Health Literacy Interventions to Overcome Disparities in CRC Screening

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In the *Implementation* phase, we will begin targeted recruitment procedures at each clinic.

Inclusion/Exclusion Criteria. Inclusion criteria will be: 1) a patient of the identified clinics, 2) age 50 to 75 (based on ACS guidelines), and 3) can speak and understand English. Exclusion criteria include: 1) previous history of cancer other than non-melanoma skin cancer, 2) up-to-date with CRC screening according to ACS guidelines (FOBT every year, sigmoidoscopy every 5 years, or colonoscopy every 10 years), 3) a first relative family history that requires a more complete history and possible colonoscopy because of their risk factor (these patients will be referred to their provider for follow-up**),** 4) an uncorrectable hearing or visual impairment, or 5) too ill to participate. (See Appendix)

Recruitment. Clinic staff will ask consecutive patients scheduled for a routine primary care visit who are 50 to 75 if they are interested in participating in a CRC screening study. If a patient agrees, the RA will take them to a private room and prescreen them for eligibility using the Eligibility Interview (see Appendix). The RA will go through the consent process using a simplified consent form and administer the structured Baseline Interview. The entire process of screening, consenting, administering the interviews and giving the FIT test and educational materials will take approximately 30 minutes. Patients usually have at least a 45-minute wait, so clinic flow will not be disrupted.

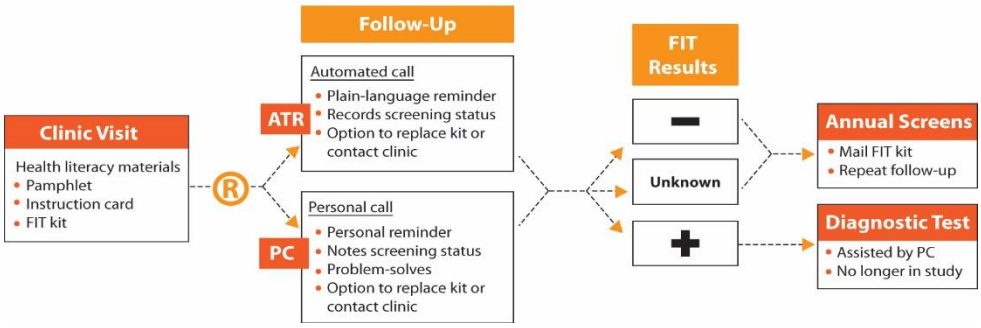
Health Literacy Best Practices. The RA will employ HL communication principles in providing a CRC recommendation and brief screening information using the CRC pamphlet and a FIT kit with simplified instructions and accompanying self-addressed, stamped envelope.[14,53,126-127] A scripted message and illustrations will model what the patient needs to do to complete the FIT. The RA will appropriately demonstrate, using the kit, and will suggest patients show the pamphlet and FIT kit to their provider that day and talk to them about screening. Follow-through with screening will be emphasized by telling participants they will receive a PC or ATR call within a day or two. Based on our experience with telephone interactions in our current R01, we will ask patients to write down two preferred phone numbers and a number of someone who will know how to reach them if they move and time of day they wish to be called. The RA will give them a business card with either the ATR information or the PC information on it so they will recognize the phone number on their caller ID. Annual screening will be further emphasized at enrollment by giving patients an empowering message about the benefits of completing a FIT annually and telling them they will be mailed a reminder letter and FIT kit and receive outreach phone calls in 12 and 24 months for the next two years as well as a post survey and satisfaction interview over the phone at 6 months.

Randomization. Randomization will be done at the patient level. Patients will be randomized by RAs to either the ATR or PC study arm. We will use a 1:1 permuted block randomization scheme within FQHC to assign patients to either study arm.

