The University of Texas Southwestern Medical Center at Dallas
Institutional Review Board

Title:
Evidence Based Colorectal Cancer Screening for the Uninsured

Introduction and Purpose:

Screening reduces colorectal cancer (CRC) incidence and mortality, but participation is low among the uninsured, resulting in poor CRC outcomes. Indeed, at John Peter Smith Health System (JPS), the safety-net health serving uninsured patients in Tarrant County and Fort Worth, TX, screening participation is just 39%, and 63% of CRC patients present with advanced stage cancer.

Through a prior CPRIT Evidence Based Prevention Program, we tested a systematic screening outreach strategy for increasing screening completion among uninsured patients, not up-to-date with screening. The intervention consisted of mailed screening invitations, with processes such as phone reminders to promote screening and follow up. Additionally, patients were randomly assigned to receive either mailed invitations to complete a home fecal immunochemical test (FIT) or a colonoscopy. We found: 1) 1 in 3 receiving mailed outreach completed screening, and 2) Screening completion was twice as high for patients offered the simple, at home FIT compared vs. colonoscopy**. Thus, we have shown our outreach invitation strategy, particularly when it includes FIT invitations, markedly increases screening completion among the uninsured.**

Several challenges remain. First, all unscreened patients must be reached. Previously, we invited 2,080 patients, but JPS has over 20,000 unscreened, uninsured patients. Second, UT Southwestern staff previously served as an intermediary between JPS patients and staff by delivering all outreach activities, a structure that is not sustainable. Now, program sustainability must be ensured by handing outreach delivery over to JPS. Third, while initial participation was highest when FIT was offered, we must determine if annual completion rates remain high, because annual testing is required for effective FIT screening. Fourth, further innovation is required. Offering modest financial incentives to complete screening, beyond offering free tests, may powerfully complement our current outreach approach. Financial incentives have been shown to improve rates of complex behaviors such as quitting smoking, but have not been evaluated for improving cancer screening rates.

Specific Aims: **We will conduct an Evidence Based CRC Prevention Program, among uninsured 50-64 year olds served by the JPS safety-net health system, not up-to-date with screening, with the following aims:**

Aim 1: Deliver mailed invitations to complete FIT screening to all eligible patients (over 20,000), with centralized processes to promote screening completion and evidence based follow up, including repeat annual FIT for patients with initial normal FIT.

Aim 2: For a randomly assigned subset of 2,000 patients, supplement the mailed outreach invitations with modest financial incentives to complete screening with either a $5 or $10 gift card.

Aim 3: Rigorously evaluate program outcomes. We will:

A) Determine screening rate improvement after expanding screening outreach to all unscreened patients.

B) Compare rates of initial and repeat screening completion among 1) Patients offered a modest financial incentive to complete screening, in addition to outreach invitations, vs. 2) Patients offered outreach invitations alone.

C) Among patients receiving financial incentives to complete screening, compare rates of initial and repeat screening completion between patients receiving $5 vs. $10 incentives.

D) Assess all CPRIT required outcomes, including increase in early stage cancer detection from baseline, as well as health system changes required to boost screening.

By completing these goals, we expect to reach over 20,000 patients with screening invitations, screen over 6,600 patients, and detect 400 patients with CRC or potentially precancerous polyps.

***Innovation*:** We will translate findings from our prior CPRIT program to usual practice by developing knowledge and infrastructure required at JPS for successful, sustainable screening outreach. Also, we will determine if offering modest financial incentives enhances mailed outreach, further advancing prevention knowledge.

***Significance and Impact*:** Locally, we will deliver potentially lifesaving screening invitations to over 20,000 patients, and create a robust, sustainable CRC screening program poised to markedly improve CRC outcomes for uninsured patients in Tarrant County, TX. Statewide and nationally, our program will advance cancer prevention knowledge, and serve as a proven, replicable model for improving CRC screening for the uninsured.

Background:

Colorectal cancer (CRC) is an important public health problem in the United States and Texas, particularly for the uninsured. CRC is the 2nd leading cause of cancer death in the United States and Texas[1, 2]. Nationwide, 150,000 individuals are diagnosed, and 50,000 individuals die of the disease annually[2]. Each year, CRC treatment results in over $14 billion in costs nationally, and over $3.7 billion in costs for Texas[2, 3]. Uninsured patients are at particularly high risk for poor CRC outcomes. Uninsured patients are more likely to present with advanced stage CRC, and have worse stage-specific survival than other groups[4]. At John Peter Smith Health System (JPS), the main safety net health system providing care to uninsured patients in Fort Worth and Tarrant County, Texas, 63% of patients with CRC have advanced stage at presentation. *Overall, it is clear that CRC is an important public health problem, particularly for the uninsured.*

CRC screening with fecal occult blood tests, sigmoidoscopy, or colonoscopy can save lives. Randomized controlled trials have shown that screening with fecal occult blood tests (FOBT) or sigmoidoscopy reduces CRC incidence and mortality[5-9]. Observational studies have demonstrated similar results for colonoscopy[10-12]. As a result, the US Preventive Services Task Force and the American Cancer Society have endorsed CRC screening for all individuals beginning at age 50 years[13, 14]. The US Preventive Services Task Force does not endorse one test over others because modeling studies suggest that regular screening with fecal occult blood testing, sigmoidoscopy, or colonoscopy results in similar outcomes[14-17]. Because FOBT, sigmoidoscopy, and colonoscopy all appear to reduce CRC mortality, and because it is uncertain whether any one test is better than others, many support the idea that "the best CRC screening test is the one that gets done[17]."

CRC screening participation is suboptimal, particularly for uninsured patients age 50-64 years and minorities. National Health Interview Survey data show that screening participation, defined as being up-to-date with stool occult blood, sigmoidoscopy, or colonoscopy testing, was 55% for all individuals aged 50 to 75 years in 2008[18]. Marked variation in screening was noted by race/ethnicity. Screening rates were 51% for Blacks and 39% for Hispanics, compared to 57% for

Table 1. Baseline screening rates among uninsured JPS connection patients age 50 to 64 seen ≥1 time in a primary care clinic in 2011

	n	Not Up-to-Date with Screening, n	Screening Rate
All patients	16,905	10319	39%
Race/ethnicity			
White	6,187	4081	34%
Black	3,968	2386	40%
Hispanic	4,774	2745	43%
Other	1,976	1107	44%

Whites. Most strikingly, uninsured 50 to 64 year olds had the lowest rate of screening participation, at just 20%, markedly lower than the 55% screening rate noted for insured patients age 50 to 64. Data from JPS has also shown low screening rates of among uninsured 50 to 64 year olds[19]. Currently, just 39% of uninsured 50 to 64 year olds seen regularly in a primary care clinic are up-to-date with screening (Table 1).

Our prior CPRIT-sponsored Evidence Based Prevention Program demonstrated that screening rates for the uninsured and minorities can be dramatically improved through screening outreach. *The goals of our prior program were to deliver CRC screening invitations to 2,080 patients, determine if an organized outreach invitation strategy to complete screening boosted screening compared to usual care, and determine if screening completion was higher when stool occult blood testing with fecal immunochemical test (FIT) versus colonoscopy screening were offered.* The program was set at JPS, a safety-net health system that serves a large, very diverse group of uninsured patients. We identified 5,994 uninsured patients, age 54 to 64 years, not up-to-date with CRC screening, and randomly assigned them to one of three screening strategies: usual care (n=3914 patients), organized invitation to FIT screening (n=1600 patients), and organized invitation to colonoscopy screening (n=480 patients). Organized outreach consisted of a mailed invitation to complete screening, information regarding the importance of screening, and, for the FIT group, a FIT kit. Patients assigned to the FIT and colonoscopy screening strategies also received processes to promote screening completion consisting of 2 automated and up to 2 "live" telephone reminders to complete screening, navigation to colonoscopy for screening or diagnostic purposes, and results reporting. Program processes were developed in close collaboration with clinical service providers at JPS such as the GI lab. The tracking database used to prompt and track outreach activities was developed and pretested at UT Southwestern.

The design of our screening outreach approach was heavily based on recommendations from the Task Force on Community Preventive Services as well as prior evidence. The Task Force previously recommended that cancer control programs use a multi-pronged approach to improve community demand for and access to cancer screening[20]. Recommendations included: 1) Use of client reminders, such as mailings advising patients that they are due for screening, 2) Use of small media, such as informational letters on importance of screening, 3) Reduction of structural barriers to screening, such as making screening more convenient, and eliminating complex administrative procedures and need for multiple clinic visits. Several lines of evidence support these recommendations. First, a systematic review of approaches to improving screening delivery demonstrated that using organized, system-level solutions to improving screening delivery were 17 times more likely to be successful than no intervention[21]. Second, prior published work has shown that mailed invitation to CRC screening, including informational material about screening and a guaiac FOBT kit can increase screening by 12 to 23%[22-24]. Third, it has been previously noted that phone reminders may increase screening participation by an additional 10-20%[25]. Fourth, reducing structural barriers to screening completion by simplifying processes for screening referral has been shown to improve screening CRC screening; most interventions in this area have consisted of mailed invitation to complete screening with a stool occult blood test[26-31]. Thus, the design of our prior outreach approach followed Task Force recommendations and was supported by multiple lines of evidence. Nonetheless, at the time we started our prior CPRIT prevention program, it was unclear whether this approach would be effective in a safety net setting among uninsured patients, and whether organized outreach would be most effective with invitation to complete FIT vs. colonoscopy screening.

