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# A Comparison between a Mail Only Outreach and a Mail Outreach with Automated and Live Phone Call Reminders for Increasing Colorectal Cancer Screening

THESIS

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MASTER OF SCIENCE

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by

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# ABSTRACT OF THE THESIS

A Comparison between a Mail Only Outreach and a Mail Outreach with Automated and Live Phone Call Reminders for Increasing Colorectal Cancer Screening

By

Michael Bin Yue Xu

Master of Science in Biomedical and Translational Science

University of California, Irvine, 2020

Professor John Billimek, Chair

Colorectal cancer is a leading cause of cancer related deaths in United States for both men and women. Despite the availability of various screening tests, the screening rate remains low, especially among the Hispanic population. This randomized pragmatic trial study compares the effectiveness of a combination of mailed package, including a pre-paid fecal immunochemical testing (FIT) kit, with automated and live phone call reminders to mailed package only. The control group received only mailed packages, whereas the intervention group received automated and live phone calls after the mail delivery. Patient data were collected from the electronic healthcare record from a primary care clinic within a federally qualified health center in Orange County, CA. Our results showed that the intervention group had a significantly more FIT returns than the control group. The results also suggested that many patients may not be available through phone calls.

# CHAPTER 1. INTRODUCTION

Colorectal cancer (CRC) is one of the leading causes of cancer related deaths in the United States, and one of the most common types of cancer among both men and women. In 2016, it was estimated that 134,000 people would be diagnosed with CRC, and 49,000 would die due to the cancer.[4] CRC is developed from untreated precancerous polyps, which are abnormal growths, in the colon or rectum. According to the Centers for Disease Control and Prevention (CDC), the risk for CRC increases with age, and over 90% of the patients are 50 years old or older. Other risk factors include inflammatory bowel disease, family history of CRC, and certain genetic syndromes. Unhealthy lifestyle, such as lack of regular exercise, unbalanced diet, tobacco and alcohol consumption also contribute to higher risks of developing CRC.[1] Despite its prevalence, if CRC is detected and treated early at the localized stage, the 5-year survival rate is as high as 90.3%. In contrast, the survival rate drops to 70.4% and 12.5% for patients with regional (the spread of cancer to nearby lymph nodes, tissues, or organs) and distant stages (the spread of cancer to distant parts of the body) respectively.[2]

In addition to contributing to significantly higher survival rates, early detection can lead to a noticeable reduction in healthcare costs. According to the National Institute of Health (NIH) and Center for Disease Control and Prevention (CDC), the direct medical cost of CRC care in 2010 was estimated to be $14 billion nationwide. A study done in 2009 shows that the medical cost attributable to CRC is lowest if cancer is found at the in situ or local stage. If CRC is detected at the in situ or local stage, the mean cost attributable to cancer was $27,551; at the regional stage, the mean cost was $30,748; at the distant stage, the mean cost was $29,933.[3] The cost of care also increases with more comorbidities.

Early detection of CRC significantly improves patient survival rate and reduces medical costs. Thus, CRC screening tests are strongly recommended by healthcare professionals and the government. The United States Preventive Services Task Force (USPSTF) encourages testing for early detection, and gave CRC screening tests a grade A recommendation for people between age 50 to 75.[4]

There are different types of screening tests for CRC, which can be categorized into 2 main types: visual/structural based exams and stool-based tests. Visual/structural based exams include colonoscopy, CT colonography, and sigmoidoscopy. Stool based tests include fecal occult blood test, stool DNA test, and fecal immunochemical test (FIT). FIT, a non-invasive test which detects human hemoglobin in the stool, is one of the most common primary CRC screening tests done in clinics or at home due to its ease of use and good psychometric properties. Use of FIT is associated with essentially no harm by itself; the harms of FIT are mainly associated with colonoscopy exams after positive test results.[6] According to a systematic review report from USPSTF, single stool specimen FIT has a sensitivity range of 73% - 88%, specificity range of 90% - 96%, and an overall fair to good quality rating, which is the same quality rating given to colonoscopy.[5] Annual FIT testing is accepted by the CDC as an acceptable screening strategy for CRC.

Despite the substantial benefits of early detection, variety of test choices, and availability of CRC screening tests, many members of the at-risk population are not up to date with their screening or have never been screened. According to the CDC, as of 2018, only 68.8% of adults between age 50 to 75 were up to date with their screenings. In addition, there are 21.7 million adults between age 50 and 75 who have never been screened for CRC. Among the many barriers to screening, the common primary barriers to screening are lack of physician recommendation, lack of screening awareness, and lack of insurance coverage.[12] In order to increase the screening

rate, healthcare professional and researchers have been continuously making efforts to increase the screening rate through quality improvement projects and studies.

Research has been focusing on improving participation in routine FIT testing through various reminder systems, such as mailed reminders, text reminder, phone calls, or a combination of them.[8-10] Among these approaches, phone calls seem to be more effective than written communication (letter or text message) in increasing FIT screening rate.[8]

The need for effective reminders for CRC screening is particularly high among Hispanic/Latino adults. In California, only 70.8% of age-eligible adults have been screened for CRC; among them, the Hispanic/Latino patient population has the lowest participation in CRC screening of 55.6% compared to Whites (77.3%) and African Americans (77.5%).[7] The difference may be attributable to Hispanic/Latino cultural beliefs, perception towards medicine and the healthcare system, lack of insurance coverage, language barriers, and general awareness of CRC screening[51-54].

