A RCT of Outreach and Inreach Strategies for Boosting CRC Screening in a Federally-Qualified Health Center

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SPECIFIC AIMS

Colorectal cancer (CRC) screening has the potential to save lives, but is underutilized, particularly among underserved populations. For example, screening rates among Latinos are just 40%, and among uninsured and those insured by Medicaid are just 20 and 25%, respectively. Low rates for Latinos are of particular concern, as they have higher than average stage at presentation and stage-specific mortality than non-Latino whites. To reduce CRC disparities, interventions to optimize screening among underserved populations, particularly among Latinos, are required. Federally Qualified Community Health Centers (FQHCs) are in a unique position to leverage their service to underserved populations to deliver the benefits of CRC screening for several reasons. FQHCs traditionally serve the uninsured, underinsured, and racial/ethnic minorities that have traditionally low rates of being up-to-date with cancer screening, and are now required to publically report screening rates due to federal mandates. For example, San Ysidro Health Center, Inc. (SYHC) is a large FQHC that includes a network of 10 clinic sites that serves over 90,000 patients annually, who come from a predominantly low-income, Spanish-speaking Latino population in the U.S.-Mexico border region of San Diego County; in 2013 the publicized CRC screening rate was just 31%. While low rates of screening at FQHCs such as SYHC are of great concern, provisions within the Affordable Care Act, such as new access to health insurance for populations that commonly utilize FQHCs, may offer a historic opportunity to develop and implement strategies for optimizing screening rates for underserved populations, including low income Latinos. In 2013, SYHC approached UCSD and SDSU partners on how to build a CRC screening infrastructure to increase screening rates.

Despite potential opportunities to deliver screening for underserved populations through FQHCs, many challenges exist. Available strategies for screening promotion have undergone limited development and evaluation among low income predominantly Spanish-speaking FQHC Latinos patients. Further, it is unclear which strategies are best for increasing screening, and whether implementing multiple approaches (e.g. inreach delivered at point of a medical visit vs. outreach not requiring an in-person visit) would be superior to taking one approach alone for optimizing screening rates. To begin to address these challenges, we have conducted pilot work that has 1) established an academic-community CRC partnership between UCSD, SDSU, and SYHC; 2) established that FQHCs are keenly interested in understanding the best and most practical strategies for screening promotion; 3) identified (through key informant interviews of providers, clinic leadership, experienced *promotoras* (community health workers), and screening experts) key themes our interventions must address; 4) adapted previous effective materials used for mailed FIT outreach and patient navigation-based in-reach for screening promotion. Now, utilizing this comprehensive partnership and pilot work, we propose the following specific aims:

Aim 1: Among 648 Latinos age 50-75 years served by the SYHC FQHC, not up-to-date with screening, compare impact of 4 strategies on screening completion via a randomized controlled trial. The strategies will include: a) a patient-navigation-based, in clinic, inreach strategy, b) a mailed FIT outreach strategy (FIT outreach), c) inreach + FIT outreach, and d) usual care (n=162 per group).

Hypothesis 1a: *The inreach strategy (with or without FIT outreach) will be significantly superior to usual care*
Hypothesis 1b: *FIT outreach (with or without the inreach strategy) will be significantly superior to usual care*
Hypothesis 1c: *FIT outreach + the inreach strategy will be significantly superior to either strategy alone compared to usual care.*

Aim 2: Conduct a process evaluation to examine the interventions' reach, effectiveness, acceptability, feasibility, and sustainability following the RE-AIM framework.

The proposed research is innovative because it seeks to identify pragmatic interventions required to optimize CRC screening in a Latino underserved population, is highly feasible, and, will allow us to determine whether a combination of outreach and inreach interventions are superior to either strategy alone for increasing CRC screening. Further, the community-based partnership approach of linking our academic medical center/NCI-designated comprehensive cancer center (UCSD), a research university/Hispanic-serving institution (SDSU), and a large community health center (SYHC) may serve as a model for developing and implementing evidence-based interventions for traditionally underserved populations. Indeed, successful interventions will be Demonstration of intervention effectiveness will support adoption by the SYHC, and disseminated through the local, regional and national CHC networks (e.g., Council of Community Clinics, California Primary Care Association, and the National Association for Community Health Centers). Overall, the research has potential to reduce cancer disparities among Latinos and other underserved populations served by FQHCs and beyond.

RESEARCH PLAN

SIGNIFICANCE

Colorectal cancer (CRC) is the 2nd leading cause of cancer death in the United States (US). CRC accounts for over 136,000 new cancer diagnoses, and over 50,000 deaths annually (1).

Screening can reduce CRC incidence and mortality, but is underutilized, particularly among underserved populations. Randomized trials and observational studies have demonstrated that screening with fecal occult blood testing (including the guaiac fecal occult blood test (gFOBT) and the fecal immunochemical test (FIT)), sigmoidoscopy, and colonoscopy can reduce CRC incidence and mortality (2-7). As a result, the US Preventive Services Task Force has recommended screening for all individuals after age 50 years. However, according to the National Health Interview Survey (NHIS) the national screening rate is 59%, far below the 70% Health People 2020 target (8). Moreover, screening rates are particularly low among underserved populations, such as Native Americans, Asians, Latinos, individuals living in rural areas, individuals with lower education and/or socioeconomic position, and the under-/uninsured (9). For example, the screening rate among the uninsured is just 21% (10, 11).

