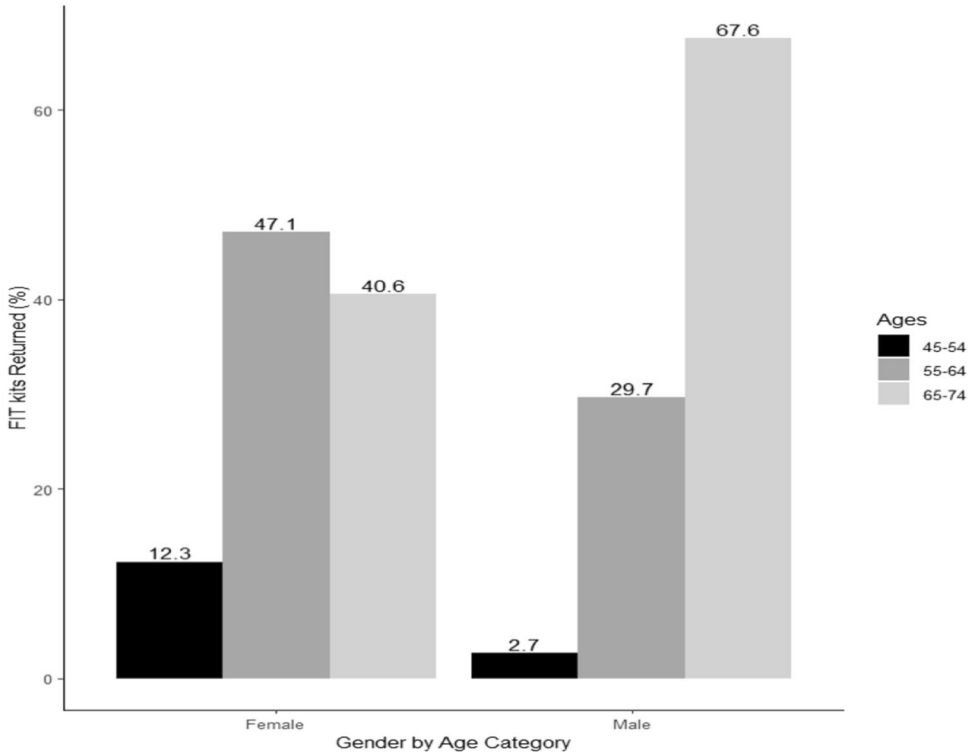

Fig. 1 Percentage of FIT kits returned by age and gender in participants who returned a FIT kit, 2022

significant predictor of returning the kit with age category in the model. No statistical interaction between age and gender was observed.

3.2 Analysis of time lag in returning FIT kits

The median number of days to return the kit was 21, the mean was 37.75, and the range was 10 to 155. The median number of days for those 65–74, 55–64, and 45–54, were 16.0, 21.0, and 31.5 days, respectively.

Table 2 Odds ratios and 95% confidence intervals for return rates by gender, age category, race, and ethnicity in 1,231 participants, 2022

Variable	Univariable model OR (95% CI)	Multivariable model OR (95% CI)
Gender		
Male	Reference	Reference
Female	1.36 (0.92, 2.00)	1.76 (1.18, 2.61)
Age Category		
45–54	Reference	Reference
55–64	2.79 (1.67, 4.64)	2.98 (1.79, 4.98)
65–74	4.30 (2.58, 7.16)	4.89 (2.91, 8.22)
Race		
White	Reference	
Nonwhite	0.96 (0.39, 2.33)	NA
Hispanic		
No	Reference	
Yes	0.61 (0.36, 1.04)	NA

A Cox proportional hazards regression model showed that the time to return the FIT kits did not have a different trajectory in females compared to males. The hazard ratio (HR) was 0.75 ($\beta = -0.29$, SE = 0.18, p-value = 0.12). However, age category was a factor in the length of time in returning the kit. Compared to the youngest age category, the 55- to 64-year-olds had a HR of 2.64 ($\beta = 0.97$, SE = 0.25, $p < 0.0001$), indicating that the 55–64 group returned the kit earlier.

Kaplan–Meier curves showed clearly that those 65–74 years old returned the FIT kits earlier than the younger age groups and that the youngest had a lower probability of returning them and took more time to do so (Fig. 2). Gender differences showed overlap in the confidence intervals in the probability of returning the FIT kit over 155 days (Fig. 2). Over the study period, males had a lower probability of returning the FIT kit as early as females did, and the gap widened across time. They not only returned the FIT kit at a lower rate, but also took more time to do so.