Automated Telephone Reminder Strategy. For patients randomized to the ATR arm, the RA will inform them they will receive an ATR call within two days to encourage them to return the FIT test. The patients will be contacted up to three time periods - within two days after enrollment; then also at four weeks and eight weeks after enrollment if they have not returned the FIT. A novel robust patient-friendly ATR using Twilio Interactive Voice System will remind the patient of the importance of completing and returning the FIT results and offer empowering messages to encourage screening completion. Automatic messages will use a person from south Louisiana speaking in a conversational tone rather than computer-synthesized speech. The automated instructions will tell the listener to press “1” if the call has reached the participant. There will also be an option where the patient can request another FIT kit be mailed to them, one to hear information on problem solving common problems with FIT completion or how to call the clinic if they have questions. No calls will be left on answering machines. The ATR system will keep track of the number of calls to each patient and their responses**.** *Successful completion of FOBTs have*

*been shown using ATRs in clinics serving **insured** patients;[84] this study seeks to determine if this approach would also be successful in clinics serving **low income, under and uninsured** patients in FQHCs.*

Figure 2. Intervention Overview



Prevention Coordination Strategy. For patients randomized to the PC arm, the RA will tell them a PC from LSUHSC will call within two days to remind them to return the FIT. One of two PCs located at LSUHSC will call patients to go over the FIT kit and address any barriers identified. Based on previous studies[68] and our own experience it is anticipated each PC will need to make 1-8 attempts to reach each participant. The PC will check the Quest lab website daily for results and record both positive and negative results in the tracking system. If the patient's FIT is not returned within 4 weeks, the same PC will call again to encourage completion. Following the same process/protocol if the FIT has not been returned by 8 weeks, the same PC will call to encourage completion and ascertain any barriers to completion. The PCs will use HL and motivational interviewing techniques described in the training section to enhance understanding and confidence and reduce ambivalence to completing and returning the FIT. The PCs will use the electronic tracking log (similar to one used successfully in current study) to track all contacts with each patient, barriers to care and actions and time taken to resolve these barriers.

FIT Results. Patients will use preaddressed postage paid envelops to mail their FIT kits to Quest Laboratories for processing. All FIT kits will be returned to this one lab. Research staff at LSUHSC (the centrally located RA for patients in the ATR arm and the PCs for patients in the PC arm) will check the Quest website daily for results and record both positive and negative results in the tracking system to update their follow-up database. The RA will update the ATR follow-up system to ensure follow-up calls for only those patients who have not returned their FIT. In the event of a positive result, the RA (in the ATR arm) or PC (in PC arm) will call the clinic nurse and speak directly with him/her, as well as fax the results, to ensure patients are called by the clinic and followed-up for additional testing. With negative results the RA and PCs will fax the results to the appropriate clinic nurse at each study site weekly. The designated clinic nurse at each clinic will put the FIT information in the patient's medical record. Patients will be mailed a letter from their clinic by the RA or PCs informing them of negative results.

Follow-up for Positive FITs. If patients in either arm have a positive screening test result, they will discontinue participation in the study and their clinic's protocol will direct their follow-up care. Patients with positive FITs will receive a recommendation for follow-up from their provider – most commonly a colonoscopy at a public hospital in LA.

In the PC arm, the PCs will continue to provide assistance to patients they have talked with who have been referred for diagnostic testing and possible treatment. The PCs will work with the clinic nurse and facilitate appropriate follow-up including calling and reminding patients about diagnostic appointments. The PCs will also work toward reducing the unnecessary complexity of patients' navigation and communication with public hospitals which can be 50 to 100 miles from the clinic.

Patients with a positive screen in either arm will continue to be followed for the length of the study. One of the investigators, Dr. Morris (a GI specialist who has conducted colonoscopies in several LA public hospitals) will assist with any problems in getting patients scheduled for colonoscopies.