The purpose of this study is to conduct a quality improvement study examining the effect of a reminder intervention on CRC screening rates in a high risk and under-studied population, English and Spanish-speaking Hispanic/Latino age-eligible patients at a federally qualified health center safety net clinic. This study is among the first to determine whether the effects of reminder interventions seen in other studies can be replicated in a primary care safety net clinic using mail and phone call outreach. In addition, few studies have been done to examine and compare the feasibility of using mailed information reminder and a combination of automated and live phone calls to increase CRC screening rate in a safety net clinic. Lastly, this study will examine the effectiveness of the outreach within different sub-groups.

This study has 3 aims: 1) compare the effectiveness of mailed reminder to a hybrid approach of automated and live phone call outreach in increasing the rate of CRC screening via FIT completion in a predominantly Hispanic patient safety net clinic; 2) examine the feasibility of using a combination of automated and live phone call reminders to increase CRC screening rate in a safety net hospital serving predominantly Hispanic patients; 3) conduct sub-group analyses to examine the effectiveness of mail with phone call outreach among groups with different genders, ages, and ethnic sub-groups.

# CHAPTER 2. BACKGROUND

## Chapter 2.1 Effectiveness, Harms, and Benefits of Screening Tests

There are two categories of CRC screening tests: stool-based tests (eg. fecal occult blood test, fecal immunochemical test, stool DNA), and visual/structural based exams (eg. colonoscopy). The gold standard test for CRC is colonoscopy, which is a visual/structural based exam recommended to be done every 10 years by experienced specialists. The sensitivity of colonoscopy for detecting adenomas of at least 10mm ranges from 89% - 98%; for detecting adenomas of at least 6mm ranges from 75% - 93%.[6] The pooled estimated sensitivity and specificity for screened asymptomatic patients were 92.5% and 73.2% respectively.[11] However, despite the good parametric values of colonoscopy, due to its extremely invasive nature, the exam carries more risks and harms to patients when compared to some other alternative tests. A systematic review for the USPSTF estimates that the risk of perforation due to colonoscopy was 4 in 10000 procedures, and the risk of major bleeding was 8 in 10000 procedures.[5] In order to avoid invasive and risky procedures, many healthcare institutions and professionals prefer using a stool-based exam, such as the fecal immunochemical test (FIT), as a preliminary screening test.

Guaiac fecal occult blood test in one of the most common types of stool-based CRC screening tests. The gFOBT, which is recommended to be done annually, examines the stool for traces of blood by detecting peroxidase, a type of protein found in the blood. However, food sources containing peroxidase, such as red meat, cruciferous vegetables, and fruits, could increase the rate of false-positives.[13] In addition, high amount of vitamin C supplements, which inhibit peroxidase reactions, could produce false-negative results.[14] In order to minimize false results, patients are instructed to avoid aspirin and other nonsteroidal anti-inflammatory drugs, vitamin C, red meat, poultry, fish and some raw vegetables.[15] The common testing protocol requires 2 samples

from 3 consecutive bowel movements, because the sensitivity increases from each additional samples.[16] The overall sensitivity and specificity of gFOBT have shown to be variable depending on many factors, such as brands and variants of the test, specimen collection techniques, number of collected samples, rehydration of specimen, interpretation, and screening interval.[16-20] The sensitivity could range from 12.9% to 79.4%, and specificity could range from 86.7% to 98.1%.[14] A study done in Scotland has shown that the positive predictive value of gFOBT to be 7.0% - 12.0% for cancer detection, and 29.1% - 36.5% for adenoma detection.[24] A Dutch study has shown that the number needed to screen according to intention to screen to find an advanced adenoma or carcinoma was 181; the number needed to screen to find cancer was 936.[24] Because of the limitations of gFOBT, there has been a shift preference from gFOBT to other stool-based screening tests.

The fecal Immunochemical test (FIT) is another stool-based exam that uses blood detection in stools to screen for CRC. Blood vessels of colorectal polyps and cancers are easily damaged by the passing of stool, and results in bleeding into the colon and rectum. The trace amount of blood usually cannot be seen by human eyes, but the hemoglobin from the blood can be detected by FIT. Different from gFOBT, the FIT detects only human hemoglobin in the stool, which makes the test specific to the detection of human blood. In addition, FIT is more specific for lower gastrointestinal bleeding, because globin is degraded by enzymes in the upper gastrointestinal tract.[14] In a meta-analysis of 19 studies in asymptomatic average-risk adults the pooled sensitivity and specificity of FIT was 79% (95% CI: 0.69–0.86) and 94% (95% CI: 0.92–0.95) for CRC.[25] The positive predictive value of FIT for cancer ranged from 2.9% to 7.8%; for advanced neoplasia, it ranged from 33.9% to 54%.[26] Although not done in the United States, several studies have demonstrated that the negative predictive value of FIT for CRC was consistently greater than 90%.[27-30] There

have been no harms related directly to the use of FIT. In addition to FIT, there is one more stool-based screening test that has been developed recently, and combines FIT with DNA testing.

CRC is the result of the accumulating genetic and epigenetic alterations, which prompted the development of sDNA test.[21] Cells from precancerous and cancerous lesions shed DNA biomarkers into the stool, which is then detected by the sDNA test. Since cancerous DNA alterations differ between CRC, the sDNA test targets multiple DNA biomarkers in order to achieve high accuracy. The test is also capable of detecting traces of blood in the stool, and is often added on to a FIT, which is why the sDNA test is also known as FIT-DNA. The testing procedure for sDNA is very similar to that of FIT, except that sDNA requires the entire stool sample to be collected. The overall sensitivity and specificity of sDNA for CRC at any stage is 92.3 (95% CI: 83.0–97.5) and 89.8 (95% CI: 88.9–90.7) respectively; the positive predictive value is 0.037 (95% CI: 0.029-0.048), the negative predictive value is 0.999 (95% CI: 0.998 – 1.00); the number needed to screen is 166 (95% CI: 130 - 217).[22]