Latinos are at particularly high risk for suboptimal screening, as well as adverse outcomes when CRC is diagnosed*.* Among male and female Latinos combined, CRC is the 2nd leading cause of cancer death, with lifetime risk ranging from 4 to 5% (12). Yet the national screening rate among Latinos is just 47%. Additionally, Latinos are more likely to be among the uninsured, the group with the lowest overall screening rates (13, 14). Compared to non-Latino whites, Latinos are more likely to be diagnosed at advanced stage (15), and less likely to survive CRC after diagnosis (12). Thus, because Latinos are the largest and fastest growing ethnic population in the US, strategies for increasing CRC screening and survival are required.

Barriers to screening among Latinos include lack of knowledge and awareness, access to care, insurance status, language barriers, culture-bound beliefs, and low literacy (16). Research along the Texas-Mexico border showed Latinos held misconceptions about CRC, including confusing CRC with prostate, stomach, and other cancers. Many had never heard of CRC or CRC screening tests (17). Cancer education interventions, such as the use of print materials, have been used to overcome these barriers and increase participation in CRC screening (18, 19) in the general population, however, it is unclear whether more culturally-appropriate intervention strategies are as effective in promoting CRC knowledge among Latinos.

Successful organized strategies to increase screening among underserved populations (including Latinos) may involve inreach and outreach approaches. Organized screening requires an "explicit policy in a defined target population with a defined implementation and quality assurance structure, and tracking of cancer in the population."(9, 20) Organized screening strategies may broadly categorized as inreach vs. outreach based on whether health care visits are required to deliver screening invitations (9). Inreach strategies promote screening at point of routine medical care. Outreach strategies target all eligible individuals within a defined population regardless of scheduled health care visits. Inreach strategies take advantage of in-person encounters with age-eligible individuals, but may be limited in reach due to requirement for health system visits, as many individuals do not access health care on a regular basis. Further, resources required to implement inreach strategies to promote screening among all eligible individuals may be substantial. Outreach strategies have the advantage of reaching a greater proportion of the population, with a centralized, potentially smaller team, but in theory might be less effective than interventions that occur in context of a face-to-face healthcare visit.

Examples of successful inreach approaches have included provider assessment and feedback, one-on-one education, patient navigation to promote colonoscopy completion after referral, and offering gFOBT or FIT at time of flu vaccination (21-27). In a single SYHC clinic, we previously piloted delivery of one-on-one patient education for Latino patients using a culturally linguistically tailored CRC self-help brochure containing information on risk factors, knowledge, culture-bound myths and screening tests, with and without scripted review of key points within the brochure by a community health advisor prior to a primary care visit (28). Compared to usual care, the brochure increased screening knowledge, and also increased frequency of discussion of screening with providers by 20%, but no differences were noted between delivery of the brochure with or without intense review. These results complement prior work that has shown one-on-one education to be effective in promoting screening (21). The main limitations of our prior work include small sample size (n=130 completed pre and post intervention surveys) and use of a surrogate outcome (knowledge rather than screening completion). Additionally, our inreach intervention did not include navigation(22, 23) (such as telephone follow up to promote screening completion), and was not supplemented by offers to complete screening at time of flu vaccination (24-27, 29), both of which have been shown effective for promoting screening. Whether one or both of these approaches might be an effective adjunct to one on one education in the FQHC is unknown, but highly relevant given that each of these strategies requires substantial resource investment to implement. We postulate that in the FQHC setting, the ideal inreach intervention would be tailored to the local clinic context and community needs based on formative research in which we work with patients, providers, and health system leaders to determine the most acceptable and practical inreach interventions that can leverage usual care medical visits for screening promotion.

Examples of successful outreach approaches have included use of mailed invitations with telephone follow up to promote screening fecal occult blood test (FOBT) completion, as well as patient navigation to promote colonoscopy completion. We conducted a randomized, comparative effectiveness trial of the impact three system-level strategies—usual care, mailed invitation to complete free colonoscopy, and mailed invitation to use and return an enclosed fecal immunochemical test FOBT (FIT) kit—among a racially- and ethnically-diverse group of 5,970 uninsured individuals served by a large safety-net health system, not up to date with screening (30). Mailed invitations were supplemented by telephone calls to promote screening completion, and help with scheduling to complete colonoscopy for screening or diagnostic follow up of abnormal FIT. At one year, screening was significantly higher for FIT (40.7%) and colonoscopy outreach (24.6%) compared to usual care (12.1%), $p<0.001$ for all comparisons. Among individuals with abnormal FIT, 82% completed diagnostic colonoscopy. Intervention effects were similar for non-Hispanic whites, non-Hispanic blacks, and Latinos. Importantly, the interventions were delivered through a safety-net health system that included a county-level sliding scale health assistance program that facilitated access to primary and specialty care (such as colonoscopy) within the health system – few such comprehensive systems exist in the US for underserved populations. Our results with mailed outreach are similar to others offering FOBT (31, 32) or colonoscopy (33, 34) outreach, thus suggesting that this approach is consistently effective for promoting screening completion compared to usual care.

However, two main limitations exist. First, as highlighted below, these interventions are under-studied among predominantly Latino populations. Second, while effective, none of the studies achieved outcomes expected to result in reaching the Health Person 2020 goal of screening 70.5% of the population if implemented on a wide-scale. Third, resources required to deliver these interventions can be substantial. For example, our intervention included two automated and up to two live phone reminders within 3 weeks, while Lasser et al. reported making a median 8.5 calls (associated with a total average phone contact time per patient of 107 minutes) during the study period to promote colonoscopy completion (33). The intensity of resources required for these prior interventions have implications for FQHCs seeking to boost screening with limited resources.