Annual Screening FITs.12 months after patients returned their initial FIT (or if they did not return the FIT, 12 months after enrollment) they will be mailed a friendly letter to remind them that it is time for their annual CRC screening and that a FIT kit will be mailed the following week. During the following week the patients will be mailed the FIT kit with addressed stamped envelope and the educational pamphlet they received at enrollment. In the ATR arm, the central RA will mail patients the letter and materials. For follow-up ATR calls, we will use the same protocol as described for the initial screening (see Figure 2). In the PC arm, the PC will mail the reminder letter followed in a week by the FIT kit, stamped envelope and the same educational pamphlet the patient received at enrollment. The same protocol for initial screening will be used for the PC follow-up**.** The RA and PCs will track FIT completion rates and results and follow the same test results follow up protocol with the clinics and patients described in year 1. This protocol will be repeated for a third annual screening. (Figure 2)

Measurement. A draft version of the interview packet can be found in the Appendix**.** The baseline, in-person interview will include assessments of knowledge, beliefs, self-efficacy, as well as perceived benefits and barriers to screening, assessments of demographic characteristics, self-reported screening history. Most questions based on Social Cognitive Theory and validated in previous studies are designed to be easy to understand and answer. A similar structured interview used in our current R01 took 20 minutes to complete. In addition, patients will be asked to take the REALM, a reading recognition test which can be administered in 2-3 minutes. Patients will be compensated $15 for their time.

Six-month interview. The central RA will administer a telephone at six months post enrollment that will include the same CRC screening knowledge, beliefs, self-efficacy, benefits, and barrier questions as the baseline interview. **In addition, the central RA will administer the Satisfaction** Survey to assess patient satisfaction with the follow-up telephone reminder strategy they received. (See appendix) Our experience with similar phone interviews in our R01 indicates it is feasible and takes less than 30 minutes; a $20 gift card will be mailed to patients for their time.

Process Evaluation: Using data from the tracking information gathered from the ATR system and PC phone logs we will determine how many calls were made, how many calls it took to reach participants, how many required another FIT to be sent and what types of questions participants asked the PCs as well as if any ATR patients called the clinic with questions.

Knowledge, Beliefs and Self-Efficacy Outcomes. 40 CRC-related items that have been validated in a previous study by the authors[129] include questions assessing CRC knowledge (14 items), beliefs about susceptibility of CRC (3), benefits of screening (5), perceived barriers (7) and self-efficacy for screening behavior (3 items), and whether participants had received CRC screening education or a recommendation from a physician or ever completed screening (8 items). Knowledge items use a 'yes', 'no', 'don't know' or open-ended set of responses; belief, barrier and self-efficacy items incorporate a 5-point Likert scale.

Rapid Estimate of Adult Literacy in Medicine (REALM). Patients' reading ability will be assessed at baseline using the Rapid Estimate of Adult Literacy in Medicine (REALM), a reading recognition test which can be administered in 2-3 minutes. The REALM, the most widely used test to assess patient literacy in health care research, is highly correlated (.80) with the Test of Functional Health Literacy in Adults (TOFHLA) and is an indicator of functional health literacy. REALM raw scores (0-66) can be converted into reading grade levels that correlate with literacy skills[132-133] (see Appendix).

Colorectal Cancer Screening Outcomes. The primary study outcome is completion of initial and repeat CRC screening. A patient will be considered screened *initially* for CRC if he/she completes a FIT within 6 months of study entry. Patients in our study will be considered to have completed *repeat* annual CRC screening if they complete a FIT between 12 and 18 months of previous screen (or baseline interview, if initial FIT was not returned). This is consistent with current screening recommendations

We will conduct analyses using SAS v9.2 (SAS Institute, Carey, NC).

Study Design. Four FQHCs will participate, and randomization will be done at the individual patient level. We will use a simple 1:1 randomization scheme to assign patients to either study arm.

Sample Size Considerations. Based on initial screening data available to date in our ongoing study, a 45% initial screening rate is assumed for the ATR arm and a 55% rate for the PC arm. The required sample size to detect 45% versus 55% is 800 total or 400 per arm. For FOBT repeat screening, if the power is conditioned on having completed the initial screening, a sample of 180 subjects in the ATR arm (45% of 400 having initial screen) and 220 subjects in the PC arm (55% of 400 having initial screen) would have 80% power to detect a repeat screening rate of 20% in the ATR arm versus 33% in the PC arm. Two-tailed tests and a Type I error rate of 5% are assumed.