Comparing the three stool based exams, both FIT and sDNA perform better than gFOBT; however, FIT is currently more cost-effective than sDNA. As mentioned previously, when compared to gFOBT, FIT is more specific to human blood and requires no dietary restrictions before testing. This could be a reason that led to FIT having a higher participation rate than gFOBT. A retrospective observational study done at Veterans' Administration San Diego Healthcare System revealed that a significant portion of patients completed a FIT than a gFOBT (42.6% vs 33.4% respectively, $p < 0.001$).[41] The study also showed than FIT detected a higher portion of advanced neoplasia than gFOBT (0.79% vs 0.28% respectively, $p = 0.003$). A meta-analysis of five different papers also demonstrated that FIT have higher participation and positivity rates, and lower false negatives and negativity rates than gFOBT.[42] Compared to gFOBT, FIT also has more

consistent sensitivity and specificity due to less variables in the testing procedures, such as hydration of specimen, number of samples, screening intervals, etc. Compared to both gFOBT and FIT, sDNA uses more advanced DNA testing technology to detect signs of CRC, has higher sensitivity, and is able to detect a greater proportion of neoplasia and cancers.[43] However, sDNA is more expensive than gFOBT and FIT. The reimbursement from Centers for Medicare & Medicaid Services per FIT is $23, whereas it is $493 per FIT plus sDNA test.[31] A study using the Markov model of average risk CRC screening determined that FIT is more cost effective than sDNA, assuming equal participation rates; for sDNA to be more cost effective than FIT, a higher screening participation rate is needed.[44] Overall, considering the advantages and disadvantages of the three screening tests, FIT is a more preferable choice as the primary CRC screening test for many hospitals and clinics. For our study, we also decided to use FIT as the screening method for our patient population.

**Chapter 2.2 Facilitators and Barriers to Screening**

A recent National Health Interview Survey (NHIS) study has shown that only 62% of Americans are up-to-date with their CRC screening, a number much lower than the goal of 80% set for 2018 by the National Colorectal Cancer RoundTable.[32] Furthermore, data from additional NHIS cohorts suggests that screening rate is plateauing around 60 to 62%.[33] In order to understand patient behaviors and attitudes towards CRC screening, many studies have been done to examine the facilitators and barriers to screening.

A systematic review and meta-study synthesis included ninety-four qualitative studies and identified several screening facilitators and barriers.[46] According to this study, the decision of participating or not participating in the screenings depended on awareness, which affected views

of CRC, attitude towards screening modalities, and motivations for screening. Specific screening facilitators were public education to address misconceptions, physician recommendations, and influence from family and friends. Attitudes toward screening can be affected by previous screening experience and knowing the purpose of CRC screening, while motivations to screening stem from intrinsic health beliefs, habits, and influence from family and friends, especially from those who were affected by CRC.

The study also reported that the barriers to screening were the converse or the lack of the facilitators, as well as negative views of cancer, negative beliefs about screening modalities, socioeconomic challenges, and cultural and gender beliefs. Negative views of cancer mainly include fatalism and fear of cancer, screening results, and treatment after diagnosis. Participants were averse to colonoscopy due to the associated pain, discomfort, and risks, while the factors of fecal test aversion were threats to hygiene and social taboo. Socioeconomic barriers were mainly composed of loss of income due to time spent at screening, lack of transportation, poor health literacy, and language barriers. Some cultural beliefs, such as belief in natural remedies, and that screening not being the cultural norm, negatively affected rate of screening. The attitude towards screening also differed between men and women. Latino and African-American men perceived colonoscopy as a threat to their masculinity due to its procedure, while some women believed CRC was a male disease.

Another systematic review focused on CRC screening barriers in rural USA produced similar findings. The review examined results from 27 surveys, focus groups, medical records, and interviews. It reported 4 categories of barriers: individual-level structural barriers, barriers related to screening procedures, and individual-level perception/knowledge barriers, and barriers at the provider level.[47] Individual-level structural barriers included costs of tests, lack of insurance, and

lack of time; screening procedure barriers were embarrassment, discomfort, fear of procedures, fear of results, and fear of burdening families; individual-level perception barriers were lack of knowledge of screening guidelines and options, lack of perceived need, and misconception that CRC is a male disease; provider-level barriers included lack of physician recommendation, distrust of providers and healthcare system, and lack of specialists or even primary care physicians.

As shown by the findings from various studies, facilitators and barriers to CRC screening fall into the following categories: awareness and knowledge of CRC and screening options, attitudes and beliefs towards screenings and the healthcare system, socioeconomic challenges, and physician recommendations. Therefore, intervention strategies need to target these categories to increase screening participation. Many studies on different intervention methods have been done to examine the effectiveness of those methods.

### Chapter 2.3 Current Studies on Screening Intervention Methods

CRC has a high mortality rate if it is left untreated and allowed to develop into late stages. However, the survival rate cab be as high as 90% if detected early.[2] Therefore, regular screening to detect CRC as soon as possible is strongly encouraged. However, despite being reminded by physicians and health care professionals during regular clinic or hospital visits, CRC screening remains low, especially among minority groups. The Community Guide to Preventive Services recommends using multicomponent methods to increase CRC screening. Multicomponent is defined as using at least 2 out of the 3 domains: (1) interventions to increase community demand (eg. reminders, education, incentives); (2) interventions to increase community access (eg. reducing structural barriers, reducing client out-of-pocket costs); and (3) interventions to increase provider delivery of screening services (eg. provider assessment/feedback, incentives,

reminders).[34] Many studies have searched for effective methods to increase CRC screening. A systematic review and meta-analysis published in JAMA found that the most common interventions associated with increased screening completion rate when compared to usual care are: fecal blood test outreach (RR: 2.26, 95% CI: 1.81-2.81; RD: 22%, 95% CI: 17%-27%), patient navigation (RR: 2.01, 95%CI: 1.64-2.46; RD: 18%, 95% CI: 13%-23%), patient education (RR: 1.20, 95% CI: 1.06-1.36; RD: 4%, 95% CI: 1%-6%), patient reminder (RR: 1.20, 95% CI: 1.02-1.41; RD: 3%, 95% CI: 0%-5%), clinician intervention of academic detailing (RD: 10%, 95% CI: 3%-17%),), clinician reminder (RD: 13%, 95% CI: 8%-19%).[45] The review also showed that multicomponent interventions are associated with greater increases in screening completion than single component interventions (RR: 1.18, 95% CI: 1.09-1.29; RD: 7%, 95% CI: 3%-11%).[45]