It is largely unknown whether prior inreach and outreach approaches can be effective among low income Latinos, and whether using a combination of strategies will be synergistic for increasing screening rates. There are few randomized trials that have focused on either inreach or outreach strategies for promoting screening using samples that included substantial (≥25%) Latino representation. In fact, little to no community-based cancer control intervention research has been conducted on border Latino populations outside of Texas. Similar to our prior outreach study, Walsh et al. and Coronado et al., have both reported increased screening completion associated with mailed invitation to complete guaiac FOBT compared to usual care with and without phone follow up (35). Walsh's study included an arm with culturally tailored telephone follow up (mean 1.7 calls with mean 17 minutes duration), while Corando's included an arm with *promotora*-based telephone follow up (mean duration 10 minutes). Compared to usual care, these interventions improved screening by 7 to 29%, with the highest rates associated with telephone follow up – 17% and 29% increases for Walsh et al and Coranado et al, respectively. Potter et al. studied an inreach strategy of offering guaiac FOBT at time of Flu vaccination at a primary care clinic within a large public hospital (24). Compared to usual care with vaccination alone, the Flu-FOBT intervention increased screening completion by 25%; the rate compared to usual care individuals not presenting for flu vaccinations was not reported. Jandorf et al.(22) studied effects of an inreach patient navigation strategy after physician recommendation for guaiac FOBT and/or endoscopic screening (sigmoidoscopy or colonoscopy) in New York City FQHC. Navigation included telephone follow and assistance with procedure scheduling if recommended. Navigation resulted in a non-statistically significant 17% increase in FOBT completion, and a statistically significant 19% increase in endoscopic screening completion. Overall, there appears to be consistent evidence that mailed outreach can be effective for promoting screening, including among Latinos. Also, there is limited evidence that inreach strategies such as offering FOBT at opportunistic times such as that of flu vaccination, as well as patient navigation can aid in screening completion among Latino populations.

Importantly, none of these interventions (including our own mailed outreach approach) have been shown to achieve optimal screening rates among individuals not up to date, and impact of using combination approaches (such as inreach and outreach approaches together) has generally not been evaluated in FQHC settings. Kaiser Permanente Northern California, a large health maintenance organization, has utilized a combination of inreach (including provider reminders), and outreach (including mailed FIT invitations with phone follow up) to achieve a screening rate of 79% in 2012 (36), suggesting that inreach and outreach may be synergistic. However, utilizing both approaches requires significant resources, and it is unknown whether a combination approach would achieve similar results among the underserved and/or Latino populations.

Federally Qualified Health Centers (FQHCs) are in a unique and historic position to use existing relationships with underserved populations to develop and implement strategies for boosting CRC screening. FQHCs have a mission to care for underserved, under- and uninsured populations. It is expected that with advent of the Affordable Care Act (ACA), many uninsured patients served by FQHCs will acquire health insurance, a prerequisite in most settings to offering CRC screening, and treatment if cancer is found. The ACA is also promoting electronic medical record uptake among FQHCs, allowing for better identification and tracking of patients and outcomes. Additionally, in 2012, the Department of Health and Human Services designated CRC screening as a publically reported Universal Data Set (UDS) measure. Thus, FQHCs have new resources and motivation that can enable them to play a central role in identifying individuals not up to date, and delivering screening. While recommendations for how to promote screening have been made (37), evidence to support efficacy of one strategy vs. another (e.g. inreach vs. outreach), and impact of a combination approach, is lacking. Thus, FQHCs have on one hand the urgent need to improve screening rates, but on the other hand have significant uncertainty as to which approaches to invest limited resources in for promoting screening. New knowledge that elucidates the best approach or combination of approaches for promoting screening among underserved populations (particularly Latinos) is thus required.

PILOT RESEARCH

In addition to our previously cited published intervention work in the area of CRC screening, this proposal is supported by pilot work that demonstrates the feasibility of the proposed work, elucidate key guiding principles for our interventions, and our commitment to the project.

First, we have established an academic-community partnership between UCSD, SDSU, and SYHC. Since the fall of 2013, representatives from UCSD Moores Cancer Center (Gupta), SDSU (Talavera, Castaneda), and SYHC (Sumek) have worked closely together to forge a partnership around understanding barriers to CRC screening at SYHC, identifying key infrastructure required to optimize screening and deliver screening interventions, and garnering the support of key leaders at SYHC for the project. This work together has facilitated the additional pilot work reported herein.

Second, we have established that FQHCs in our region are keenly interested in understanding the best and most practical strategies for screening promotion. In January of 2014, a continuing medical education and needs assessment was conducted with 14 directors, administrators and clinic managers from over 10 Council of Community Clinic member FQHCs to determine interest and readiness for implementation of CRC screening programs in San Diego. The meeting included a presentation by Dr. Gupta in which evidence-based “best practices” as well as opportunities for future research were identified; this presentation was rated as the most important aspect of the meeting in our post-presentation survey. All participants reported that they are interested in adopting evidence-based strategies for CRC screening programs and needed technical assistance to move forward. Major needs expressed included: 1) additional, more widespread staff and provider education, 2) desire to leverage electronic health record (EHR) data to promote screening, and 3) a desire to incorporate follow up for CRC screening into existing case management/navigation and referral programming, such as those that exist for BC screening and follow-up.