Statistical Analysis Plan. Prior to formal statistical analysis, all data will be summarized descriptively by study arm and by FQHC within arm. Frequency distributions of all categorical variables will be calculated. For continuous variables, means, medians, ranges and standard deviations will determine distributional properties and compliance with the normal distribution. Any extremely non-normal data will be log-transformed before comparative analyses. The statistical analysis plan will follow the specific aims. This is a two-group study, with the overall aim to compare screening rates and other outcomes between the two groups.

Generalized mixed model analysis[136-137] will be used. 'Mixed' indicates the study arm (intervention group) is fixed and FQHC is random. 'Generalized' indicates that different metrics of the dependent variable may be analyzed by selecting the link function. The model is for the primary outcome variable of screening for which a logit or cumulative logit link is used. In all analyses using these models, data at the patient level are used in the model, and the model adjusts for clustering by FQHC. The mixed model will be applied (using either the logit or identity link) to the categorical and continuous measured at baseline. The logit link will be used to compare dichotomous variables such as gender and race between groups. Continuous variables (e.g. age) will be compared using the identity link. These analyses are expected to show that the two study arms are similar at baseline. Should that not occur, then measures which are significantly different between the groups at baseline will be used as covariates in models for further comparative analyses. Traditional epidemiologic demographic variables (age, education level, income, and race) will be included as covariates.

Analyses for Aim 1. *Compare the effectiveness of the PC and ATR strategies to improve initial and repeat CRC screening in FQHC patients*. To assess primary Specific Aim 1, initial screening is a binary variable and a generalized linear mixed model analysis will be applied to evaluate the intervention effect adjusting for covariates. Within a subject, initial screening must occur within the first 6 months to count as 'initial'. Repeat screening will be analyzed as a 4-category variable using a cumulative logit link. The four categories will be (1) did not complete initial screening, (2) completed initial screening but did not complete follow-up screening (3) completed initial screening and completed follow-up screening (4) completed initial screening and completed follow-up screening but not on time (i.e. completed initial screening, did not complete 2nd year screening but then completed year 3 screening). The statistical significance of the fixed intervention effect will determine whether the two groups differ on screening outcomes. Separate models will be run for initial and for repeat screening.

Analyses for Aim 2. *Compare the cost effectiveness of the PC and ATR strategies for initial and repeat CRC screening*. Cost effectiveness analysis compares the marginal cost of the proposed intervention to its marginal benefits. To the extent that effectiveness can be measured in a manner that allows benefits to be directly compared to other interventions, it becomes more useful.

Therefore, it is often suggested that measures include a utility analysis that allows one to compare the change in quality-of-life years due to an intervention. For the current intervention, the endpoint is whether the patient is screened. The health and quality-of-life implications of screening will occur far beyond the endpoints of this study. We will focus on cost per additional patient screened, an outcome that can be compared to previous work in the area of CRC and other screening programs.

To assess primary Specific Aim 2, incremental cost effectiveness ratios (ICERs) will be calculated comparing ATR with PC. Cost for each of ATR and PC strategies will be determined in a manner similar to that used by Wolf et al.[138] Fundamental costs we recognize should be the same for both study arms include: 1) costs associated with printing and mailing health literacy materials, 2) orientation of clinic staff to the intervention and training of study personnel to perform tasks for disseminating materials, processing mailed FIT kits, and repeating these behaviors annually, 3) costs linked to tracking patients and phone calls as was done in the Khankari et al study led by Dr. Wolf.[138] Additional costs unique to the two study arms include, for the ATR arm: 1) cost of the ATR Twilio Interactive Voice System, 2) time for training central RA to maintain the system, including processing the data, tracking and mailing kits. For the PC arm, additional costs will include: 1) salary and fringe benefits costs associated with the hiring, training, and maintained staffing of the PCs, 2) any costs associated with office space, equipment, monthly costs and added staff time for supporting the PC in conducting calls and mailings. We will systematically track costs and work with clinics in both arms to get estimations of costs monthly, per time spent on each of the above activities, as well as actual costs incurred by others. We will also perform sensitivity analyses to examine modifications to certain assumptions related to costs in both study arms (i.e. presence of electronic health records for chart review, use of a medical assistant to serve as PC).