Mailed outreach, containing patient reminders, CRC education materials, and fecal blood testing kits is one of the most common multicomponent outreach methods. It increases community demand by educating patients the importance of CRC and reminding the overdue patients, as well as reducing access barriers by mailing testing kits to the homes of patients. Compared to standard care, which is having care providers reminding patients that they are overdue for CRC screening during patient visits, mailed outreach has shown to increase screening. A 2019 systemic review and meta-analysis examined seven randomized controlled trials (n = 12,501) comparing mailed outreach offering stool tests (both FIT and gFOBT) to usual care showed a 28% (95% CI: 25-30%) absolute and 2.8 (95% CI: 2.03-3.45) fold relative increase in screening completion.[32] This review also showed that there was no significant difference in screening completion rate when comparing FIT to gFOBT, and that the number needed to invite to achieve one patient up-to-date with screening was estimated to be 3.6. Out of the seven RCT studies, this review also compared those

that focused on underserved and/or minority populations to those that did not; the absolute increase in screening did not differ significantly.

A cluster randomized pragmatic clinical trial also demonstrated increased screening completion with mailed outreach, although the effect size is much smaller. The trial consisted of 26 federally qualified health centers, and 41,193 participants in total; 13 clinics with 21,134 patients were assigned to the intervention arm, and 13 clinics with 20,059 patients were assigned to usual care. In the trial, the adjusted FIT completion proportions from intervention clinics, were 3.4% (95% CI: 0.1-6.8%) higher than those from usual care clinics; in addition, the trial also showed that the proportion of patients completing any CRC screening was 3.8% (95% CI: 0.6-7.0%) higher in intervention clinics than in usual care clinics.[35] This trial estimated the number needed to mail to be 4.8. A secondary analysis of this cluster randomized pragmatic trial showed that the increased FIT screening was consistent across various subgroups, such as gender, primary language, insurance status, federal poverty level, etc.[40] Although the exact effect sizes differ, results from other randomized trials also indicate that mailed outreach is superior than usual care in increasing screening.[36-39]

Demonstrated by several randomized trials, phone call reminders are another common outreach method to increase CRC screening participation. One large trial study randomized 5905 patients to either usual care and automated phone call intervention group. The results showed that 22.5% of the patients in the intervention group returned a FOBT, compared to only 16% in the usual care group; patients in the intervention group were significantly more likely to complete and return a FOBT than the usual group, with a hazard ratio of 1.31 (95% CI: 1.10 – 1.56).[48]

In another study, automated phone calls, live phone calls, and a combination of automated and live phone calls were compared to mail reminders. The study analysis showed that the live

phone call group and the group with a combination of automated and live phone calls had the highest FIT return rate, with odd ratios of 1.73 (95% CI: 1.16 – 2.58) and 1.74 (95% CI: 1.17 – 2.60) respectively.[49] However, there seems to be differences in the effectiveness of automated or live phone call interventions based on language preference. English-speakers (n = 1467) responded better to live calls (OR, 2.17; 95% CI: 1.31–3.59), a combination of a reminder letter and live call (OR: 1.78; 95% CI: 1.07–2.97), an automated and live call (OR: 1.73; 95% CI: 1.04–2.88), or text message and live call (OR: 1.90; 95% CI: 1.15–3.14) compared to mail reminders alone. However, for Spanish-speakers (n = 384), only the combination of automated and live phone calls produced had higher odds of FIT return compared to mail-only reminders (OR: 3.45; 95% CI: 1.42–8.39).[49] Similar results were found in another study, in which Spanish-preferring (n = 106) patients were more likely to return FIT if they were in the automated call only group than in the automated and live call group (62% vs 39%, p = 0.02), while English-preferring patients (n = 279) showed no difference in modes of phone call intervention.[50]

**Chapter 2.4 Current Knowledge Gaps**

Past research has identified many facilitators and barriers to CRC screening, has suggested that English-speaking versus Spanish-speaking patients may respond differently to different interventions, and has shown that effective intervention strategies to increase CRC screening should include multiple components to target different screening obstacles. However, these studies were conducted at settings where Hispanics were the minority. We lack further information on the effectiveness of different intervention strategies in Hispanic dominant safety net primary care settings.

In our study, we will examine the effectiveness of mailed outreach and automated plus live phone call reminders in increasing the CRC screening rate in a safety net hospital with predominantly Hispanic patients. We will also study the feasibility of phone call interventions by examining variables such as number of subjects reached, FIT completion rate of subjects reached by phone, and whether patients received the packages and understood the written FIT instructions.