Third, we have identified, through key informant interviews of providers, clinic leadership, experienced *promotoras*, and patients key themes our interventions must address. Ten key informants (non-patients) who were knowledgeable about CRC, early detection, SYHC/health care system level issues related to cancer, EHR, and the Latino community of focus, participated in 60-minute semi-structured interviews to obtain information regarding recommendations for intervention methods and opinions on intervention readiness, adoption and implementation issues. Interviews were analyzed using content analysis techniques to describe emergent salient themes. Major results from interviews of non-patients included perceptions that 1) tests are not offered in a systematic, consistent manner; 2) health literacy among patients with regards to knowledge of cancer and specifically CRC is limited, 3) patients have limited knowledge of CRC screening tests, 4) providers have limited time to promote and order screening tests, 5) participation in CRC screening needs to be "normalized", 6) navigation-based interventions need to be delivered by an individual perceived to be a peer rather than a "*jefa*" or boss. These observations among non-patients were complemented to some extent by observations taken from group interviews of SYHC patients that included questions about needs surrounding reducing cancer risk, topics they would like to learn more about regarding CRC, and preferences for how information should be presented. SYHC staff recruited 46 Spanish-speaking Latinas age 40-70 waiting for a routine health visit; 140 were approached and 92 agreed to participate. When asked about what things that came to mind about reducing cancer risk the top responses included a desire for information on how to understand how to reduce risk, request for information on how to have regular screening exams, and concerns about fear and death. When asked to share 3 topics they would like to learn more about specifically regarding CRC screening, major themes included a desire to obtain more information about screening that is easy to understand, wanting to know more about symptoms, risk factors and prevention, information on how to manage concerns about embarrassment and shame associated with CRC testing.

Fourth, we have adapted and evolved our prior FIT outreach and patient navigation-based inreach strategies for screening promotion suitable for the SYHC clinic setting.

Outreach strategy: As mentioned above, we previously conducted a randomized comparative effectiveness trial that demonstrated the potential for mailed invitation to use and return an enclosed FIT kit, with telephone follow up to promote completion, to increase screening rates compared to usual care. In our pilot work, we have adapted the mailed FIT strategy for use at FQHCs, and, in the process, also address several potential limitations of the prior work. The new proposed strategies that were modified include: 1) mailed invitation to complete an enclosed FIT in English and Spanish, 2) low literacy pictorial home-based FIT completion instructions, 3) FIT result reporting to patient and primary provider via culturally sensitive means (e.g., by phone and in person, not via mail), and 4) telephone assistance with colonoscopy referral and completion for individuals with abnormal FIT. To improve on the prior strategy, first, telephone assistance will be done by SYHC-based patient navigator, whereas in our prior work telephone assistance was done by a university-based nurse and medical assistance. Second, we have revised our English and Spanish-language invitation letters for use in SYHC's clinic population, that is largely a low income, unacculturated and low literacy population. Third, we will streamline the phone follow up required. The prior intervention utilized two automated, and up to two live telephone calls within 3 weeks of mailed invitation to promote screening. Because automated phone reminders may not be able to be reliably implemented across FQHCs, we will not include this approach in the intervention. Further, an increased, 4-5 week window for delivery of reminder phone calls will be allowed to increase the chances of feasible implementation. Fourth, we will develop a process for referring individuals with abnormal FIT for diagnostic colonoscopy outside of SYHC based on best practices currently utilized by the clinic for breast and cervical cancer screening and follow-up. This step is critical, because FQHCs generally have to refer elsewhere for specialty services. Prior to initiation of the randomized trial, we will, in additional preparation to research work, conduct a focus group with a random sample of 30 patients meeting inclusion/exclusion criteria (men and women, age 50 to 75, not up-to-date with screening) recruited from SYHC waiting rooms to review the interventions and study materials to help fine tune the outreach strategy. As part of this process, we will procure feedback on additional features (such as inclusion of links to internet videos on how to complete the FIT kits, timing of follow phone calls during the day/evening) that might improve the effectiveness of the mailed FIT strategy.

Inreach strategy: We have similarly adapted prior inreach strategies tested by our group in the past for the specific goal of promoting CRC screening awareness and completion.(38) For example, lessons learned from a prior breast cancer navigation study used by the partnership at SYHC show that the average patient load a navigator can manage per week is roughly 10 to 12 given the extended time needed for one-on-one patient empowerment, motivation, education, and follow-up to link patients with appropriate care. In addition, the navigation assistance required to initiate screening is quite often less than that required for follow-up to abnormal exams (e.g., which requires diagnostic colonoscopy at an external specialty care site and the potential for cancer treatment) due to the individual psychosocial barriers associated with seeking treatment (e.g., disbelief in efficacy of treatment, myths about cancer, unawareness of resources available etc). This research suggests that culturally appropriate interventions such as in-depth patient navigation can facilitate Latinas' successful entry into, and progression through, the cancer care system and improve time from screening to diagnosis. As with our mailed FIT strategy, prior to initiation of the randomized trial, we will conduct a focus group with a random sample of 30 individuals meeting inclusion/exclusion criteria for the trial to review the interventions and study materials to help fine tune the inreach strategy.