Results show our outreach approach successfully boosted screening among the uninsured (Table 2):

Table 2. Outcomes of prior CPRIT sponsored Evidence Based Prevention Program among patients receiving outreach invitations after 12 months (n=2080)

Group	Invited, n	Completed Screening, n	Screening Completion Rate
All Outreach Patients	2080	601	29%
FIT	1600	532	33%
Colonoscopy	480	69	14%

- ***Strikingly, 29% of patients receiving organized outreach completed screening within one year.*** All these patients were not up-to-date with screening at baseline, despite being age-eligible for screening, and having access to care through JPS' medical assistance program for the uninsured. Results of comparisons of the intervention group to the usual care group not receiving organized outreach were subject of ongoing statistical analyses at time of this grant submission.
- **4 *patients with CRCs, and 60 patients with one or more adenomas have been identified*.** Therefore, our outreach approach has successfully identified patients with CRCs and potentially precancerous polyps.
- ***The rate of screening completion was <u>two times</u> higher for patients invited to FIT vs. colonoscopy screening.*** 33% of patients assigned to the FIT invitation completed screening, compared to 14% of patients assigned to the colonoscopy invitation, a 19% absolute difference in screening completion rates**.** These data demonstrate that screening rates are highly dependent on which screening test is offered. Because test participation in any test is likely to be more closely associated with positive CRC outcomes than which screening test type is completed, our preliminary data support future mailed outreach invitations with FIT, rather than colonoscopy (Table 2). Accordingly, in our expanded outreach program, we will invite patients to complete FIT screening, and use colonoscopy to follow up patients with abnormal tests. This approach has the added advantage of allowing us to offer organized outreach invitations to all eligible uninsured patients not up-to-date with screening (over 20,000), whereas with a colonoscopy based approach we could only offer screening to a small subset of patients due to budget and colonoscopy capacity constraints.

CHALLENGES REMAINING DESPITE PRIOR CPRIT PROGRAM SUCCESS

We must expand this organized outreach program to all uninsured individuals age 50 to 64 not up-to-date with screening at our safety-net health system. We have extracted health system encounter data for all patients age 50 to 64 seen $\geq$1 times in a primary care setting in 2011 who participate in JPS' medical assistance program for the uninsured. Out of 16,905 patients meeting these criteria, 6,586—39%—are up-to-date with screening, defined by having an FOBT in the last year, sigmoidoscopy within 5 years, or colonoscopy within 10 years (Table 1). Thus, as of 2011, 10,319 patients need screening. Screening rates are suboptimal among all major racial/ethnic groups (Table 1). Our prior CPRIT program delivered screening invitations to 2,080 patients, a much smaller group, and limited invitations to patients age 54 to 64. Now that our outreach program has been developed and shown to substantially boost screening, we need to expand outreach to all eligible individuals.

To enable sustainability of program activities, primary responsibility for screening outreach delivery must be transferred from UT Southwestern to JPS staff, and JPS must be equipped to run the outreach program. Previously, all screening outreach was delivered by UT Southwestern personnel. Specifically, a UT Southwestern Moncrief Cancer Institute nurse manager, and a UT Southwestern medical assistant created and mailed all invitations, made all reminder phone calls, delivered all testing results, arranged all follow up colonoscopy tests for patients requiring colonoscopy, and managed our screening tracking database. All UT Southwestern personnel were supervised on a day to day basis by a gastroenterologist and clinical researcher at UT Southwestern. Because the colonoscopy tests and all pre and post colonoscopy visits were conducted at JPS, this work required close interfaces with the JPS clinics and gastrointestinal endoscopy laboratory, as well as intermittent consultation with two JPS primary care physicians who were key physician champions of our program. This meant that UT Southwestern in effect served as an intermediary between JPS patients and JPS staff, and also worked through JPS physician champions to mediate any challenges

that came up during interfaces with JPS staff. Having an intermediary between JPS patients and JPS is not the ideal way to deliver screening because it sometimes lead to back and forth phone calls, at times leading to delays in care, and more importantly, because it is not sustainable. UT Southwestern cannot indefinitely commit to serving JPS patients. We propose implementing a much more streamlined and sustainable approach, in which JPS staff will deliver all organized outreach. This will equip JPS staff to conduct the outreach program, deliver screening more efficiently, and, most importantly, set JPS up to sustain the organized outreach program for its patients on an ongoing basis. As described in Section F, JPS has the experience, institutional commitment, and resources required to successfully take on primary responsibility for all screening outreach activities. The training program described in detail below will ensure an effective, sustainable transfer of program activities.

We must also determine if FIT participation rates remain high when screening is offered annually. Our prior CPRIT outreach program only offered one-time invitations to complete screening. Whether our approach can be successful in prompting repeat participation is unknown. Effective CRC screening with stool occult blood tests such as the FIT requires annual testing[14, 15]. Prior trials of stool occult blood testing only showed substantial reductions in CRC incidence and mortality after several years of testing, likely because there are a substantial number of patients who may initially have normal tests, but have an abnormal test on repeat testing due to either a new cancer or a cancer that was missed by the initial stool occult blood test screen[32].

Though repeat testing is important, there are limited "real world" data outside of clinical trials on rates of repeat stool occult blood test participation. A study of a program offering mailed outreach invitations to complete stool occult blood test among rural Australians reported 75% of patients initially completing a test completed a repeat test the following year[33]. An integrated health insurance program in Washington State serving over 350,000 beneficiaries reported contrasting results[34]. Just 44% of patients who completed an initial stool occult blood test subsequently completed repeat testing within 2 years. The report from Australia may conflict with the Washington State health plan for several reasons. First, the Australian study reported results from an organized outreach program, in which screening was not contingent on a clinic visit, whereas the results from the Washington insurance program were based on usual care stool occult blood test use, in which patients were offered testing at intermittent primary care visits (e.g. "opportunistic screening"). Second, a large number of patients in the Australian report were offered screening with FIT, rather than the guaiac stool occult blood tests studied in the Washington state report. FITs require fewer samples, and do not require diet restrictions. Prior data clearly demonstrate that initial participation rates in CRC screening are much higher with offers to complete FITs, rather than guaiac based stool occult blood tests[36, 37]. Thus, it is plausible that differences between the Australian and Washington reports may be due to type of stool occult blood test offered. Fundamental differences in the patient populations may also be relevant, though are difficult to assess. Overall, it is clear that there is a paucity of data on whether repeat rates of participation in stool occult blood testing are adequate for longitudinally effective screening. Available data suggest that repeat participation may be variable, and perhaps influenced by whether or not repeat testing is offered with the more convenient FIT vs. guaiac-based stool occult blood test. We anticipate that our program, which uses the more convenient FIT and organized outreach to encourage repeat testing, may be associated with high rates of repeat completion, but this requires formal evaluation. Further, if rates of repeat participation are suboptimal, new interventions will need to be developed to supplement our current efforts.

New, innovative, strategies to further improve screening participation are required. Our program resulted in screening completion for 29% of patients not up-to-date with screening at baseline. Thus, despite the clear benefit of our outreach strategy, this approach alone will be inadequate for achieving optimal rates of screening. Effectiveness of our outreach program may (and should) be improved with added interventions. The Task Force on Community Preventive Services review of interventions to increase breast, cervical, and colorectal cancer screening recommended use of client reminders (e.g. letters alerting patients of need for screening), small media (e.g. letters

discussing importance of screening), and reducing structural barriers to screening (e.g. making screening more convenient)[20]. As discussed previously, our screening outreach program already includes all of these intervention approaches. Thus, further innovation is needed to determine if other interventions can serve as adjuncts to approaches currently recommended by the Task Force.

Adding financial incentives to complete screening to mailed outreach invitations is a promising strategy for boosting CRC participation. Client financial incentives for screening are "small, noncoercieve rewards (e.g. cash or coupons) to motivate people to seek cancer screening for themselves…"[20]. In its most recent evidence review, the Task Force on Community Preventive Services found insufficient evidence to determine effectiveness of financial incentives for increasing cancer screening[20, 38]. Nonetheless, prior data on use of financial incentives for behaviors much more challenging to prompt than completing a one-time FIT at home have demonstrated that financial incentives can powerfully boost healthy behaviors[39-41].

A randomized trial of offering cash financial incentives for completing a smoking cessation program and maintaining abstinence from smoking showed an absolute 10% increase in rates of program completion and smoking abstinence[39]. In this study, employees of a multinational company were offered quitting information alone, or information plus incentives, including $100 for completing smoking cessation education, $250 for abstinence at 6 months, and $400 for abstinence at 12 months from enrollment.

More complex financial incentives have been shown to be effective in inducing short term weight loss[40]. A study of 57 obese U.S. Veterans randomly assigned to receive standard weight loss counseling, vs. counseling plus addition of one of two financial incentives, found that financial incentives were associated with a 40% absolute increase in meeting a goal of 16 pound weight loss at 16 weeks. The financial incentives consisted of either entry into a lottery for cash, or a deposit contract, in which participants were offered the opportunity to deposit cash on a daily basis with the chance to earn 1:1 matching return on the investment if they met a pre-specified weight loss goal.

Financial incentives have also been shown to be effective for improving substance abuse disorders. A meta-analysis of 40 studies using financial rewards for promoting abstinence, clinic attendance, and/or medication compliance found that financial incentives often increase healthy behaviors substantially[41]. *Taken together, prior work suggests that financial incentives may boost participation in healthy behaviors.*

Financial incentives may be particularly effective for boosting participation in our FIT outreach program. Completing a FIT test once a year is much easier than quitting smoking, losing weight, or stopping substance abuse. Patients receiving our outreach approach are delivered information on CRC screening tailored to their age-specific risk for CRC, and have the FIT kit in their possession. All that is required for screening completion is obtaining one non-diet restricted stool sample with a simple collection device, and placing the collection vial in a postage paid return envelope. Therefore, it seems very possible that offering a financial incentive to complete a FIT may successfully motivate patients with positive attitudes toward screening.