# CHAPTER 3. METHODS

## Chapter 3.1a Participant Selection

Eligible study participants who were overdue for CRC screening were randomly selected from primary care clinics in the UCI Family Health Center in Santa Ana (FHC-SA). UCI Family Health Center in Santa Ana is a Federally Qualified Healthcare Center affiliated with UCI Medical Center and UCI School of Medicine. The clinic serves a large proportion of Hispanic/Latino patients with low socioeconomic status. Study eligibility criteria were: 1) age between 50-75 years; 2) current patients of the Family Health Clinic in Santa Ana; 3) no documented history of completing a FIT in the past year or colonoscopy in the past 10 years; 4) having a Medicaid insurance plan that covers 100% of the out of pocket costs of the FIT test employed in the study; 5) had a preferred language of English or Spanish listed in the EHR; and 6) had a valid phone number listed in the EHR. Patients were excluded from the study if they: 1) had a previous diagnosis of CRC; 2) previously had a total colectomy; or 3) were in hospice care during the time period of the study.

## Chapter 3.1b Rationale for Study Eligibility Criteria

Health disparity has been a big issue in the United States, with the Hispanic population often experience worse health outcomes and services. In California, the CRC screening rate of Hispanics is only 55.3%, the lowest compared to non-Hispanic whites, African-Americans, and Asians.[7] Therefore, we focused our intervention study on the Hispanic population in an attempt to address this screening disparity.

Previous studies have already shown that lack of insurance prohibits screening participation in CRC screening, however, in California, only 67.3% of the insured have been

screened for CRC.[7] Therefore, we wanted to determine if our intervention would be effective to increase screening rate among those who are insured.

Lastly, our study only included patients between age 50 to 75, because the USPSTF concluded with high certainty that screening for colorectal cancer in average-risk, asymptomatic adults aged 50 to 75 years is of substantial net benefit; For older adults aged 76 to 85 years, the benefits of screening for colorectal cancer decline, and the risk of experiencing serious as sociated harms increases. Therefore, after assessing the risks and benefits, it was decided to include only patients within this recommended age range.

**Chapter 3.2 Study Design**

Based on patients' medical records at the UCI Family Health Center at Santa Ana, patients who were overdue for CRC screenings and fit our study criteria were identified.

The control group received only mailed reminders, which consisted of a signed letter (written in both English and Spanish) from a physician educating patients on CRC and the need of screening, a map of clinics and laboratories to return FIT kits, and the FIT kits along with instructions. The intervention group received the same mailed reminders as the control group, and a combination of automated and live phone call reminders. Patients in the intervention group received phone call reminders at two instances of time. The initial automated phone calls were made at the time of sending out the mails to inform them of their overdue status for CRC screenings and the incoming FIT kit mails. If patients have not returned their FIT kits within two weeks, live follow-up calls will be made to remind them. Both the initial calls and follow-up calls were attempted three times per patient; if patients did not answer on at least one of the three attempts, patients were left with brief voicemails. Automated and live phone calls were in either English or

Spanish based on the preferred language indicated in patient medical records.

Participants could return FIT kits to any of the clinics and laboratories indicated on the map included in the mailed reminders, or via prepaid mail included inside the FIT kits. The primary outcome of this study is the return of completed FIT kits. The secondary outcomes are the number of patients reached with phone calls, number of patients who understood the written FIT instructions, and number of patients who recall receiving the FIT mailed packages. We also conducted three sub-group analyses comparing the return of FIT between men and women, at or above median age and below median age, and non-Hispanic Whites, Hispanic English speakers, Hispanic Spanish speakers, and non-Hispanic non-Whites. The primary outcome and sub-group analyses were conducted using the Fisher's exact test. The secondary outcomes will be presented as descriptive statistics. All statistical analyses were done using SPSS version 25 (IBM Corp, Armonk NY).

# CHAPTER 4. RESULTS

## Chapter 4.1 Participant Characteristics

Of 491 eligible patients identified, 300 were randomly selected and randomized into the intervention and control groups. Four patients in the intervention group were lost to follow-up because their electronic health records had restricted access. Therefore, outcomes were analyzed for a total of 296 participants, 146 in the intervention group and 150 in the control group (see Figure 1).

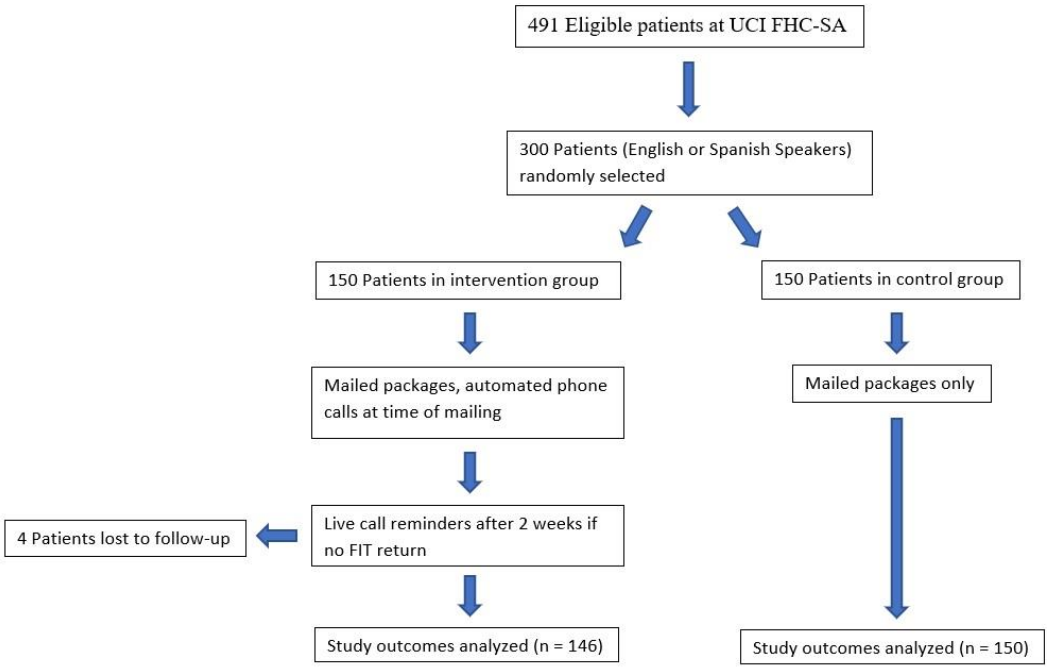


**Figure 1. Study Flowchart**

The demographic information of patients is shown in Table 1. The mean ages of the control mail only group and intervention group were 59.2 (SD 5.7) and 58.8 (SD: 6.8) with a p-value of 0.65. There were 62 (42.5%) male patients and 84 (57.5%) female patients in the control group, and 54 (36%) male patients and 96 (64%) female patients in the intervention group with a p-value

