Evaluation of Letters Promoting Colorectal Cancer Testing
(NCT04548765)

Study Protocol with Statistical Analysis Plan

June 16, 2021

Study Protocol

Purpose

The purpose of this study is to evaluate, prospectively, the potential impact of different mailer conditions (standard letter, letter highlighting risks, letter highlighting risks and different options, letter highlighting risks, options, and consequences for inaction) on colorectal cancer screening.

Introduction

Colorectal cancer (CRC) is the third most common cancer diagnosed in the US. Mailing fecal immunochemical (FIT) kits to at-risk patients is an effective way of increasing CRC testing uptake, as this test can be done at home and is less intrusive compared with colonoscopies. As part of an existing program, the health system mails FIT kits to eligible patients each year. Although this test needs to be conducted annually, not everyone who receives a test kit returns the kit for processing. In this study, the researchers aim to test different letters with the goal of encouraging the use of FIT kits or scheduling of colonoscopies.

As part of this study, kits were mailed with everything the patient needed to conduct the test at home and mail a sample back to the hospital. They also included introductory letters informing patients about the program and inviting them to use the kits. The researchers are comparing a standard version of the introductory letter against three versions that include different combinations of behavioral nudges, specifically framing effects (loss, default, decoy) and fear appeals.

Methods

Sample

Geisinger Health Plan members who were currently enrolled in specific plans (Medicare Health Maintenance Organization [HMO] and Preferred Provider Organization or Commercial HMO in one large employer's group) and had a flag indicating that they were due for a colon cancer screening were included. Those who were part of a do-not-contact list were excluded.

Experimental conditions

All participants were mailed a Fecal Immunochemical (FIT) kit with instructions for their use and return. The mailers also included an introductory letter. Participants were randomly assigned to receive one of the four introductory letters detailed below.

Standard Letter (V1): The standard letter described the importance of getting screened and included general instructions on how to use the FIT kit for screening at home.

Letter with Risks (V2): The standard letter was enhanced with language that described the risks of late detection in greater detail but also clearly described how early detection with a test could

reduce those risks; it also explained why test kits were being sent, to disarm skepticism about the program.

Letter with Risks and Options (V3): In addition to the enhancements added by the letter with risks, the letter also included a table comparing FIT kit and colonoscopy in terms of convenience, frequency of testing, and effectiveness. Presenting different screening options was intended to make participants feel empowered to make the choice that best suited them. In addition, presenting multiple options was intended to increase the chance that recipients got screened by one of the two methods. This letter also included contact information to schedule a colonoscopy in case participants preferred that procedure over using the FIT kit.

Letter with Risks, Options, and Consequences for Inaction (V4): In addition to the enhancements added by the letter with risks and options, the comparison table included comparisons of the mortality rate when getting screened vs. waiting for symptoms to appear.

Outcome measures

The primary outcome measure was colorectal cancer screening, defined as either returning the FIT kit (yes/no) or ordering a colonoscopy (yes/no) 6 months from the intervention date. FIT kit return and colonoscopy were initially two separate outcomes, but they were collapsed into one, since doing either was the desired response to the intervention, that is, taking action to get screened for colorectal cancer. Further increased colonoscopies, which can be done without a FIT kit, could contribute to lower FIT kit returns and falsely suggest that there were fewer people screened in a particular group.

The secondary outcome measures were FIT kit return at 12 months (yes/no), colonoscopy order at 12 months (yes/no), FIT kit result at 12 months (lab notes), colonoscopy completion at 12 months (yes/no), and colonoscopy result at 12 months (lab notes).

Statistical Analysis Plan

As of the writing and posting of this plan, all mailers have been sent and the data have not yet been examined.

Primary Research Question: Do the enhanced mailers outperform the standard mailer?

H1a: V2 will lead to increased colorectal cancer screening at 6 months compared with V1
H1b: V3 will lead to increased colorectal cancer screening at 6 months compared with V1
H1c: V4 will lead to increased colorectal cancer screening at 6 months compared with V1

The following logistic regression model will be used for this analysis: Outcome ~ Condition. In this model, V2, V3, and V4 will be entered as predictors with V1 as the reference group. For all tests, two-tailed p-values < 0.05 will be used to determine statistical significance.

Secondary Research Question 1: Do the enhanced mailers outperform the standard mailer, specifically focusing on FIT kit returns and colonoscopies ordered?

H1a: V2 will lead to increased FIT kit returns at 6 months compared with V1
H1b: V3 will lead to increased FIT kit returns at 6 months compared with V1
H1c: V4 will lead to increased FIT kit returns at 6 months compared with V1

H1d: V2 will lead to increased colonoscopy orders at 6 months compared with V1
H1e: V3 will lead to increased colonoscopy orders at 6 months compared with V1
H1f: V4 will lead to increased colonoscopy orders at 6 months compared with V1

The following logistic regression model will be used for this analysis: Outcome ~ Condition. In this model, V2, V3, and V4 will be entered as predictors with V1 as the reference group. For all tests, two-tailed p-values < 0.05 will be used to determine statistical significance.

Secondary Research Question 2: Do the enhanced mailers outperform the standard mailer in the long term (12 months after)?

H2a: V2 will lead to increased colorectal cancer screening at 12 months compared with V1
H2b: V3 will lead to increased colorectal cancer screening at 12 months compared with V1
H2c: V4 will lead to increased colorectal cancer screening at 12 months compared with V1

H2d: V2 will lead to increased FIT kit returns at 12 months compared with V1
H2e: V3 will lead to increased FIT kit returns at 12 months compared with V1
H2f: V4 will lead to increased FIT kit returns at 12 months compared with V1

H2g: V2 will lead to increased colonoscopy orders at 12 months compared with V1
H2h: V3 will lead to increased colonoscopy orders at 12 months compared with V1
H2c: V4 will lead to increased colonoscopy orders at 12 months compared with V1

The following logistic regression model will be used for this analysis: Outcome ~ Condition. In this model, V2, V3, and V4 will be entered as predictors with V1 as the reference group. For all tests, two-tailed p-values < 0.05 will be used to determine statistical significance.

Secondary Research Question 3: Do the enhanced mailers outperform the standard mailer in the long term (12 months after)?

H3a: V2 will lead to increased colonoscopy completions at 12 months compared with V1
H3b: V3 will lead to increased colonoscopy completions at 12 months compared with V1
H3c: V4 will lead to increased colonoscopy completions at 12 months compared with V1

The following logistic regression model will be used for this analysis: Outcome ~ Condition. In this model, V2, V3, and V4 will be entered as predictors with V1 as the reference group. For all tests, two-tailed p-values < 0.05 will be used to determine statistical significance.

Exploratory Research Question: Which of the enhanced mailers had the best performance?

The researchers did not have hypotheses regarding which of the enhanced versions will perform better with regards to FIT kit returns, although they expect V3 and V4 will lead to more colorectal cancer screenings, and more specifically, colonoscopy orders and completions since information on how to schedule a colonoscopy was included in those letters.

For these outcomes, logistic regressions will be used. The following basic model will be used for the above analyses: Outcome ~ Condition. For each outcome, two models will be run in parallel: (1) V2 and V3 will be entered as a predictor with V4 as the reference group; (2) V3 and V4 will be entered as predictors with V2 as the reference group. For all tests, two-tailed p-values < 0.05 will be used to determine statistical significance.

Examination of Additional Outcomes

Only descriptive statistics will be reported for positive screens from the FIT kits and colonoscopies. These will be used to illustrate how many people detected CRC due to the program and to estimate the costs to the hospital system.