Overall, because our outreach program already includes all outreach intervention components recommended by the Task Force on Community Preventive Services, and because financial incentives show promise for changing health behaviors that are far more complex than completing FIT screening, we need to determine whether financial incentives boost CRC screening over and above our organized outreach program. *Our proposed prevention program will determine whether offering financial incentives, in the form of either a $5 or $10 gift card in exchange for screening completion, are an effective adjunct to our organized outreach approach.*

BACKGROUND SUMMARY. CRC is an important public health problem, particularly for the uninsured, who have the lowest screening rates and worst CRC outcomes. Our prior, CPRIT sponsored Evidence based Prevention program focused on the uninsured was successful in boosting

screening participation by 29%. Organized outreach was twice as effective when patients were offered FIT vs. colonoscopy screening (33% vs 14%). Our program was highly evidence based and successful, but several challenges remain. We must expand our organized outreach to all individuals eligible for screening. Program sustainability must be ensured by transferring primary responsibility for screening promotion delivery to JPS. We must determine if participation rates remain high when screening is offered annually because effective, evidence based FIT screening requires annual test completion. Finally, innovation is required. Offering modest financial incentives to complete screening, beyond offering free tests, may be a particularly effective adjunct to our current outreach approach. The specific aims and outreach approach outlined below have been carefully crafted to leverage the screening needs of the uninsured, our prior experience with a successful outreach program, and innovative ideas for screening to improve CRC screening to deliver screening and advance evidence based screening practice.

Concise Summary of Project:

Screening for colorectal cancer (CRC) can lower rates CRC death and even prevent some cancers from developing. However, screening rates are low, especially for uninsured patients. As a result, uninsured patients are more likely to develop CRC and die. For example, at John Peter Smith Health system (JPS), the main health system serving uninsured patients in Tarrant County and Fort Worth, Texas, just 39% of uninsured patients served have had screening, and the majority of patients who develop CRC have advanced cancer at time of diagnosis.

UT Southwestern and JPS previously received a grant from CPRIT to develop and test a CRC outreach program for uninsured patients at JPS. The program sent mailed invitations to complete screening to over 2,000 uninsured patients who needed screening. To figure out which screening test was most likely to be completed, some patients received a simple, at home kit that checks the stool for blood called a fecal immunochemical test (FIT), while others were invited to schedule and complete a colonoscopy. All patients received phone calls to encourage screening completion, answer questions, and help with scheduling tests and follow up.

The prior program was a big success. At the end of 12 months, 1 in 3 patients who were not up-to-date with screening at the beginning of the program got screened. Screening was two times higher when patients were offered the simple at home FIT compared to when offered a colonoscopy. We found 4 patients with CRC, and another 60 patients with potentially precancerous polyps.

Since the program was such a success, we would like to now expand the outreach program to benefit all 20,000 uninsured patients at JPS. Also, we need to equip JPS to run the program on its own, so that JPS can deliver the program to its patients on an ongoing basis. Because screening with FIT needs to be done every year, we need to also expand the program to deliver the outreach invitations yearly. Finally, we know that the program can be improved even more. Offering patients a small financial reward may help nudge them to complete healthy behaviors. Therefore, we also plan to see if adding a small $5 or $10 reward for screening to our outreach program results in more patients completing initial and repeat screening.

As a result of the new program, we will create a sustainable CRC screening outreach program for uninsured patients in Tarrant County and Fort Worth, Texas. The program will serve as a model for other health systems which care for uninsured patients across Texas and beyond. Also, we may discover new ways to convince more patients to be screened that can be used locally and nationally. Most importantly, we will offer potentially lifesaving CRC screening to over 20,000 patients, expect over 6,600 patients will get screened, and predict we will find 38 patients with CRC and 364 patients with potentially precancerous polyps.

Study Procedures:

Overview: Our program is set at John Peter Smith Health System (JPS), a safety-net health system serving Tarrant County, TX. Our prevention program will systematically identify uninsured, 50 to 64 year old patients, not up-to-date with screening, and deliver over 20,000 organized invitations to complete screening with a FIT. Organized outreach will consist of a mailed invitation to complete screening, information regarding importance of CRC screening, and a FIT kit. Screening participation will be promoted with automated phone reminders before and after invitation delivery, as well "live" phone reminders. Guideline appropriate follow up will be delivered, including facilitation of colonoscopy for patients with abnormal FITs, and annual repeat FIT invitation for patients with normal FITs. To understand impact of offering financial incentives on screening completion, for a subset of randomly assigned patients, screening promotion will be supplemented with an additional modest $5 or $10 gift card incentive for completing screening.

Program Setting. JPS is the primary safety net provider for uninsured patients in Fort Worth and Tarrant County, TX. The system consists of 12 community and hospital based primary care clinics, a free standing outpatient surgical and endoscopy center, as well as a tertiary care hospital that provides surgical, oncologic, and endoscopic services. Annually, over 457,000 encounters are delivered. JPS offers a taxpayer subsidized medical assistance program for the uninsured (JPS Connection) that facilitates access to primary and specialty care, including surgery and cancer care, with low copays. ***Thus, for uninsured patients, participation in JPS Connection ensures access to specialty care if a cancer is diagnosed through screening.*** JPS has a longstanding history of working with UT Southwestern Medical Center to improve health outcomes for JPS patients, including successful work on the prior CPRIT sponsored CRC evidence based prevention program outlined previously.

JPS Screening Outreach Team. The screening outreach team will be responsible for sending out all invitation letters, tracking results, and facilitating follow up for patients with normal and abnormal FIT tests. The team will consist of a nurse manager, as well as two medical office assistants who are JPS health system employees; at least one will be bilingual. This structure closely resembles the team for our prior CPRIT program, which was composed of a nurse manager and a single medical office assistant. The team will be directly supervised by Dr. Elizabeth Carter and Dr. Mark Koch. Both Drs. Koch and Carter were close collaborators for our prior CPRIT prevention program, and have extensive experience with our program procedures. Dr. Carter's primary responsibilities will include leading all administrative aspects of the program. Dr. Koch will manage day to day operations of the screening outreach team by helping the team set daily, weekly, and monthly goals. Further, he will take a leadership role in coordinating screening activities across JPS primary care clinics and the JPS GI lab.

Training in CRC screening knowledge. At the outset of the program, we will conduct a two day, small group seminar focused on developing CRC screening knowledge for the 5 outreach team members. Topics covered will include: 1) Public health importance of CRC, 2) Basics of why and how CRC develops, 3) Evidence to support CRC screening, 4) Screening guidelines, including guidelines and rationale for appropriate follow up, and 5) Evidence based approaches to boosting screening. Presentations will emphasize the importance of these topics for the uninsured. The presentations will be based on available scientific literature, including CRC screening guidelines, results of national surveys such as the National Health Interview Survey, and Surveillance Epidemiology and End Results and Texas state cancer registry data.

Training in outreach program processes. Training in outreach program processes will be based on our previously developed screening outreach program manual, through a separate two day seminar. The following topics will be addressed:

- **Process for identifying the screen eligible population.** We will teach the screening outreach team how to obtain the JPS administrative data required to identifying patients meeting program inclusion/exclusion criteria. This will involve working with data managers at JPS who previously

generated such data for our prior published screening analyses of screening rates at JPS[19, 42], and our baseline screening data (Table 1). In order to reach our goal of sending FIT screening invitations to the approximate 20,000 patients who meet program eligibility criteria, a maximum of 40,000 individual patient records will be reviewed by study personnel to obtain the study dataset.

- **Process for importing patient contact data for screen eligible individuals to the tracking database**. The tracking database has a straightforward data import function that allows for importing patient contact data required for program procedures. This function was used to import patient data to the tracking database for our prior CPRIT program patients, and thus has been previously developed, tested, and implemented.
- **Screening outreach**. We will train the outreach team how deliver all of the screening outreach processes described in detail below, including mailed invitations and phone reminders.
- **Screening follow up**. We will train the outreach team how to conduct all of the guideline appropriate follow up described in detail below, including follow up of patients with abnormal FITs.
- **Screening tracking database**. Will train the outreach team how to take full advantage of the tracking database, which can generate lists of patients requiring follow up (e.g. patients due for phone reminders to complete screening), document patient interactions (e.g. delivery of phone reminders or documentation of triage for colonoscopy for patients with abnormal tests), and document screening outcomes (e.g. FIT test completion, FIT results, and colonoscopy results for patients with abnormal tests).
- **Program management**. We will work with the team to learn how to set daily, weekly, and monthly goals for the screening program. For example, each cohort of patients invited to complete screening through a given year has a timeline of events that must occur over a two month period that includes invitation delivery, phone reminder delivery within 2 to 3 weeks post invitation, and follow up of abnormal tests (described in detail below). Dr. Carter has extensive experience with management of other disease management programs, and in developing and implementing quality improvement initiatives at JPS. Through his work as a family physician and endoscopist, Dr. Koch has extensive experience in leading medical care teams. Thus, the physician champions of the program at JPS have the expertise and experience necessary to take on primary program management responsibilities.