Pilot work summary. Our pilot work demonstrates that the proposed work is feasible, that we are fully committed to seeing the work through, and that we have taken significant steps to optimize our proposed strategies for the target population. Though our prior work and pilot work has been substantial, we recognize several limitations that we will address in the process of the current work. First, while we have developed our intervention and intervention materials through community-based participatory research strategies, guided by prior work and pilot work, we have not yet pretested the near-final versions among individuals sampled from the target population. Second, key informant patient interviews were conducted among women, but have yet to be conducted among men. These two limitations will be addressed as part the research approach outlined below.

INNOVATION

The proposed research is innovative for several reasons:

First, the study will be set at a within one of many FQHCs across the country which share a mission for caring for underserved populations and are expected to have an influx of newly insured patients who are candidates for screening. SYHC serves over 82,000 unique patients. 84% are Latino, 40% are uninsured, 51% have MediCal/Medicaid insurance, and 99% of patients are at or below 200% of the Federal Poverty Level. Just as at all FQHCs, many uninsured patients are expected to be newly eligible for insurance under the ACA.

Second, the FQHC selected serves a predominantly low income Latino population – a group that has particularly low screening rates and has been understudied with respect to interventions to increase screening.

Third, we will leverage our expertise and infrastructure across three institutions that have a commitment to improving health outcomes among underserved populations: SYHC, SDSU, and UCSD. Both through and outside of the U54 partnership, these three institutions have a sustained track record of funded community based research and publications (*See Rationale for Partnership for details*). For example, currently there are 2 SDSU/SYHC large RCTs at SYHC testing the chronic care model for childhood obesity and multiple cardiovascular disease (CVD) risk factors. There are also currently 2 cancer-screening promotora-based and navigation-basedprojects at SYHC in partnership with SDSU and UCSD. Theses and prior studies demonstrate the feasibility of conducting research in this setting.

Fourth, we propose to test whether inreach and outreach interventions can be effective for increasing CRC screening among low-income Latinos and others served by FQHCs. To date, there are no published examples that have compared the relative effectiveness of inreach vs. outreach interventions for boosting screening, even though these approaches require disparate resources.

Fifth, we will conduct our study using a randomized controlled trial design that will allow our study to not only determine whether inreach and outreach strategies can be effective, but also provide valuable data regarding whether there is an interaction associated with using inreach and outreach strategies combined. To date, there have not been randomized trials examining whether a combination of inreach and outreach might be synergistic for promoting CRC screening – such a combination might be required to achieve Healthy People 2020 goals for screening 70.5% of the population.

APPROACH

Conceptual Framework: The conceptual framework proposed from this study stems from the Chronic Care model with emphasis on re-design of the clinical delivery system, decision support and enhance clinical information systems with an application to proactive promotion of clinical preventive services (Figure 1)(39).

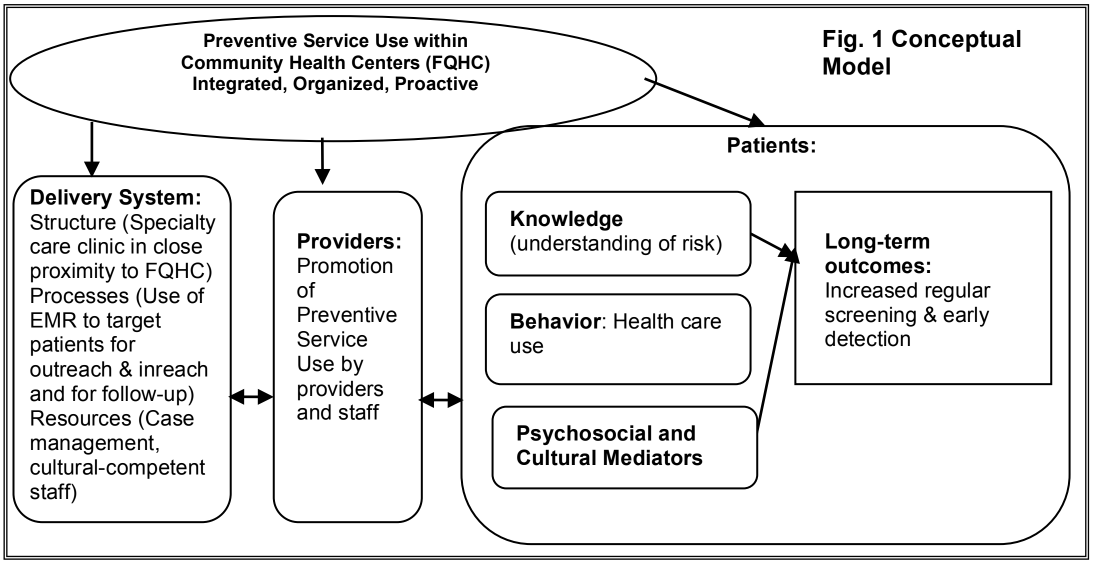

Fig. 1 Conceptual Model

Overview: We propose a randomized trial of a) an inreach strategy, b) FIT outreach, c) the inreach strategy plus FIT outreach, and d) usual care for increasing CRC screening among individuals age 50 to 75, not up to date with screening served by the SYHC. In Aim 1, we will test the impact of these strategies on screening completion (alone and together) among individuals not up to date with screening at SYHC. The primary outcome will be screening completion, defined by completion of a CRC screening test (home fecal immunochemical test, home guaiac fecal occult blood test, sigmoidoscopy, or colonoscopy) within 6 months of randomization. We will assign 162 patients (n=648 total) to each group. In Aim 2, we will conduct a process evaluation to examine the interventions' reach, effectiveness, acceptability, feasibility, and sustainability following the RE-AIM framework.