4 Discussion

In our study, age and gender were determinants of the return rate of CRC FIT kits. In our sample, females were 1.76 times more likely to return the completed FIT kit compared to men. In contrast, in a cross-sectional study of Nebraska residents, males were more likely to be up to date on CRC screening using any method [18]. However, our results are consistent with the higher proportion of females being up to date on CRC screening with stool-based tests or any test in the overall United States [19]. Among both genders, the likelihood of returning a FIT kit increased with age. Again, this is consistent with patterns of screening with stool-based tests or any test in the United States [19]. With the increasing incidence of CRC among younger adults, future interventions should be targeted to younger populations [20]. In our sample, the return rate was low in all age groups. In individuals who were not up to date on their CRC screening, only 15.6% returned their FIT kit.

Of those that returned the FIT kit, the median time to return the kit was 21 days, which is consistent with other studies of mailed FIT kit interventions [8]. In our study, those who were older tended to return the kit with less delay than those who were younger. A study of Kaiser Permanente records found that older adults returned FIT kits 4 days faster than younger adults [21]. Potential reasons for screening non-compliance in younger adults include lower knowledge, perceived susceptibility, and perceived benefits [22]. It is also likely that those younger adults are working populations, and thus have less time to return FIT kits in their busy daily schedules. As suggested by previous studies on non-response, the late responders may look like the non-responders and need further prompting to encourage participation. Future studies may consider more reminder strategies for younger adults to increase their return rates.

Interestingly, we found that there was a distinction between early responders and late responders in our sample. At the 100-day point, there is a drop off in return rates, which can be seen in Fig. 2. Incentivizing these late responders to respond earlier is important to early detection since we found no difference in the percentages of positive CRC tests

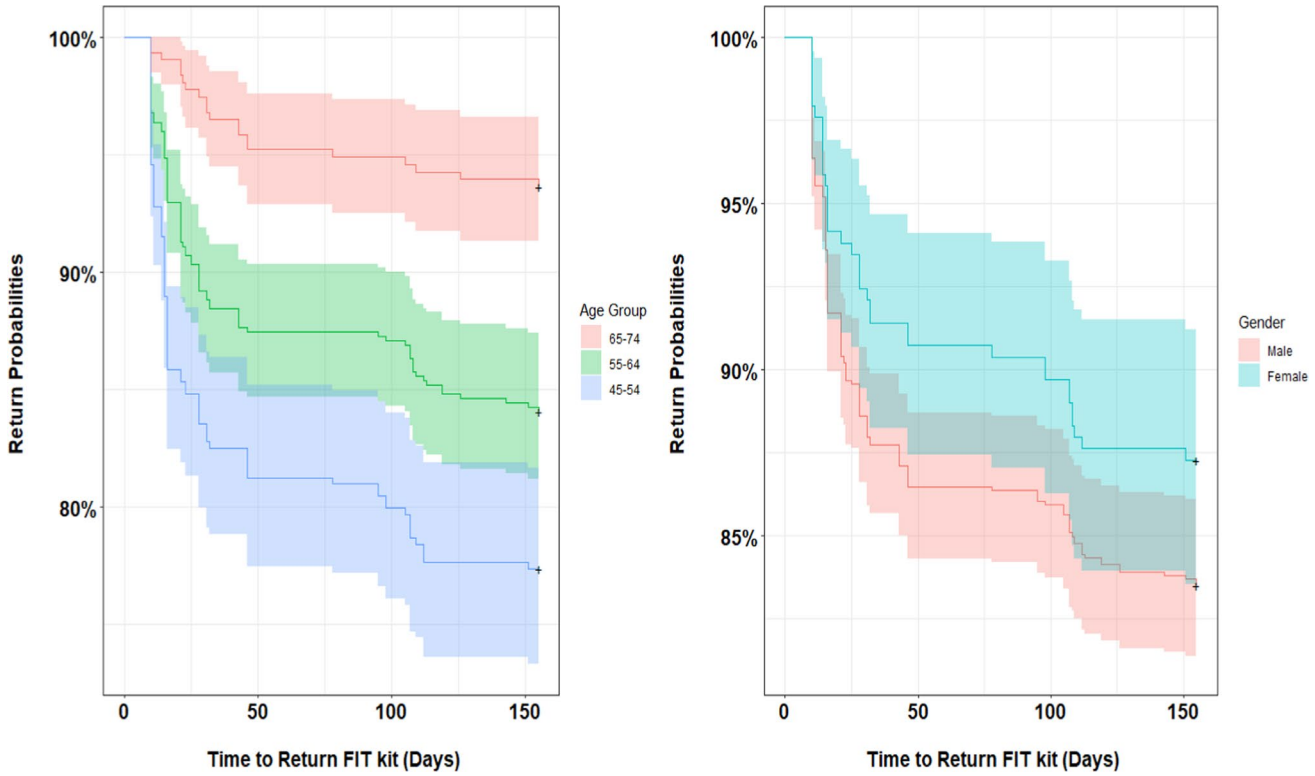

Fig. 2 Kaplan–Meier curves showing return probabilities by age category and gender in 192 who returned the FIT kit, 2022

in younger compared to older respondents. If late responders are likely to behave like non-responders, then greater encouragement is important because early detection is critical for increasing survival rates. Earlier studies have combined mailed FIT kit interventions with reminder phone calls to increase participation among non-responders [23, 24]. Targeting late responders may be important, especially since late responders tended to be younger in our sample. About 14% of completed FIT tests in our sample were positive; further research is needed to also examine predictors of time to completion of colonoscopies following these positive tests, particularly among rural residents who may face added barriers to receiving access to care [25, 26].