Approach to Screening Invitation and Promotion

All patients meeting inclusion/exclusion criteria will receive mailed invitation to complete screening, with processes to promote screening completion. The list of eligible patients will be divided into multiple groups so that the expected group of 20,000 patients will receive invitations spread out in time, so as to avoid overwhelming the system. All screening processes were included in our prior CPRIT sponsored outreach program, and therefore are already developed and ready for use. The specific components of outreach include:

- **Screening invitation letters.** These letters were previously developed in English and Spanish and pretested as part of our prior CPRIT sponsored CRC outreach program. The letters emphasize importance of CRC screening, encourage the patient to complete FIT screening with the enclosed FIT kit, and will be signed by Drs. Koch and Carter as representatives of JPS primary care physicians. For patients receiving repeat invitations, new English and Spanish letters will be developed to emphasize importance of repeat screening for preventing adverse CRC outcomes.
- **FIT kit.** The invitation kit will include a 1-sample Polymedco OC Sensor FIT, including simplified instructions on how to perform the test, as well as a return mailer with prepaid postage. Diet/medication restriction will not be required. Kits will be returned to JPS and processed per manufacturer recommendations. A sensitivity threshold for hemoglobin of 50 mg/mL will be set to maximize sensitivity for CRC[44]. This FIT has been shown to have sensitivity for CRC of over 85%, and specificity of over 90%[44]. Preliminary data from our prior CPRIT outreach program show that 12% of patients will have an abnormal FIT, and $\geq$60% of those completing colonoscopy after abnormal FIT will have an adenomatous polyp or cancer detected.
- **Automated and "live" phone call reminders to encourage screening completion.** Automated messages will be sent at time of invite and within week 1 of the invitation. Up to two "live" phone

call reminders will be attempted 2 to 3 weeks post invitation, with our English and Spanish standard scripts.

Centralized processes to promote guideline-based follow up. *Follow up for patients with a normal test in Year 1 will consist of repeat screening invitations in Year 2 and Year 3.* This is consistent with guideline recommended annual FIT for CRC screening[13, 14]. *Follow up for patients with an abnormal FIT will consist of navigation to complete a colonoscopy*. Up to 10% of individuals with an abnormal FIT have a colon cancer, and up to 50% may have a potentially precancerous polyp[44, 45]. Thus, colonoscopy follow up is imperative. Patients with abnormal FIT will be called by the screening team within 1 week to report the result and facilitate direct scheduling of colonoscopy or a pre-colonoscopy visit. During their pre-colonoscopy visit patients will receive a Gatorade Bowel Prep kit with instructions on how to prepare for their colonoscopy. If colonoscopy scheduling is delayed, there is a possibility that the Dulcolax tablets in prep kits may expire. Expiration dates will be monitored by the study team. In the event tablets will reach expiration before a scheduled colonoscopy, the patient will be mailed a letter with replacement tablets. The goal will be to schedule colonoscopies within 12 weeks of the abnormal FIT. In our prior outreach program, all patients willing to have their colonoscopies done within 12 weeks were accommodated, most within a much shorter period of time. Patients who do not keep their scheduled pre-colonoscopy or post-colonoscopy appointment will be contacted by phone to reschedule their missed visit. Patients who the study team are unable to contact by phone will be mailed a "No-Show" letter asking them to call the JPS clinic to reschedule their appointment. Similarly, patients who do not keep their scheduled colonoscopy will be contacted by phone to reschedule their colonoscopy. Those patients that the team is unable to contact by phone will be mailed a "No-Show" letter asking them to contact the JPS clinic to reschedule their colonoscopy. After multiple attempts to reach No-Show patients by phone and certified letter, a final letter will be mailed to them. The letter informs patients that this is the final attempt to remind them that they had an abnormal FIT and to contact the JPS staff to schedule an appointment for further evaluation, possibly with colonoscopy. All three letters will be on JPS letterhead signed by Dr Koch and include a contact phone number for the study team.

Follow up of patients with a CRC will consist of navigation to first treatment consultation visit. We will arrange for a surgery or oncology clinic follow up for all patients with a CRC diagnosis if such follow up is not already scheduled by the colonoscopist who diagnosed the CRC. These calls will be made daily for up to one week. The goal will be to have a first treatment consultation visit within 2 weeks of CRC diagnosis. Patients will be reminded of these visits 5 days and 1 day prior to the scheduled appointment. *All results/recommendations will also be sent to the patient via mail, and to the patient's primary provider within 1 week of the result.*

Financial incentives.

A group of 2,000 individuals will be randomly assigned to receive a modest financial incentive to complete screening, in addition to the organized outreach program. The incentive will be sent in exchange for screening completion. Incentives will be sent to a subset of patients, rather than all patients included in the screening outreach program for two main reasons. First, it is unknown whether offering financial incentives results in meaningful increases in screening participation. By selecting a subset, rather than all patients to receive financial incentives, we will be able to determine if offering financial incentives, in addition to the current program, is more effective for promoting screening than outreach invitations alone. Evaluating impact of incentives as an adjunct to organized screening outreach for promoting CRC screening will address the lack of evidence on impact of incentives highlighted by the Task Force on Community Preventive Services[20]. Second, budget constraints preclude offering incentives to all patients. To randomly assign the 2,000 individuals who will receive the financial incentive, we will use SAS procedures. The rationale for choosing 2,000 individuals to receive incentives is discussed in below. To determine whether offering a $10 vs. $5 incentive results in substantially

higher screening completion, 1,000 patients will receive an incentive for $5, and 1,000 patients will receive the $10 incentive offer.

The incentive will consist of either a $5 or $10 gift card to a local retailer that will be sent to the patient upon return of an FIT kit. Incentives will be mailed by the JPS outreach team, in exchange for successful FIT completion, after the FIT has been returned. $5 and $10 incentives were chosen for several reasons. First, these levels of incentives, if shown effective, could be potentially sustained by the JPS system beyond the timeframe of the grant. Higher incentives, while potentially more powerful in inducing participation, would be unsustainable and therefore do not merit study at this time. Comparing $5 and $10 incentives is important because if offering incentives is effective in boosting screening, it is important to know the minimum incentive required for meaningful changes in participation. Incentives are to be offered to all patients who are assigned to the incentive strategy. We considered, but rejected, restricting incentives to only patients who initially do not respond to screening invitations. This was because restricting incentives to non-responders would logistically complicate outreach activities. It is important to note that patients meeting study inclusion criteria must have a minimum of 1 visit to a JPS Primary Care clinic within the last year. Considering these patients have an established baseline relationship with the JPS primary care system, the addition of a modest financial incentive should not create undue influence in patients that otherwise would still have exposure to information on the benefit of screening. Since participation in this standard of care screening poses minimal to no risk, the chances that incentives may motivate research participants to take unnecessary risks are low.

Screening Completion Follow Up. Follow up for determining screening completion for all included patients will be through the end of Year 3 regardless of whether or not patients respond to screening invitations. As is explained below, screening rates will be measured for all patients included for outreach invitations. For patients who die on follow up or who do not have additional health system encounters, follow up will be censored at time of death or last health encounter, respectively.

Data Sources and Data Tracking. *Our approaches to data acquisition, as well as data tracking have been previously developed and previously used to evaluate CRC screening rates and deliver screening.* The primary data source used to identify patients eligible for our outreach program will be JPS administrative claims database and Epic electronic medical record. At baseline, these data will be queried to identify all 50 to 64 year old patients potentially eligible for program inclusion. Demographic data, such as sex and race/ethnicity, as well as visit data, such as dates of any health system visits and any associated CPT codes with health system visits will be extracted and analyzed to determine which patients are eligible and up-to-date with screening. Data required for inviting patients to screening and tracking follow up, such as names and addresses, will be imported into a tracking database that has been previously developed and tested for this purpose. The tracking database facilitates all day to day program activities and associated data collection. For example, daily, a report is generated of patients who have been mailed FIT, and are due for follow up phone reminders to complete the FIT and return it. The database also allows for updating patient results, such as results of FIT and colonoscopy tests.

Sub-Study Procedures:
A sub-study will be conducted with the goal of identifying strategies that may further increase rates of 1) initial participation in colorectal cancer screening, and 2) follow up of abnormal colorectal cancer screening tests with colonoscopy. This sub-study involves 2 parts:

Part 1) Participants scheduled to receive mailed fecal immunochemical test (FIT) outreach for the first time late in the 2nd year of the study (currently ongoing) will be randomly assigned to receive one of three invitation letters, which vary slightly from one another. These letters represent small, but potentially impactful modifications to our original invitation letters.

All participants randomized to the original $5 and $10 incentive groups were enrolled during Year 1 of the study. After the incentive groups reached full enrollment, all new participants received the

standard (non-incentive) invitation only. For the sub-study, the standard invitation letter will be replaced with one of the 3 modified letters. All new participants will be randomized to receive one of the 3 letters during 2 predetermined rounds of invitations (involving n=2,124 individuals).

Rationale and plan for sub-study part 1: Over nearly 2 years of our prevention program, we have tested a systematic screening outreach strategy for increasing screening completion among uninsured patients, not up to date with screening. Through these carefully evaluated interventions, we have shown that our outreach invitation strategy, particularly when it includes FIT invitations, markedly increases screening completion among the uninsured. Indeed 36% of individuals invited to complete FIT return the test. While this rate of participation is substantial, it may be improved by making changes to our invitation letters. In 2 predetermined rounds of invitations (involving n=2,124 individuals), we will slightly modify the invitation letters to test our hypothesis that providing information in the letter about the value of the kit and attenuating concern about future cost will further increase FIT and follow-up response rates.