Community-based Research Setting. This study will take place at **San Ysidro Health Center, Inc., (SYHC),** a federally-qualified community health center (CHC), located in the community of San Ysidro in San Diego County, California's most southern county, less than 1 mile from the U.S.-Mexican border entrance to Tijuana, Baja California Norte, Mexico. According to the 2010 United States (U.S.) Census, Latinos comprise the second largest ethnic group in the U.S and over 37% of Californians and about 29% of San Diegans are Latino; yet > 70% of the South San Diego communities of San Ysidro, Chula Vista, and Imperial Beach, are Latino(40). SYHC provides comprehensive health care to 85,731 registered patients annually in South and Central San Diego through a service delivery network of 9 primary care clinics, 3 high school clinics, 2 HIV centers, 1 adult day health center, 5 WIC centers, 3 mobile clinics, 6 dental clinics, and 6 behavioral health service centers. SYHC's patient profile is predominately Latino (first, second and third generation), with high rates of: poverty, uninsured individuals, low education levels, and Spanish speaking households. In 2013, SYHC's patient population profile was highlighted by the following demographics: 76% of SYHC patients were Latino (65,440); 90% of patients lived at or below 100% of Federal Poverty Level (76,982); 53% of patients were uninsured (45,103); and 32% of patients were ages 0-12 (27,068).

Approach, Aim 1. In Aim 3, we will test the impact of our inreach and mailed FIT outreach strategies on CRC screening completion using a rigorous, randomized controlled trial design.

Prep to research focus groups. As previously mentioned, prior to initiating recruitment for the randomized trial, we will conduct focus groups among a random sample of 30 SYHC patients recruited from waiting rooms to review our outreach and inreach strategies, and fine tune the interventions. Key points of feedback will include clarity of intervention materials, completeness of key educational components, and any need for supportive components.

RCT inclusion/exclusion criteria. We will **include** individuals age 50 to 75 years, with one or more SYHC visits in the last year, at average-risk for CRC but not up-to-date with screening, insured by a MediCal provider, Medicare, or private health insurance. We will **exclude** individuals with personal history of CRC or colorectal polyps, as well as the uninsured. Uninsured individuals will be excluded because in absence of health insurance, we cannot guarantee that screening (and cancer care if CRC is found) will be financially possible. Inclusion and exclusion criteria will be applied through queries of the SYHC EHR.

Identification of candidate patients and recruitment. Using the SYHC EHR we will enroll and randomize 648 individuals meeting inclusion/exclusion criteria: 162 to usual care, inreach, mailed FIT outreach, and the inreach strategy plus FIT outreach, respectively (see sample size and power calculations below). A waiver of documentation of informed consent will be obtained for randomization and intervention delivery based on two primary factors: 1) goal of increasing screening for as many individuals as possible, and 2) scientific advantage of observing as close to “real world” impact of the planned strategies on asample of patients. We reviewed with our Institutional Review Board a potential strategy for complete waiver of informed consent, but were advised that maximizing patient autonomy and awareness of potential loss of confidentiality associated with research data collection merited at minimum a one-page informational research “fact sheet” that would provide patients with information about the research project. In the letter, patients will be the option to specifically note a desire not to participate in the intervention or subsequent data collection. Recruitment will continue until a sample size of 162 individuals per group who do not opt out of the research is achieved. In our primary, intent to screen analysis, we will analyze all randomized individuals who do not opt out of the research.

The EHR will be queried 4 times over a 1 year period. At time of each query 1/4 of the target sample will be identified and randomized, and have the assigned interventions initiated. Each group will be followed for 12 months for the primary outcome: completion of any CRC screening test (guaiac fecal occult blood test, FIT, sigmoidoscopy, or colonoscopy), measured by evidence of screening documented within the EHR. Thus, the total recruitment period will last 12 months, and the duration through completion of 6 month follow up of all patients will be 24 months. Measurements will include demographic information (race, ethnicity, sex, and age), number and location of health center visits, primary provider, and comorbid medical conditions. In secondary analyses, we will determine whether screening rates vary across these characteristics, and also assess whether for significant interactions between characteristics and intervention effects.

Analytic approach and sample size, Aim 1. We estimated the sample size for 5 comparisons (usual care vs. inreach, usual care vs. outreach, usual care vs. inreach + outreach, inreach + outreach vs. outreach alone, and inreach + outreach vs. inreach alone), assuming alpha = 0.01 across all groups and power $\geq$0.8. For these assessments, we assumed the following rates of screening on follow up among individuals not up to date at baseline: 10% for usual care, 25% for inreach, 25% for outreach, 45% for inreach + outreach combined. The 10% rate for usual care and 25% estimate for outreach were conservative assumptions based on our previously cited work (30). The 25% rate for inreach was a conservative estimate based on observations that inreach interventions such as patient navigation have boosted screening completion (among patients referred for colonoscopy) by 41 to 78%. Finally, the 45% rate for both interventions combined was considered the minimal clinically significant difference that would justify implementing two different interventions for increasing screening. Under these assumptions, we computed need for a sample size of n=648 patients (n=162 for each group) to have sufficient power for all primary comparisons of interest.