of 0.28. The most dominant ethnicity group in this study was Hispanics of any race. There were 95 (65.1%) Hispanics in the control group, and 101 (67.3%) in the intervention group. There was no significant difference in any demographic information between the two groups. Four patients in the mail only group had restricted electronic health record access, therefore, their demographic and study outcomes data were not abstracted or analyzed.

**Table 1. Patient Demographics**

| | Mail Only (n = 146) | Mail with Phone Call (n = 150) | p |
|---|---|---|---|
| Age, Mean (SD) | 59.2 (5.7) | 58.8 (6.8) | 0.65 |
| Gender, n (%) | | | 0.28 |
| Male | 62 (42.5%) | 54 (36%) | |
| Female | 84 (57.5%) | 96 (64%) | |
| Ethnicity, n (%) | | | 0.40 |
| Non-Hispanic White | 31 (21.2%) | 26 (17.3%) | |
| Hispanics | 95 (65.1%) | 101 (67.3%) | |
| African American | 6 (4.1%) | 9 (6.0%) | |
| Asian | 10 (6.8%) | 6 (4.0%) | |
| Pacific Islander | 1 (0.7%) | 1 (0.7%) | |
| Mixed Race | 3 (2.1%) | 3 (2.0%) | |
| Unknown | 0 (0%) | 4 (2.7%) | |

## Chapter 4.2 Study Outcomes

The primary outcome of the study is displayed in Table 2 and Figure 2. The control group returned 26 (17.3%) completed FIT kits, whereas the intervention group returned 49 (32.7%). The p-value from the Fisher's exact test was 0.001.

**Table 2. Comparison of FIT Completion Between Control and Intervention Group**

| | Mail Only (n = 146) | Mail with Phone Call (n = 150) | p |
|---|---|---|---|
| Returned FIT | 26 (17.8%) | 49 (32.7%) | 0.005 |

*P value was computed from Fisher's exact test. Patients who received mail packages with phone call reminders had a significantly higher proportion of returned FIT compared to patients who received only mail packages.

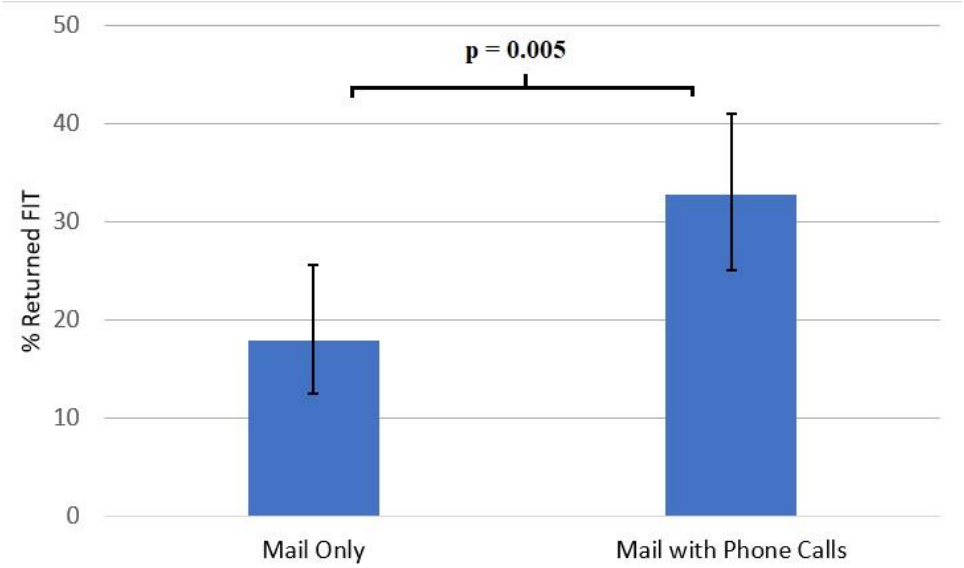


**Figure 2. FIT Return Rate Between Mail Only and Mail with Phone Calls.** Error bars represent the 95% confidence intervals. P value was computed from the Fisher's exact test. 17.8% (95% CI: 12 – 25%) of the mail only group returned FIT; 32.7% (95% CI: 25 – 41%) of mail with phone call group returned FIT. Patients who received mail packages with phone call reminders had a significantly higher proportion of returned FIT compared to patients who received only mail packages.

Table 3 and Figure 3 show the results of the live call follow-up. Within the intervention group (n =150), 16 (10.7%) patients returned their FIT kits prior to the start of live call follow-up; no live phone call attempts were made for these patients. The live calls, attempted three times on different days, were only able to reach 77 (51.3%) patients; out of these 77 patients, 20 (26%) returned their FIT kits after the calls. 57 (38%) patients of the intervention group could not be reached with live calls, but 13 (23%) patients returned their FIT kits. A pie chart showing the distribution of the live follow-up calls is shown in Figure 3.