There will be 3 conditions for the invitation letter and individuals will be randomly assigned 1:1:1 to each condition. The 3 conditions contain just slight differences in the information provided in the letter, as follows: (i) a control invitation letter (similar to letters in previous studies with some slight wording and grammatical improvements, (ii) the control letter plus the addition of one line informing recipients of the average value of the procedure (~$200), and (iii) a letter with the average value and a sentence assuring patients that should a follow-up test be requested, it will be provided free of charge.

The addition of this pragmatic trial to the ongoing prevention program provides no additional risk to individuals and will allow us to assess a hypothesis that will contribute to our success in increasing screening completion rates among this population. From a statistical standpoint, assuming a control invitation letter response rate of 36% with the planned sample size of n=708 per group, we will have over 80% power to detect absolute increases of $\geq$8% between the control invitation and the first alternate letter, as well as between the control invitation and the second alternate letter, assuming two-sided alpha=0.125 for each comparison.

Part 2): In part 2 of the sub-study, participants will receive their FIT responses in either a white envelope (normal results, no immediate follow-up necessary) or a red envelope (positive result, need to follow-up with doctor). The only change to this portion of the study is the color of the envelope patients receive.

Rationale and plan for part 2: With our current program, the rate of follow up to diagnostic colonoscopy after an abnormal FIT is 58%. Since indivdiuals with abnormal FIT have an increased chance of having colorectal cancer, identifying alternate strategies to improve compliance with diagnostic colonoscopy is desirable. Accordingly, we propose to employ a simple alerting tactic through the color of the envelope (red for abnormal and white for normal). We hypothesize that more people will follow-up after receiving a positive FIT result as a result of the messaging importance of abnormal tests with a red envelope. Because these changes will be employed in 2 predetermined rounds of invitations, we will have the opportunity to conduct an pre-post analysis of the follow-up rates to test our hypothesis that this alerting tactic will increase follow-up rates. From a statistical standpoint, pre-intervention, we assume there are at least 329 individuals with abnormal FIT, and that 58% (n=191) complete diagnostic colonoscopy. Post modification, we expect a minimum 107 patients with abnormal FIT. With these sample sizes, assuming two-sided alpha=0.05, we will have 80% power to detect a difference post intervention of $\geq$14.9%.

Change in risks to participants
The sub-study does not substantially change risks to study participants. Accordingly, no change to our process for recruitment or waiver of informed consent for invitation is proposed.

Criteria for Inclusion of Subjects:

Uninsured patients not up-to-date with CRC screening meeting the following criteria will be included:

- **Age 50-64.** This age group is at highest risk for screening non completion. Patients younger than age 50 will be excluded because screening is not routinely recommended for patients under 50. Patients older than 64 will be excluded because most of these patients would have screening access through Medicare insurance.
- **Uninsured, but participants in JPS's medical assistance program for the uninsured.** Uninsured patients have the lowest rates of screening participation, and therefore are most likely to benefit from screening outreach. ***Selecting patients who are uninsured, but enrolled in JPS's medical assistance program for the uninsured will ensure that any patient found to have a cancer or unresectable polyp will have access to surgical and/or medical oncology services.*** This is critical, because CPRIT funds do not allow for cancer care; offering screening without a system to care for patients with cancer would be unethical.
- **One or more visits to a JPS primary care clinic within a year.** This criterion establishes that patients have a baseline relationship with the JPS primary care system.
- **Not up-to-date with colorectal cancer screening**. We will apply National Committee on Quality Assurance Healthcare Effectiveness Data and Information Set (HEDIS) criteria to determine if patients are up-to-date with screening, defined by having had a colonoscopy within 10 years, a fecal occult blood test within one year, or a sigmoidoscopy within 5 years[43]. HEDIS criteria allow for using administrative claims data, including Current Procedural Terminology (CPT), International Classification of Diseases-9 (ICD9), and Health Care Common Procedure Coding System (HCPCS) codes to determine whether patients have had CRC screening tests. Logical Observation Identifiers Names and Codes (LOINC) will not be used because these are not routinely used within the JPS system.

Table 3: HEDIS codes used to measure CRC Screening

Description	CPT	HCPCS	ICD-9-CM Procedure
FOBT/FIT	82270, 82274	G0328, G0394	
Sigmoidoscopy	45330-45335,45337-45342,45345	G0104	45.24
Colonoscopy	44388-44394,44397, 45355, 45378-45387, 45391, 45392	G0105, G0121	45.22, 45.23, 45.25, 45.42, 45.43

- HEDIS criteria were selected because these are standardized criteria that the National Committee on Quality Assurance uses to compare rates of CRC screening across different insurance carriers. The criteria are clear, and widely available, and using these criteria will improve generalizability of our program procedures. In prior published analyses, we previously demonstrated ability to determine screening rates and identify patients not up to data using a similar approach, and validated the approach for this purpose[19, 42]. Table 3 shows codes that will be used to assess whether patients are screening up-to-date.

Criteria for Exclusion of Subjects:

Patients with a history of CRC or colon resection, no address and/or phone number on file, or who are incarcerated will be excluded. Patients with history of CRC/colon resection will be excluded because they require specialized screening, usually with colonoscopy. Addresses and phone numbers are required to deliver outreach. Incarcerated patients will be excluded because they cannot keep FIT kits in their cells.

Once included, patients will remain in the program unless they no longer meet age criteria. Patients in both the standard (non-incentive) and incentive invitation groups who do not respond to initial invitation will be followed for screening outcomes, but will not receive repeat

invitations. Through the program period, we expect that some patients will no longer participate in the JPS connection program, or not see a primary care provider within a year. We considered excluding these patients in subsequent years, but decided against this. Many of these patients remain uninsured, and if they were to develop late stage CRC, would present to JPS for treatment. We anticipate that most of these patients would then again access the JPS medical assistance program for the uninsured as well as primary care clinics, because JPS is the main safety-net health system for uninsured patients in Tarrant County and Fort Worth, TX. Continuing screening outreach will potentially allow for boosting detection of such patients when their CRCs are early, rather than late stage.

Additional patients will be assessed for inclusion/exclusion criteria annually in Years 2 and 3 of the program. Each year, patients who newly meet our inclusion/exclusion criteria will be included in the program. For example, patients newly turning 50 in year 2 or 3 meeting all other inclusion/exclusion criteria will receive screening outreach. Similarly, a 60 year old patient new to the JPS system and meeting inclusion/exclusion criteria will also receive screening outreach. We think this approach reflects the ideal implementation of a standing CRC outreach program.

Sources of Research Material:

There are several sources of research material for this project:

- **Administrative and electronic medical record databases at JPS**. These data systems will be used to identify patients meeting inclusion/exclusion criteria, and to record outcomes of screening invitation.
- **Results of fecal immunochemical tests (FIT).** Patients will be invited to complete screening with a one-sample FIT. These kits will be processed by the JPS clinical lab, and the results will be recorded in the electronic medical record. Results of testing, including whether the test was abnormal or normal, and the level of hemoglobin present in the sample, will be collected
- **JPS cancer registry**. This resource will be accessed to identify patients enrolled in the screening program who develop CRC during the follow up time frame.
- **Study tracking database**. This database will record in real-time delivery of all screening interventions, and outcomes of the interventions. In addition, process variables, such as time spent on phone with patients, failed mailings due to wrong address will be collected. The study tracking database has been created for exclusive use by screening program personnel.
- **Interviews of JPS personnel who will be conducting outreach interventions.** The purpose of these interviews will be to understand the challenges to implementation of the outreach program within the health system.

A complete list of variables to be abstracted, including justification for variables, is in the table below.

Variable	Justification	Source
Baseline characteristics and eligibility criteria		
first name, last name	Required for delivery of screening invitations	JPS administrative and electronic medical record databases
date of birth	Required for eligibility criteria	
Sex	Screening rates can differ by sex	
Race/ethnicity	Screening rates may differ by race/ethnicity	
Primary language	Use to identify preferred language for study interventions	
Home address	Required for screening invitations	

Telephone numbers	Required for screening invitations	
Prior history of CRC	Required for eligibility criteria	
Prior history of CRC resection	Required for eligibility criteria	
Past exposure to CRC screening tests, including colonoscopy, sigmoidoscopy, fecal occult blood tests, and barium enema	Required for eligibility criteria	
Insurance type	Required for eligibility criteria	
Incarceration status	If currently incarcerated, not eligible for study	
Screening Outcomes		
Incident CRC	Key outcome	JPS administrative and electronic medical record databases, pathology records, cancer registry data
Stage of incident CRC	Key outcome	
Date of incident CRC		
Treatment for incident CRC		
Incident colorectal polyps	Key outcome	
Size of incident polyps		
Histology of incident polyps		
number of incident polyps		
Completion of CRC screening tests, including colonoscopy, FIT, fecal occult blood testing, barium enema, or sigmoidoscopy		
Date of completion of CRC screening tests		
Results of CRC screening tests		
Screening Process Variables/Outcomes		
Number and duration of phone calls		Program tracking database
Failed mailings		
Wrong phone numbers		

Recruitment Methods and Consenting Process:

Recruitment Methods:

Our goal is to recruit all patients who are not up to date with CRC screening, and meeting all of the inclusion/exclusion criteria above, for screening interventions. Recruitment will occur with the following steps:

a) The administrative and electronic medical record databases at JPS will be used to identify patients age 50 to 64, with at least one primary care visit in the one year period prior to the data pull, who are participants in the JPS Connection medical assistance program for the uninsured. We anticipate that up to 40,000 records may be pulled for this step.
b) Study inclusion/exclusion criteria will be applied to the dataset.
c) All patients meeting inclusion/exclusion criteria will be recruited to the study. We anticipate that 20,000 patients will meet inclusion/exclusion criteria, but seek permission to recruit up to 22,000 patients in case the total meeting inclusion/exclusion criteria is higher than expected. This will allow us to deliver screening promotion interventions to all eligible patients.
d) All patients meeting inclusion/exclusion criteria will receive mailed invitations to complete screening, and processes to promote screening completion outlined above.

e) Additionally, a subset of patients recruited to the study will be randomly assigned to receive financial incentives, in addition to all screening interventions, to boost screening completion. n=1,000 will be assigned to receive $5 incentives, and n=1,000 will be assigned to receive $10 incentives.