The primary outcome is completion of any CRC screening test (guaiac fecal occult blood test, FIT, sigmoidoscopy, or colonoscopy) within 12 months of randomization. The analytic approach taken will depend on whether or not an interaction exists between the outreach and inreach strategies on screening completion. If no interaction is present, screening rates for inreach vs. usual care and outreach vs. usual care will be compared using a Chi-square test of proportions, requiring p<0.01 for statistical significance. If interaction is noted, we will compare screening rates with a Chi-square test of proportions for inreach without outreach vs. usual care, as well as inreach with outreach vs. usual care separately, using a p<0.025 to indicate statistical significance. In both cases (interaction or no interaction), secondary comparisons will include inreach plus outreach vs. usual care, as well as inreach plus outreach vs. either strategy alone. We will conduct additional analyses treating screening completion as the dependent variable, and examine the relationship of group assignment, demographic characteristics, primary provider, and clinic visit frequency to this outcome. Factors associated with screening completion on univariate analyses will be considered as part of a logistic regression model examining factors independently associated with screening completion; in the case of interaction by group assignment a term for interaction will be included in our models. Additionally, interactions between other factors (e.g. gender, age, language preference, income, inreach strategy and frequency of clinic visits) will be considered.

Approach, Aim 2 Process Evaluation. Following the RE-AIM framework(41-43), a quasi-experimental process evaluation of intervention programs is proposed as part of the research protocol using validated measures developed in previous studies(44). This process evaluation is designed to examine the intervention’s acceptability, feasibility, and sustainability(45-47). Process measures include: intervention fidelity, recruitment and retention issues, dosage delivered and received, participant satisfaction, and *navigator* perceptions on areas for improvement in each one-on-one session. Dr. Castañeda, Ms. Sumek, and Ms. Espinoza will lead trainings to ensure intervention fidelity and standardized intervention delivery and dosage.

Team Management Plan. The study team includes Samir Gupta, Greg Talavera, Sheila Castañeda, Kristi Wells, Lin Liu, and Caryn Sumek. All have extensive experience with conducted research and promoting health among underserved populations. The research team currently has 2 NIH- funded and 1 ACS funded RCT studies at SYHC focusing on chronic disease, and cancer navigation (**see Biosketches**). Successful recruitment, intervention, and measurement methods and from these studies will be used in the proposed study for formal protocol development. The team will work collaboratively to set goals, timelines, and achieve study objectives. Drs. Talavera, Castañeda, and Wells will lead the final prep to research work required for finalizing study interventions. Dr. Gupta will lead planning and evaluation of Aim 1. Dr. Liu will serve as the lead biostatistician for analyses. Dr. Castañeda will lead the Aim 2 process evaluation. Ms. Sumek will play a critical role in leading the execution of activities under Aims 1 and 2 at the SYHC setting, including day-to-day management of study activities and interventions. All investigators will participate in analysis, interpretation, and publication of results.

Threats to Validity. Contamination due to the potential exchange of information between the intervention groups is a recognized threat to the integrity of the proposed study design due to nature of the study setting. Evidence from our pilot work suggests this has not been an issue to date. The SYHC has over 90,000 registered patients that it serves in the target area. As recruitment proceeds, eligibility screening will include examining if family members are already participating in the proposed study. The staff selected for the interventions have comparable experience working within the community of interest, knowledge and training of selected topics to be covered during the navigation sessions, are bilingual (Spanish/English) and bicultural (Mexican-heritage). Findings would have external validity for other community health center settings, but limited validity to organizations that target middle and upper class populations.

Data Management and Quality Control. Data management will be an on-going activity designed to ensure the highest quality data possible. Activities include data-coding, computer data entry, data quality control and tracking, data confidentiality and development of data files for statistical analysis. Prior to data entry, forms will be examined for completeness and accuracy. A tracking system will be developed to ensure all forms have been administered to participants. Completed forms will be entered into the database using a double data entry verification system. All identified errors will be resolved using the original hard data. All corrected fields will be noted for a detailed audit trail. Forms will be kept in locked files at the SYHC. Subjects will be assigned study ID numbers to be linked with SYHC medical record numbers on data management and data analysis files. No identifiable information will be used in reports. Data entered and stored will be periodically archived on the secure SYHC server. Data entry and analysis will be performed on Pentium-based computers. Analyses will be carried out using SPSS and SAS by the study statistician (Dr. Lin Liu at UCSD) who will receive a deidentified dataset from SYHC.

Timeline

Timeline (anticipated start date September 1, 2015)												
	Year 1				**Year 2**				**Year 3**			
TASKS	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4
Weekly academic-community partnership team meetings	■	■	■	■	■	■	■	■	■	■	■	■
Prep to research finalization of interventions	■	■										
Aim 1: Compare CRC screening rates associated with use of a) the inreach strategy, b) the mailed FIT outreach strategy (FIT outreach), c) inreach + FIT outreach, and d) usual care among n=648 individuals randomized across these groups.												
a. Random Assignment and Intervention (1/4 sample size per Q, Q1-4)			■	■	■	■						
b. Completion of 12-month follow up for outcomes							■	■	■	■		
c. RCT Analyses										■	■	■
Aim 2: Process evaluation										■	■	■
a. Process evaluation data collection			■	■	■	■				■	■	■
b. Process evaluation data analyses										■	■	■
Dissemination of results through community and academic conferences and publications, Preparation of subsequent grant applications										■	■	■