**Table 3. Result of Number of Patients Reached with Live Reminder Phone Call**

| | Mail with Phone Call (n = 150) |
|---|---|
| Returned FIT Before Live Call, n (%) | 16 (10.7%) |
| Patients Reached with Live Call, n (%) | 77 (51.3%) |
| Returned FIT, n out of 77 (%) | 20 (26%) |
| Patients Not Reached with Live Call, n (%) | 57 (38%) |
| Returned FIT, n out of 57 (%) | 13 (23%) |

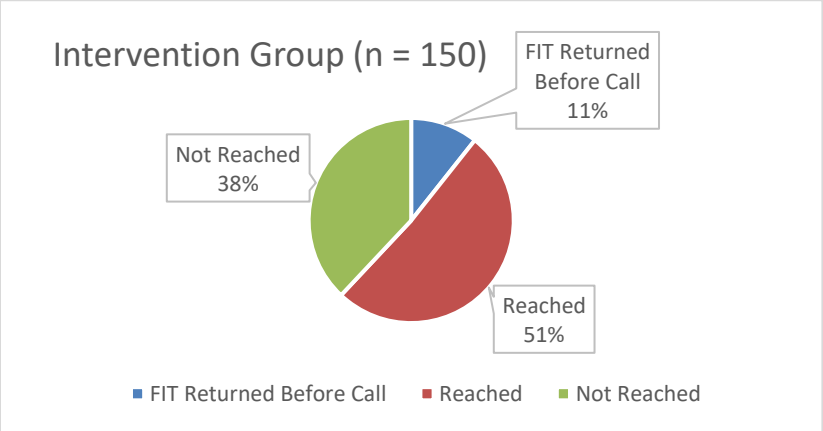


**Figure 3. Distribution of Live Follow-up Calls.** 11% of the patients in the intervention group returned

their FIT before the initiation of live phone call reminders. 51% of the intervention group were reached via live phone calls. 38% of the patients in the intervention could not be reached by the live phone call reminders.

Patients who were reached on the live calls were asked three questions, and their responses are shown in Table 4. When asked whether they received the initial automated phone calls from the clinic, 12 (15.6%) patients responded "yes", 42 (54.5%) patients responded "no", and 8 (10.4%) responded "unsure". When asked if they understood the written instructions inside the FIT kit, 44 (57.1%) responded "yes", 2 (2.6%) responded "no", and 3 (3.9%) responded "unsure". The unsure category for this question means the patient has not yet opened or checked their mailed FIT package. When asked if they received the mailed FIT packages, 50 (64.9%) patients said "yes", 8 (10.4%) said "no", 2 (2.6%) said "unsure". The "unsure" response for this question means the patient has not yet checked their mailbox.

**Table 4. Patient Responses to Questions Asked During Live Phone Call**

| | Patients Reached with Live Phone Call (n = 77) | | |
|---|---|---|---|
| | Yes | No | Unsure |
| Did you receive automated calls from clinic? | 12 (15.6%) | 42 (54.5%) | 8 (10.4%) |
| Did you understand FIT written instructions? | 44 (57.1%) | 2 (2.6%) | 3 (3.9%) |
| Did you receive FIT package in mail? | 50 (64.9%) | 8 (10.4%) | 2 (2.6%) |

*Patients were asked three questions when they answered the live phone calls. "Unsure" means patients were unsure of whether they received the automated calls, did not open FIT package yet to see instructions, and did not check mailbox yet at the time of the calls.

Table 5 shows the results of the comparison between male and female patients in their completion of FIT. In this study, there were 116 men and 180 women. Among the men, 26 of them (22.4%) completed their FIT, whereas 49 (27.2%) of the women completed their FIT. The difference between genders was not significant.

**Table 5. Comparison of FIT Return Between Men and Women**

| | Men (n = 116) | Women (n = 180) | p |
|---|---|---|---|
| Returned FIT | 26 (22.4%) | 49 (27.2%) | 0.41 |

*P value was computed from Fisher's exact test. There is no significant difference in the proportions of returned FIT between men and women.

The median age of all patients is 58 years old. There were 167 patients who were at or above median age; among them, 41 (24.6%) returned their FIT. There were 129 patients below the median age; among them, 34 (26.4%) returned their FIT. There was no statistically significant difference between these two subgroups in the return of FIT. The results are shown in Table 6.

**Table 6. Comparison of FIT Return Between Patients At or Above Median Age and Below Median Age (58 years old)**

| | At or Above Median Age (n = 167) | Below Median Age (n = 129) | p |
|---|---|---|---|
| Return of FIT | 41 (24.6%) | 34 (26.4%) | 0.79 |

*P value was computed from Fisher's exact test. There is no significant difference among the two age groups in the proportions of returned FIT.

We compared the number of FIT returned among non-Hispanic Whites, Hispanic English speakers, Hispanic Spanish speakers, and non-Hispanic non-Whites. The results of this

comparison are shown in Table 7. The non-Hispanic non-Whites group consists of Asians, African Americans, Pacific Islanders, mixed race, and unknowns. Non-Hispanic non-Whites had the highest proportion of returned FIT (37.2%), while the Hispanic English speakers exhibited lowest FIT return (12.5%). The p-value of this comparison was 0.008, which suggests a significant difference in FIT return among the sub-groups.

**Table 7. FIT Return between non-Hispanic Whites vs Hispanic English Speakers vs Hispanic Spanish Speakers vs non-Hispanic non-Whites**

| | NHW (n = 57) | HE (n = 48) | HS (n = 148) | NHNW (n =43) | p |
|---|---|---|---|---|---|
| Return of FIT | 9 (15.8%) | 6 (12.5%) | 44 (29.7%) | 16 (37.2%) | 0.008 |

*NHW = non-Hispanic White, HE = Hispanic English Speakers, HS = Hispanic Spanish Speakers, NHNW = non-Hispanic non-White. P value was computed from Fisher's exact test. There is no difference in the proportions of returned FIT among the ethnic groups.