Consenting Process:
A waiver of informed consent is requested for this study, including recruitment, delivery of screening interventions, and assignment of a subset of patients to financial incentives for increasing screening.

Justification for waiver of written/informed consent:

The main components of this study that constitute research include: 1) systematic measurement of screening participation rates and screening outcomes among patients offered CRC screening through mailed outreach, 2) systematic measurement of screening participation and screening outcomes among patients offered financial incentives, in addition to mailed outreach, versus mailed outreach alone to complete screening. The screening test being offered—FIT—is a positive sign of health welfare. Completion of this screening test is considered a positive outcome as part of the National Health Interview Survey, and is part of National Health People goals. Additionally, the US Preventive Services Task Force has recommended FIT as one of the options for CRC screening. Overall, we are not studying a new CRC screening test, but rather whether implementing a large scale outreach program results in better CRC screening outcomes, and, whether offering a modest financial incentive substantially impacts screening rates compared to mailed outreach alone.

a. Minimal risk is anticipated.
Minimal risk is anticipated because fecal immunochemical testing and colonoscopy are accepted standards of care for CRC screening, promoted by the US Preventive Services Task Force. No experimental screening procedures are planned. Even without the presence of the study, through the course of usual medical care individuals would have a chance of being offered CRC screening by a primary physician.

The study will evaluate outcomes of large-scale outreach invitation, as well as whether financial incentives have an impact on screening participation in this outreach invitation. All individuals, regardless of the screening group to which they are randomly assigned, will be free to engage in usual medical care, including usual care CRC screening.

b. The waiver would not adversely affect the rights and welfare of the subjects.
The rights and welfare of subjects is not at risk because individuals maintain autonomy, and are being offered standard-of-care CRC screening test with evidence-based benefits. Absence of consent is not anticipated to infringe on the participant's autonomy, as all patients recruited may chose to participate or not participate in screening. Moreover, individuals invited to screening could refuse our invitations and choose to follow up with primary providers to seek screening as part of usual practice.

For patients assigned to receive financial incentives, the level of incentives are likely non coercive. We are studying impact of modest $5 and $10 incentives for completing screening. These levels of incentives are unlikely to be coercive. Additionally, for patients in who are not assigned to receive financial incentives in addition to screening promotion, absence of these interventions is unlikely to result in financial hardship. It is important to note that patients meeting study inclusion criteria must have a minimum of 1 visit to a JPS Primary Care clinic within the last year. Considering these patients have an established baseline relationship

with the JPS primary care system, the addition of a modest financial incentive should not create undue influence in patients that otherwise would still have exposure to information on the benefit of screening. Since participation in this standard of care screening poses minimal to no risk, the chances that incentives may motivate research participants to take unnecessary risks are low.

The intervention does not interfere with usual medical care, which would otherwise include opportunities for participation in CRC screening. The invitation interventions are not anticipated to decrease the rate of screening as compared to usual medical care. Further, the health system could have introduced one or more of the invitation interventions proposed without research. In many practices, such as Kaiser Permanente Northern California, mailed outreach to promote screening with FIT is standard of care.

For patients who have abnormal FIT, requiring follow up diagnostic colonoscopy, clinical consent, as required during the usual medical practice of colonoscopy, will occur, allowing patients the opportunity to understand the risks and benefits of the colonoscopy procedure prior to procedure conduct, further reducing any risks to patient autonomy.

In terms of welfare, waiver of consent for study invitation interventions is not expected to decrease rates of screening, because all participants in all groups will have opportunities for screening through the course of usual medical care. Moreover, it is possible that requiring consent could have a negative impact on welfare, as it might dissuade some patients from completing beneficial screening. Indeed, this patient population that has been shown to be more vulnerable to low rates of screening, and poor colorectal cancer outcomes, requirement of consent may place a burden on patients that reduces the chances of participation in potentially lifesaving screening. These burdens could include worry, as well as distrust of the screening procedures (which are non-experimental, and associated with positive health welfare). *From a welfare perspective, positive health outcomes associated with screening completion, in conjunction with avoided consent-associated distrust and worry that could lower participation rates, both suggest that a waiver of consent may actually be beneficial rather than harmful.*

c. Study cannot be practically conducting without waiver.
The study could not be practically carried out without a waiver because requiring consent would bias study results and change the research questions under study. To do a study of interventions that boost participation in CRC screening, and require that only those with prior informed consent participate would markedly bias the study results, and greatly limit generalizability. This is because the study would be biased towards including individuals who were particularly motivated to complete CRC screening or particularly interested in research, rather than focusing on all individuals who are candidates for CRC screening.

Further it would mean that we would have to contact and receive consent from each of the anticipated 20,000 subjects before they received one of the study invitations. This method change would result in a smaller sample size (perhaps too small for the proposed analyses).

It would also change the research from an effectiveness study – showing how the different invitations to screening would work in routine practice in the safety net system – to an efficacy trial that only shows outcomes of the different invitation methods among volunteers who could be reached by the study staff and who agreed to study participation. Results from a study design that required informed consent would be inconclusive. For example, it would be unclear whether non-response to the study intervention was because of inadequacy of the intervention, or because of non-interest in participating in research. Additionally, gaining

prior consent would change the science away from the method that has received the peer-reviewed funding.

Having to gain prior consent would also markedly increase the budget via additional major costs in staff time, tracking, postage, telephone charges, etc. The budget for this project does not include the resources for these changes.

d. The subjects will be provided with additional information after participation.
We will publicize results of the study, with specific mailings to all participants informing them of the knowledge gained.

Summary of justification for waiver of informed consent
In this research proposal, the most scientifically valid approach (waiving informed consent) is likely to be the most ethical, as it will: 1) maximize participation in potentially life-saving, standard-of-care colorectal cancer screening, 2) maximize local generalizability of results if the program were to be funded on a sustained basis, and 3) maximize overall generalizability of program results to public health entities seeking to optimize colorectal cancer screening. Minimal risk is anticipated because the screening test being offered is an accepted standards of care, and the level of financial incentives being proposed are non-coercive The rights and welfare of the participants is preserved because individuals will retain the right to not participate in screening and because the screening tests offered are non-experimental--indeed completion of these screening tests is considered a marker of positive welfare. The study cannot be conducted without the waiver because requiring consent will substantially bias study results and change the research question under study. Finally, the subjects will be provided with additional information after participation.

Potential Risks:
Potential risks to study subjects may include the following:
Loss of confidentiality of personal health information. The likelihood of this complication is low, as substantial steps will be taken to ensure the safety of personal heath data. The seriousness to subjects is moderate to severe.

Psychological harm of screening invitation. Psychological harms, such as anxiety, depression, and adverse reactions to negative or positive tests have been suggested as a concern for population based screening. Positive tests may occur in the form of a positive fecal immunochemical test (up to 10% of responders), cancer diagnosis (no more than 25% among responders to fecal immunochemical testing with positive tests), and advanced polyp diagnosis (no more than 30% among responders to fecal immunochemical testing with positive tests). Data from a large trial of stool based screening suggest no statistically significant increase in psychological harms such as anxiety after a positive stool blood test, depression, or suicide among individuals invited to stool based screening as compared with controls not offered screening. Overall, the seriousness of psychological harm is judged to be moderate, but the likelihood of psychological harm is projected to be low.

Physical harm-fecal immunochemical testing. Harms associated with stool occult blood screening for CRC are generally limited to risks conferred by colonoscopy performed in follow up of positive stool tests. Up to 10% of individuals will have positive stool tests and require colonoscopy, and be exposed to the risks outlined under “physical harm-colonoscopy” below. In modeling studies, of CRC screening with fecal immunochemical testing for occult blood the life-years gained from fecal immunochemical testing based screening relative to no screening has been estimated to be substantial, estimated at 227 life-years gained per 1000 persons screened. Further, in a large randomized trial that closely evaluated physical risks associated with mass-scale fecal occult blood testing, the rate of physical harm was low. Thus, the seriousness of complications

associated with fecal immunochemical testing if one occurs is moderate to severe, but the likelihood of occurrence is low, and the balance of benefits associated with fecal immunochemical testing versus risks appears favorable.

Physical harm-colonoscopy performed for follow up of abnormal FIT tests. Colonoscopy has a known complication rate of 3 per 1000, including bleeding, perforation, and heart or lung complications, and a mortality rate of 1 per 14,000. However, in modeling studies of CRC screening with colonoscopy, the life-years gained from colonoscopy based screening relative to no screening has been estimated to be substantial, estimated at 230 life-years gained per 1000 persons undergoing screening. Thus, the seriousness of colonoscopy complications if one were to occur is moderate to severe, the likelihood of occurrence is low, and the balance of benefits of colonoscopy versus risks appears favorable.