Impact and Next Steps. Several outcomes are anticipated as a result of this work. First, we will optimize two interventions for increasing CRC screening among underserved populations, particularly low income Latinos. We will then conduct a rigorous randomized trial of these interventions, including an assessment of whether inreach and outreach interventions are complimentary (and perhaps even synergistic) for boosting CRC screening among underserved populations. Locally, if successful, this program would be adopted into ongoing standard of care for patient preventive service utilization at SYHC. Integrated implementation is highly likely at SYHC because the program fits with the health center’s strategic organizational restructuring to align with health care reform and the new “Patient-Centered Medical Home” initiative, which promotes patient-centered integrative care, patient empowerment, care coordination, and a deeper focus on meeting clinical preventive service guidelines for all patients. Regionally and nationally, we will disseminate findings, lessons learned, and best practices to key community groups, research experts, and policy-makers facilitated through meetings of our local Council of Community Clinics, the National Association of Community Health Centers, the California Colorectal Cancer Coaltion, and national and international scientific organizations. Extramural grant applications to study impact of implementing our findings in usual practice will be proposed (particularly considering the large number of FQHCs based in San Diego County), along with grant applications designed to test novel and/or improved interventions for boosting screening informed by the results of our work. To inform public health policy, we also expect data from this and future work to be used for cost-effectiveness analyses of our intervention strategies for boosting screening, as well as to support funds for implementation of population-based screening programs to promote CRC screening.

RATIONALE FOR SDSU, UCSD, and SYHC COLLABORATION

The collaboration proposed for this proposal meets many of the ideal criteria specified in the U54 RFA.

First, we propose a *hypothesis-driven* cancer prevention outreach project focused on reducing disparities in CRC screening among low-income Latinos. Our proposal includes randomized trial that will allow for highly interpretable results, whether or not our hypotheses are correct. Setting the study at a FQHC ensures that the research is focused on an underserved population, but also increases the chances that findings might be implementable in other, similar settings across the nation.

Second, each of the partners (UCSD, SDSU, and SYHC) brings unique expertise and opportunities to the partnership. UCSD/Moores Cancer Center is represented by Dr. Gupta, a gastroenterologist with significant clinical expertise in CRC screening, as well as research expertise and experience in the use of randomized controlled trials to test intervention strategies for increasing screening among underserved populations. He is a member of the Reducing Cancer Disparities program at the Moores Cancer Center, and also plays a role in promoting awareness of screening disparities and implementation of strategies to address disparities at a national level, as exemplified by invitations to speak at scientific forums and publication of his work in high impact journals.

SDSU is represented by Drs. Talavera, Castañeda, and Wells, who are members of the Institute for Behavioral and Community Health (IBACH) and the Reducing Cancer Disparities program at the Moores Cancer Center. IBACH's mission since 1987 has been to build the evidence-base regarding social, cultural, and built environmental factors associated with chronic disease risk and design interventions that ameliorate these factors. Dr. Talavera is a Professor at SDSU, Graduate School of Public Health, and Co-Director for IBACH. Dr. Talavera is a bilingual bicultural physician scientist who has been working in the field of Latino cancer disparities for over 25 years. Since 1987, Dr. Talavera has collaborated with SYHC on ~15 health promotion/research projects that have involved clinic patients directly or the community they serve, 11 of which included subcontracts to SYHC and 4 of which were randomized clinical trials. His grants and contracts have totaled over $20 million in costs. Dr. Castañeda is a Research Assistant Professor at IBACH, and the Graduate School of Public Health at SDSU. She is a community psychologist who has specialized training in community empowerment, capacity building, community-based participatory research, mixed-methods, Latino cancer disparities, partnership development, and evaluation. Dr. Castañeda has held many key community-based leadership positions, such as for the NCI-funded *Redes en Accion* Outreach Core and Dissemination efforts. She has over 14 years of community-based cancer research experience and over 23 publications reflecting this experience. Dr. Wells is an Assistant Professor in the Department of Psychology at SDSU, and has graduate training in Clinical Psychology and Public Health, followed by post-doctoral training in behavioral oncology. Since 1997, she has been engaged in public health research focused on improving the quality of cancer care delivered to underserved populations, with a specific specialty in patient navigation and community-based research, reflected in over 50 publications in this area.

SYHC and its Center for Health Promotion and Research (CHPR) are represented by Ms. Sumek, the Community PI for this proposal. Ms. Sumek has training and experience in community-based program development, strategic planning, grant writing, health promotion, and community-based intervention implementation. Ms. Sumek manages several other grants funded by SDSU. Ms. Sumek will be responsible for overseeing the project planning and implementation, the research staff and project supervisor, and working with the academic PIs to ensure intervention fidelity and that the goals are met. CHPR currently houses 13 grant-funded projects, 2 clinic-wide initiatives, and ~40 staff. CHPR serves SYHC patients and the surrounding community by researching health issues that have a direct impact on disparities, and providing culturally- and linguistically-appropriate health promotion interventions. SYHC has organizational capacities necessary for developing, adapting, and implementing evidence-based programs, such as financial means, personnel and management structure.

Third, the partnership will provide valuable training opportunities; for learning about disparities and participating in research that resolves disparities, and for training under-represented minorities to become cancer research scientists. Drs. Gupta, Castañeda, and Wells have had significant success in research in the area of cancer disparities, yet none has served as PI of a NIH/NCI R01 grant; completing the proposed study will markedly increase the chances that both will be in a position to compete as a team for R01 level grants. Additionally, the project itself will offer numerous opportunities for underrepresented minority students from various levels (undergraduate, graduate, and post doctoral) to participate in research activities ranging from intervention delivery and data collection, to secondary analyses of study data to explore novel hypotheses. Thus, our partnership will work with senior investigators among the U54 partnership training core to utilize the results from this study to help advance our research careers

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