For each intervention (ATR, PC), components of the intervention identified above will have an actual cost attached to them. These costs will be added to obtain a total cost for each intervention. The difference in this total cost between PC and ATR will be the numerator of the ICER. The denominator will be the between group difference in the number of patients with initial screening, calculated by applying the observed initial screening rates to the average group sample size and taking the difference. The denominator will be calculated as the larger number minus the smaller number. The numerator will then be calculated in the same direction. A negative ICER will indicate that for a given intervention (determined by the direction of the calculations), more people are being screened for less cost and that intervention would then be the intervention of choice. A positive ICER will indicate that for a given intervention, more people are being screened for a greater cost. Wolf et al. set a benchmark of $200 as the ICER for an intervention that provided initial training and feedback to physicians over and above reminders through electronic medical records. A confidence interval for the ICER will be calculated using the methods described in Briggs & Fenn.[139] Separate ICERs will be calculated for the initial and repeat screening. For repeat screening, the numerator cost difference will be the same, but the denominator will be different. The denominator for the initial screening will be as described above (the difference in the number of patients completing initial screening between the two arms). The denominator for repeat screening will be the difference in the number of patients having repeat screening between the two arms, which is calculated by applying the observed repeat screening rates to the average group number initially screened and taking the difference.

Analyses for Aim 3. *Conduct a process evaluation of both interventions to investigate their implementation and identify any barriers.* The purpose of Aim 3 is to understand, in detail, to what degree either intervention was able to be implemented as intended, and whether any evidence can suggest further ways to improve upon these strategies. Data sources will include post-study interviews with the two PCs, clinical staff, research assistants, and data obtained from the

satisfaction survey with patients. Response to Likert scale items detailing satisfaction will be comparable among patients in each arm, therefore scores will be additive and treated as a continuous outcome that will be compared using t-tests and linear regression models. Other aspects of intervention fidelity that may be the same, including the rate of specific tasks or deliverables reaching patients (i.e. proportion of patients followed-up, proportion of requested FIT kits mailed) will also examined using chi-square tests to reflect dichotomous outcomes. In addition, since each intervention is unique, detailed qualitative reports that summarize overall impressions of the intervention, descriptions of any specific impediments or barriers that were identified during the study and suggestions for improvement will be organized and presented to the team for consideration. This process has been used by Drs. Davis and Wolf previously for another earlier intervention to promote CRC screening in a VA population.[140] We will follow a root cause analysis (RCA) framework for addressing and understanding and system-level failures that do occur with either intervention and to identify proper remediation. RCA is a structured problem-solving method often applied to resolve organizational problems that usually stem from ineffective policies and procedures. Dr. Wolf has also used this methodology successfully in understanding and addressing clinical trials issues.

Analyses for Aim 4. *Determine if the effects of either strategy vary by patients' literacy.* To assess literacy in Specific Aim 4, the analysis plan will be similar to that described for Specific Aim 1 except that a term for literacy level (at or below 9th grade versus above 9th grade reading level) and a term for literacy by arm interaction will be added to the linear model. The statistical significance of the interaction term would indicate that the intervention effects on screening differ by literacy level.

Analyses for Aim 5. *Explore patients' understanding, beliefs and self-efficacy toward CRC screening over time.* To assess the knowledge, beliefs and self-efficacy are dichotomous variables or variables measured on a 5-point Likert scale. The Likert variables will be dichotomized with dichotomization depending on the distribution. Our experience is that dichotomizing Likert data lends it to a more understandable interpretation of the results. While these measures will be compared between arms in a manner similar to the comparison of screening, further analyses will investigate inter-relationships between these measures taken at baseline and screening. These analyses will be done using mixed logistic regression analysis. Since we will be taking these measures at two points in time, we will analyze change in these dichotomous variables using conditional logistic regression within the general analysis framework described above. To determine whether these measures mediate screening outcomes selected, understanding, beliefs and self-efficacy measures will be entered as covariates into the models in Specific Aim 1 to determine whether study group remains significant after controlling for these measures.