Financial harm--screening. There will be no financial cost associated with completion of the fecal immunochemical test to subjects invited for fecal immunochemical testing, as the tests will be provided free of charge, with return postage included, and no cost for processing of the test. Colonoscopies associated with the study will be free of charge. Participants may incur travel and parking costs that will not be reimbursed. Thus, the seriousness of financial harms associated with screening is limited, and the likelihood of some financial cost is low to moderate.

Financial harm—treatment of cancer or unresectable polyps. Through the course of the trial, it is conceivable that a few individuals may be diagnosed with CRC and/or polyps not amenable to colonoscopic removal. Because all individuals included in this study will be participants in the JPS Connection medical assistance program, which allows for cancer care with mild-moderate utilization based co-pays (see above), any participants diagnosed with CRC should have affordable access to cancer care. Overall, the seriousness of financial harms associated with treatment of cancer is minimal to moderate, and the likelihood of some financial cost is low, mainly because the prevalence of cancer is expected to be low.

Legal harms. No legal harms are anticipated as a result of this trial.

Overall risks/benefit assessment: Overall, the potential risks of this research are similar to the risks of standard medical care, mainly because only standard of care CRC screening tests are being offered as part of the program interventions.

Subject Safety and Data Monitoring
Description of monitoring plan
The principle monitoring entity will be the PI, with daily monitoring. The Institutional Review Boards at University of Texas Southwestern Medical Center and John Peter Smith Hospital Health System will monitor the trial on an annual basis, and on an ad hoc basis in the case of adverse event report to the one or more of the IRBs. Serious adverse events will be reported to the principle investigator immediately, and to both the UT Southwestern and JPS Hospital Health System immediately (within 1 business day). Safety and efficacy data will be evaluated formally at the end of the study period, beginning 13 months after first intervention invitation; no interim safety or efficacy analyses are planned as the risks associated with the study are similar to those a participant would undergo in the course of usual medical care.

Any adverse events associated with program outcomes will be recorded and characterized. These will include, but are not limited to items in Table D.

Table D. Adverse events that will be recorded and characterized	
Event	**Monitoring procedure**

Breach of confidentiality of participant data	Monthly review with all program staff of data security
Patient anxiety associated with program intervention	Passive follow up, i.e. record of any anxiety expressed by patients during course of program procedures
Colonoscopy complications	Monthly review of all colonoscopies associated with program procedures, and any complications within 30 days of procedure completion, including, but not limited to: bleeding, perforation, myocardial infarction, death.
Any unanticipated serious or non serious adverse event	Monthly review with all program staff Passive reporting by the clinical lab, endoscopy lab, JPS physicians, or any program participants to program staff.

Plans for medical or professional intervention in the event of adverse effects

1. Procedure for responding to loss of confidentiality. The study participant who experiences loss of confidentiality will be informed by one of the study primary investigators in writing and by phone of the loss of confidentiality. The IRB will be informed in case of this event.
2. Procedure for responding to physical harm from colonoscopy. The study participant will immediately be informed of the physical harm, and appropriate medical and surgical interventions will be facilitated. The IRB will be informed in case of this event.
3. Procedure for responding to psychological harm from screening. The study participant who experiences psychological harm will be informed by one of the study primary investigators in case of this event. Appropriate referrals for medical and/or psychological care will be facilitated. The IRB will be informed in case of this event.

The protocol will be stopped for any of the following reasons:

- Unanticipated serious adverse event such as loss of confidentiality
- Unanticipated death resulting from any study activity
- Request of either Institutional Review Board
- Unanticipated event deemed appropriate indication for stopping the trial by the PI

Plans for assuring data accuracy, data security, and protocol compliance include:

- Access to study data only by designated study personnel
- Study data will be kept in a locked room, on a password protected computer, with password protected file. All paper case-report forms will be destroyed after data entry, and kept in a locked room within a locked filing cabinet until data entry and subsequent destruction
- Daily backup of study data to a central, firewalled, password protected server at Moncrief Cancer Institute, University of Texas Southwestern Medical Center
- Daily monitoring of protocol compliance through conversations between the principle investigator and research assistants

The mechanisms for reporting unanticipated problems will include:

- Report of the unanticipated problem to the Institutional Review Boards at University of Texas Southwestern Medical Center and John Peter Smith Hospital Health System immediately (within 1 business day).

Continuing Review will be performed by the IRB on an annual basis, or more frequently, if required. As part of the Continuing Review submission to the IRB:

- On the IRB Form for continuing review, items referencing unexpected and serious adverse events will be completed appropriately with a comment to describe the event(s) according to IRB template instructions.
- The Progress Report will be completed according to IRB template instructions and include the principal investigator's a summary of unexpected and serious adverse events and protocol deviations with an analysis of the safety profile of the research.
- If not already done, protocol documents (e.g. protocol, project summary) that require changes based on changes to the risk profile of the research will be submitted as a Modification with the Continuing Review according to IRB instructions.
- A declaration of on-going operational feasibility. If the enrollment rate in the previous year is not sufficient to reasonably reach planned enrollment, a plan will be offered to assure completion of the study.

ClinicalTrials.gov
The trial will be registered in ClinicalTrials.gov prior to being started.

Procedures to Maintain Confidentiality:
Plans for assuring data accuracy, data security, and protocol compliance include:

- Access to study data only by designated study personnel
- Study data will be kept in a locked room, on a password protected computer, with password protected file. All paper case-report forms will be destroyed after data entry, and kept in a locked room within a locked filing cabinet until data entry and subsequent destruction
- Regular backup of study data to a central, firewalled, password protected server at Moncrief Cancer Institute, University of Texas Southwestern Medical Center
- Daily monitoring of protocol compliance through conversations between the principle investigator and research assistants
- Database and patient records accessed by research staff from JPS Network computers, connected by VPN to UT Southwestern Medical Center, and Moncrief Cancer Institute

Potential Benefits:
Individuals in the age range from 50 to 64 are most likely to benefit from CRC screening[23]. Modeling studies suggest that a life expectancy of at least 8 years is required for a given patient to realize the benefits of screening over non-screening[13]. In fact, one group has suggested that Medicare consider supporting screening for those under 65, as this could prevent CRC associated morbidity and mortality when individuals acquire age of Medicare eligibility[24].

Biostatistics:
EVALUATION STRATEGY
Overview. Our overarching evaluation goal is to rigorously evaluate program outcomes. The evaluation will be strengthened by our prior experience and systematic approach to evaluating program outcomes. Our evaluation strategy has been designed to provide the most interpretable results possible, and position local and state public health officials to assess program impact and areas for improvement. The evaluation will be lead by Dr. Chul Ahn, a biostatistician, Dr. Bijal Balasubramanian, an epidemiologist, and Dr. Samir Gupta, a physician and clinical researcher. We have a track record of completing sophisticated program evaluations, and have worked together on prior analyses. We have developed several primary evaluation aims, as well as a number of secondary evaluation aims. It should be noted that all CPRIT required program evaluations are addressed.

Consistent with Goal 3, for our primary evaluation aims, we will:

Evaluation Aim A) Determine screening rate improvement after expanding screening outreach to all unscreened patients. *We predict the population screening rate will be ≥10% higher after outreach expansion compared to baseline.*

Evaluation Aim B) Compare rates of initial and repeat screening completion among 1) Patients offered a modest financial incentive to complete screening, in addition to outreach invitations, vs. 2) Patients offered outreach invitations alone.

Evaluation Aim C) Among patients receiving financial incentives to complete screening, compare rates of initial and repeat screening completion between patients receiving $5 vs. $10 incentives.

Evaluation Aim D) Assess all CPRIT required outcomes, including increase in early stage cancer detection from baseline, as well as health system changes required to boost screening.

Approach to Evaluation Aims

Evaluation Aim A) Determine screening rate improvement after expanding screening outreach to all unscreened patients. The denominator population for evaluating baseline and end of Year 3 screening rates will consist of patients meeting the following criteria: 1) Age 50-64, 2) Uninsured, but participants in JPS's medical assistance program for the uninsured, 3) One or more visits to a JPS primary care clinic within a year, 4) Address and phone number on file, 5) No history of CRC or colon resection, 6) Not incarcerated

Thus, the denominator population for our baseline and end of Year 3 follow comparisons of screening rates generally includes patients age-eligible for screening outreach. The numerator for calculation of screening rates will be the number of patients who are up-to-date with screening based on colonoscopy within 10 years, sigmoidoscopy within 5 years, or stool blood test (guaiac FOBT or FIT) within the last year, measured by HEDIS criteria. Thus, the screening rate at baseline and at end of Year 3 will be defined by:

$$\textit{Screening Rate} = \frac{\textit{\# up-to-date with screening}}{\textit{\# patients eligible for screening}}$$

We will compare groups using a Chi-square test, and use a 2-sided p-value <0.05 to indicate a statistically significant difference between baseline and follow up screening rates.

We predict the screening rate will increase by 10% from 39% at baseline to 49% at end of Year 3. The prediction is based on several assumptions. First, we expect that initial FIT completion rates will be similar to the 33% rate observed in our prior CPRIT program among patients invited to FIT screening (Section A.2). Second, we expect colonoscopy follow up rates for patients with abnormal FIT will be 75%, similar to our prior program. Third, we considered various levels of repeat FIT participation rates. As is explained in Section A.3, there are limited data on "real world" repeat stool occult blood/FIT participation rates, with available estimates of repeat participation ranging from 40 to 75%[33, 34]. We estimate this range of FIT repeat participation is consistent with a screening rate increase of 5 to 15%, from 39% at baseline, to between 43 and 54% at end of year 3. Thus, we conservatively predict an increase of 10%. As is noted below, we will have statistical power to detect the entire range of estimated screening rate increases.