*FIT test results*

Out of all the patients who completed and returned their FIT, three of the 75 tests (4%) yielded a positive result. All three patients were from the intervention group, and were referred to complete colonoscopies. As of the end of the study period, none have yet completed the colonoscopy.

## CHAPTER 5. DISCUSSION

Our study showed significant differences between the control and intervention group for the number of FIT kits returned. This indicates that phone call reminders along with mailed FIT kits, information on CRC, and a signed physician letter is significantly better than mailed contents alone at encouraging patients to complete and return FIT kits and improving CRC screening rate at a safety net hospital in a predominantly Hispanic community.

Our results are comparable to other studies conducted in primary care settings where the patient population were predominantly non-Hispanic whites. Randomized trials conducted by Coronado et al, Nielson et al, Fiscella et al, and Hendren et al showed the proportion of patients who completed CRC screening in the study arm with automated and live calls to be 28.9%, 39%, 28.8%, and 37.7% respectively.[8, 10, 36, 39] Our study result of 32.7% FIT return rate overall in the intervention group is similar to the results from these studies, and seem to suggest that there is no difference due to ethnicity in level of patient response to mailed and phone call CRC screening interventions. However, after excluding the number of patients in the intervention group who returned FIT before the live phone call reminders, the conversion of phone calls into completed FIT was 26% in patients who were reached with live phone calls. Assuming those who returned FIT without answering the live phone calls did so due to voicemails (33 out of 134), the conversion of live phone calls was approximately 25%. This conversion rate is lower than results seen in prior studies. This suggests that reminder phone calls might not be able encourage the majority of Hispanic patients to complete their CRC screening, and unawareness might not be the major contributing factor for the low screening rate in the Hispanic population. Prior studies have shown that attitude, motivation, and beliefs towards screening and medicine all contribute to patients' decisions. Our results suggest that phone calls were insufficient to address these factors. Future

research should focus on ways to effectively influence and affect patient attitudes, motivation, and beliefs towards screening tests and medicine.

In our study, only 38% of the patients in the intervention group was reached via live phone call, which suggests that improvement is needed for the phone call method of outreach. While the reason for the unsuccessful live phone call attempts is outside the scope of this study, we suspect the timing of the calls might be a contributing factor; patients might be busy during regular work hours and unable to answer the calls. Another potential reason could be that the patients were not aware of the phone number of the clinic, and thus were less likely to answer calls from an unknown phone number. More studies should be done to determine the most successful phone call schedule and method for reaching patients.

Based on responses from patients who answered the three questions during live phone calls, a significant number of patients stated that they did not receive automated phone calls. The reason for this was unclear. This study did not measure how many patients answered the automated calls, so there was no direct measurement of how many automated calls reached the patients.

Only one of four sub-group analyses completed showed a significant difference in FIT return. It seems non-Hispanic non-Whites were more likely to complete and return FIT than other groups, and that Hispanic Spanish speakers have a higher proportion of FIT return than Hispanic English speakers and non-Hispanic Whites. However, the distribution of patients was not even; the Hispanic speaker group had many more patients than the other groups, which could confound the comparison and makes the result nonconclusive. Further research should look into CRC screening behaviors between Hispanic English speakers and Hispanic Spanish speakers.

Based on the findings of this study, a few suggestions may improve the FIT return rate. In addition to reminder strategies, there is a need to improve the effectiveness of messages regarding

good healthcare practices so that patient attitudes and beliefs can be addressed. One way to achieve this is to involve key community leaders, so that they can speak on behalf of the clinic, spread the message, and better address the attitudes and beliefs of the community towards screening. Since a significant number of patients could not be reached on phone calls, the current phone call approach needs to be adjusted. The clinic should ask patients when checking in for appointments to obtain their preferred time of the day to be contacted by the clinic if needed. During check-ins, patient contact information should also be verified and updated if necessary. The phone number of the clinic should be made known to the patients so that they know when the clinic tries to contact them. Lastly, if there are enough resources, the clinic should conduct regular follow-ups to patients to foster trust in the clinic and good relationships, so that patients would be more likely to listen to the advice of the clinic.

There are a few limitations to this study. The first limitation is that the mailed packages were sent at different times to the control group and the intervention group; the intervention group received their package and was contacted prior to the start of COVID-19 in the US, whereas the control group received the packages during the first few months of COVID-19 and was affected by the quarantine. According to a systematic review done by Jager et al, the estimated fecal test return from mail outreach ranges from 26-59%,[32] which is higher than what we saw in this study; however, other studies have longer period of intervention and multiple mail attempts, whereas in this study, there was only one mail attempt. The difference in mail results could also be attributed to the effect of COVID-19. Future studies should be done to examine the effect of COVID-19 on screening behaviors, as well as attitudes and beliefs towards medicine and preventive measures. The second limitation is that there is incomplete data for the descriptive secondary outcomes in the intervention group, which prevented this study from generating a complete examination of how

well can phone call reminders be used to access patients. Lastly, there was no record on the time of the day when the phone calls were made, so we could not determine if there was a specific time of the day when patients were more responsive. However, what is lost in experimental design, we gained in realistic results, and provided some insight into the practicality of conducting a pragmatic trial in a primary care safety net clinic serving mostly Hispanic and underserved patients.

Our study was able to show that phone call reminders aimed to increase CRC screening is more effective than mailing alone in a safety net hospital serving a predominantly Hispanic patient population. Our results also suggested that many patients may not be accessible through automated or live phone calls. For those that were reached, the conversion of phone calls to completed FIT tests, while comparable to other studies, could still be improved. More research should be done to determine the most effective approach to contact patients, including the time of the calls, contents of the information given to address negative patient attitude and beliefs, and to increase the conversion rate.

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