With the Federal Drug Administration's approval of Shield (Guardant Health) in July of 2024, a blood test for CRC may become available to rural residents who have access to a rural health clinic. The blood test was shown to be 83% effective in identifying CRC, but primarily in its later stages [32]. It was only 13% effective at indicating the presence of polyps and requires a colonoscopy to confirm the results. Agricultural operators may be more comfortable with a blood test than with using an at-home stool-based test. This test will be an option for rural individuals if Medicare and private health insurance companies cover the costs of the test, and FDA approval makes this more likely in the future.

A strength of this study was the targeting of a rural population with low CRC screening rates and the highest CRC rates in the state. However, it was primarily a White population and other race/ethnic groups were not represented. Results are generalizable to other similar rural-based populations where the intervention was executed similarly. Additionally, the study did not include information on other potential predictors of screening behaviors such as income, health insurance, and family history of cancer. An added limitation is that it cannot be known how much of the gender difference is related directly to CRC screening since there is a tendency for women to be more likely to respond to surveys in general [27]. Increased response rates by women may be related to increased perceived risk of CRC and less distrust in medicine [28]. A limitation of the study was that one of our databases was specifically designed for breast and cervical cancer screening in women and males may not be adequately represented in this sample.

The age differences are harder to explain because the sample were all adults who were at least 45 years of age. Response rates are thought to be declining in individuals older than 50 [29]; however, we saw an increase in the

response rate with increasing age, which is likely due to the perceived risk of CRC in older age groups [30]. As individuals age, they have greater contact with the healthcare system and are more likely to have screening conversations with their physician. An additional limitation is that although FIT kits were mailed to individuals who were not current on their CRC screening, we do not know whether any of the recipients of the FIT kits had prior experience with using the FIT kit. This may have been a factor in deciding whether to return the kit or not. This is an area of investigation that needs further attention. An additional avenue for future research is the feasibility of providing the MT-sDNA (Cologuard) kit as a testing option. Although it has better sensitivity than the FIT kit [31], it is considerably more expensive than the FIT kit, making it infeasible for screening a large number of people using public health funding.

In conclusion, our study revealed age- and gender-based differences in FIT kit completion among rural Nebraskans. More efforts are needed to increase CRC screening among rural residents, especially in adults between 45 and 55. Developing messaging to fully explain the risk of CRC at all ages and the importance of early detection that addresses perceived barriers to screening is key to reducing the higher mortality rate due to CRC in rural populations compared to urban populations. Partnering with local healthcare providers when sending out FIT kits might promote return of the FIT kits. Consistent, on-going messaging about the importance of CRC screening needs to come from many different trusted sources in the community, including Extension professionals who have frequent interactions with rural residents. Qualitative studies to understand who prefers stool-based tests to colonoscopy or sigmoidoscopy could make targeted screening more cost-effective.

Author contributions C.B.: study conceptualization and design, acquisition of data, analysis and interpretation of data, drafting of manuscript and critical revision; J.K.: study conceptualization and design, drafting of manuscript and critical revision; M.Le.: acquisition of data, analysis and interpretation of data, drafting of manuscript and critical revision; R.S.: study conceptualization and design, analysis and interpretation of data, and critical revision; T.R.: study conceptualization and design and critical revision; K.F.: study conceptualization and design, analysis and interpretation of data, and critical revision; J.F.: study conceptualization and design and critical revision; S.H.: study conceptualization and design and critical revision; A.Y.: study conceptualization and design, acquisition of data, analysis and interpretation of data, and critical revision; E.H.: conducted the literature review, assisted in writing the background, and reviewed the text; S.W-G.: study conceptualization and design, interpretation of data, drafting of manuscript and critical revision.

Susan Harris—Retired

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Data availability Data is available upon request to the corresponding author.

Code availability Software code is available upon request from the corresponding author.

Declarations

Ethics approval and consent to participate This study did not involve experiments on humans or use of human tissue samples so ethical guidelines are not relevant to the current study.

Consent for publication Informed consent is not relevant to this study because the study did not involve human subjects research or any experiments involving humans. The study was designated as exempt research as a public health project by the Institutional Review Board at the University of Nebraska Medical Center.

Competing interests The authors declare no competing interests.

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