Sample size for Evaluation Aim A. Unlike sample size estimates for clinical research trials, sample size estimates for these comparisons are not based on the minimum number of patients required to detect clinically significant differences in outcome rates. Rather, the sample size for these comparisons will be based on the number of patients potentially qualifying for screening outreach program. This is because the primary goal of CPRIT Evidence Based Prevention Programs is to maximize screening delivery. Nonetheless, because the sample we expect to identify is very large, we will have more than enough power to detect clinically significant differences in the outcome of interest. We estimate that at baseline and at follow up, at least 20,000 patients will qualify for our screening outreach program if not screening up-to-date (Table 1). With an expected sample of at least 20,000 patients eligible for screening at baseline and at end of year 3, assuming alpha=0.05, we will have over 90% power to detect our predicted screening rate increase of ≥10%, from 39% at baseline to 49% at end of Year 3 with a two-sided significance level. Moreover, with the expected sample sizes,

we will even have 90% power to detect a smaller screening rate increase of ≥5% (Power was computed with nQuery Advisor Software v.7.0).

Evaluation Aim B) Compare rates of initial and repeat screening completion among 1) Patients offered a modest financial incentive to complete screening, in addition to outreach invitations (n=2,000), vs. 2) Patients offered outreach invitations alone (n=~18,000). The rate of initial screening completion will be defined by:

$$\textit{Initial Screening Completion Rate} = \frac{\textit{\# patients completing a FIT Year 1}}{\textit{\# of patients sent FIT invitation Year 1}}$$

We will compare the initial screening completion rate for patients offered the financial incentive, in addition to screening outreach, to the initial rate for patients offered screening outreach alone using a Chi-square test of proportions, with a 2-sided p value <0.05 considered statistically significant. The rate of repeat screening for Years 2 and 3 will be defined by:

$$\textit{Year 2 Repeat Completion Rate} = \frac{\textit{\# patients completing FIT screening Year 2}}{\textit{\# patients completing FIT Year 1 with normal result}} \qquad \textit{Year 3 Repeat Completion Rate} = \frac{\textit{\# patients completing FIT screening Year 3}}{\textit{\# patients completing FIT Year 2 with normal result}}$$

We will compare initial FIT completion rates for the financial incentive plus organized outreach vs. organized outreach alone groups using a Chi-square test, with a 2-sided p value <0.05 considered statistically significant. The same approach will be taken for comparing repeat FIT completion rates for Years 2 and 3.

Sample size for Evaluation Aim B. The sample size for this aim will be 2,000 for the financial incentive group plus outreach group, and at least 18,000 for the outreach group alone. The sample size for the financial incentive group was chosen based on sample size required for sufficient power to detect expected differences between offers of $5 and $10 gift card incentives outlined in Aim C below. The sample size for the outreach group alone was based on including all patients included in the screening outreach program who will not receive financial incentives. With 2,000 patients assigned to the financial incentive plus outreach group, and 18,000 patients assigned to the outreach alone group, we estimate over 90% power to detect differences in initial screening participation of 5% or more at a 5% two-sided significance level. Thus, we will have more than enough power to detect clinically meaningful differences of 10% or more in initial FIT completion. Because of the lack of prior data on repeat FIT participation rates, and under the sample size discussion for Evaluation Aim A above, we do not present formal power calculations for comparisons of repeat FIT completion rates, but expect that we will be able to make meaningful comparisons based on the large number of patients included for evaluation.

Evaluation Aim C) Compare rates of initial and repeat screening among patients receiving $5 vs. $10 financial incentives in addition to outreach invitations. For this comparison, we will use the same definitions outlined under "Evaluation Aim B" above for the initial screening completion rate, and the Year 2 and 3 repeat completion rates. For these outcomes, we will compare the outcome rate for patients receiving the $5 vs. $10 incentive, using a Chi-square test of proportions, with a 2-sided p value <0.05 considered statistically significant.

Sample size for Evaluation Aim C. The sample size for Evaluation Aim C is based on comparing the initial screening participation rate between the $5 vs. the $10 incentive groups. As is outlined in Section A.3, previous data suggest that financial incentives are effective for promoting complex healthy behaviors such as quitting smoking[39-41]. Further, we believe that incremental (modest) incentives are likely to significantly increase screening completion. First, we assumed that a 10% or more difference in initial screening participation would be clinically meaningful. Second, we assumed that the screening completion rate associated with the $5 group would be 43%, and that the rate for the $10 group would be at least 53%. The 43% rate was chosen because our response to FIT invitations with our prior outreach program was 33%, and we would consider a 10% or more increase

in screening completion associated with the $5 intervention over organized outreach alone to be clinically meaningful. Similarly, the 53% rate was chosen for the $10 group because we would consider a 10% or more increase in screening completion associated with the $10, rather than the $5 group to be clinically meaningful. Under these assumptions, with an alpha=0.05, we estimated 1090 patients (n=545 in the $5 group and n=545 in the $10 group) would be required for 90% power to detect a statistically significant difference of 10% or more in initial screening participation. Because we recognize uncertainty in the estimating the expected difference between the two groups, and because we wanted to increase our ability to conduct exploratory comparisons of repeat FIT participation rates associated with the $5 and $10 groups, we increased the planned sample receiving financial incentives to 2,000 (n=1,000 in the $5 group and n=1,000 in the $10 group). Thus, we will have more than enough power to detect differences of 10% or more in initial screening participation.

Evaluation Aim D) Assess all CPRIT required outcomes, including increase in early stage cancer detection from baseline, as well as systems changes required to boost screening. ***To assess increase in early stage cancer detection from baseline, we will compute proportion of CRC patients with early stage cancer at baseline and at end of Year 3***. JPS Cancer Registry data will be used for this computation. Rate of early stage cancer will be defined as:

$$\textit{Early Stage Cancer Detection Rate} = \frac{\textit{\# CRC patients with SEER Summary Stage 0 or Stage 1}}{\textit{\# CRC patients}}$$

We will use a Chi-square test of proportions for comparing groups, and a p value <0.05 to signify statistical significance.

To assess systems changes required to boost screening, we will plan additional evaluations focused on the JPS health system. In addition to evaluating outcome change (as described above), it is also important to evaluate changes in processes related to transferring and expanding our outreach program at JPS. The purpose of this process evaluation is to gather information about the roll out process to enhance sustainability of the screening program, and enable translation of this program to other safety-net settings. To meet these objectives, we will monitor the screening program on a real-time basis. During weekly meetings between UTSW nurse (TBA) and JPS screening outreach team, the UTSW nurse will ask members of the outreach team about their experience with the program. She will maintain a detailed log of problems and successes. She will also document strategies and workarounds that JPS staff develop to tailor the program to their needs and resources. Similarly, barriers and facilitators of the outreach program at the health system level identified during JPS physician champion meetings with the principal investigator will be documented. Sustainability of the program will be enhanced because JPS staff will have access to systematically collected information about on the ground strategies that worked and did not work at the screening delivery level as well as at the health system level. In addition, this information will also enable us to apply our knowledge of successfully establishing this program at JPS to other safety-net systems.

Secondary analyses. We plan to conduct several secondary analyses. First, we recognize that results from Evaluation Aim A, in which baseline screening rates will be compared to follow up screening rates at year 3, could be confounded by time trends in CRC screening rates, which generally have been increasing over time. Accordingly, we will compare the observed rate of CRC screening in Year 3 to the expected rate of CRC screening based on time trends in screening at JPS. The expected rate will be estimated using the secular trend for CRC screening using annual screening rates for each of the 7 years 2006-2011 prior to start of our prevention program in 2012. All rates will be standardized by gender and age strata (50-54, 55-59, and 60-64 years) to the population distribution of men/women and these age strata for 2012, and a standardized incidence ratio (SIR) will be computed. An SIR greater than 1, with an associated 95% confidence interval that does not cross 1 will be interpreted as evidence to support impact of our outreach intervention beyond time trends in CRC screening rates. We have previously used this approach to assess impact of a University of Texas health plan policy that waived copays for colonoscopy screening on CRC screening rates which began in 2009, in which we compared colonoscopy uptake 2002-2008 to uptake after policy institution[46].

Second, to identify factors independently associated with screening outcomes, we will construct several logistic regression models. For example, to identify predictors of initial screening completion, we will create a model using initial screening completion rate as the primary outcome (dependent) variable, and several potential predictors of completion. Predictors considered for model inclusion will include age, sex, race/ethnicity, frequency of primary care visits, exposure to the screening outreach program, and exposure to financial incentives. A similar model will be created with the outcome of programmatic screening as the dependent variable. For these exploratory analyses, 2-sided p values of 0.05 will be considered statistically significant.

Third, we will quantify the number of patients who have CRC and potentially precancerous polyps detected through screening outreach. CRC and polyp data will be collected by reviewing all colonoscopy and associated pathology reports for patients who undergo colonoscopies after having abnormal FIT tests. Additionally, we will query the JPS tumor registry to identify any program participants who had CRC diagnosed, and determine, through chart review, whether the CRCs were detected as a result of our screening outreach or through other mechanisms. With our plan to invite over 20,000 patients, taking into account our prior rates of FIT screening participation (33%), abnormal FIT results (12%), and detection rates of CRC (4.8%) and adenomas (46%) after abnormal FIT, we estimate that 38 patients with CRC and 364 patients with adenomas will be identified through our program.

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