

Increasing Colorectal and Breast Cancer Screening in Women

A. Specific Aims

The cancer burden in women could be significantly reduced by increasing participation in recommended screening for colorectal cancer (CRC) and breast cancer (BC) in all eligible women. Colorectal and breast cancers account for 36% of all cancer mortality among women in the United States.^(1, 2) Women diagnosed with localized-stage CRC or BC realize at least a 95% five-year survival, whereas those diagnosed with distant disease have only a 20% chance of living 5 years.⁽²⁾ Although regular CRC and BC screenings are widely available and a national priority,⁽²⁾ rates for CRC screening adherence are low and rates for yearly screening for BC have recently decreased. Nationally, only 52% of persons report having had CRC screening with either fecal occult blood test (FOBT) or endoscopy within the past 5 years.⁽³⁾ During the same time period, mammography rates have shown a disturbing decline; adherence for women ages 50 to 64 has declined by 7%, and for women older than 65 years the decrease has been 4.2%.⁽⁴⁾

A new paradigm of multiple behavior change is emerging that is supported by theoretical and practical considerations. Today's health care providers are challenged to encourage preventive care and early detection behaviors at the same time they are treating acute and chronic illnesses. There is limited opportunity for counseling on cancer screening during the average clinical visit. Multiple health behavior change research is emerging as a new model to change the way in which interventions can be packaged.⁽⁵⁾ To date, intervention trials have focused on only one behavior even though we know that screening behaviors for BC and CRC are related.⁽⁶⁾ If we can find an efficacious and cost-effective intervention to increase both BC and CRC cancer screening simultaneously, we can not only decrease overall cancer morbidity and mortality in women but do so in a more efficient and cost-effective manner. This research will test an intervention to simultaneously increase both CRC and BC screening using behavior change strategies and providing access to recommended screening tests by enabling appointment scheduling or mailing of FOBT cards through phone contact with a nurse who has access to their medical records.

Routine population-based CRC and BC screening are recommended for women over 50 providing an ideal situation to combine screening interventions. First, both screenings are recommended for women ages 50 to 75. Secondly, both screenings require an appointment outside of a regular health care visit. Third, research demonstrates that the behaviors are correlated⁽⁶⁾ and that common variables predict adherence to both screenings. Additionally, although cervical cancer screening is also recommended, this screening test is conducted during a health care provider visit and requires a thorough history of sexual activity and prior screening results. Cervical cancer incidence and mortality rates in the United States are extremely low and the American Cancer Society estimates that over half of the 65.6 million Papanicoulau tests done annually are not needed.⁽⁷⁾ Finally, appropriate testing for cervical cancer is most important in a younger age cohort--not women 50 and older.⁽⁸⁾ Therefore, this proposal will address innovative approaches to increase adherence to screening tests for two cancers that have the greatest impact on female cancer mortality in the United States – colorectal and breast cancer.

We are now ready to test a new paradigm that integrates interventions for two screening behaviors simultaneously. Our previous randomized trials demonstrated efficacy for interventions that promote screening for CRC and BC separately.⁽⁹⁻¹¹⁾ Using a theoretical paradigm for multiple health behaviors, we will build on previous work to develop an individually tailored interactive computer program that promotes CRC and BC screening simultaneously. We will test the program using a tailored interactive website (TIWeb). Because research has also demonstrated the effectiveness of telephone counseling to promote screening, we will test a cancer screening call (CSC) alone and in combination with the TIWeb. The CSC includes counseling tailored to the same constructs included in the TIWeb. In each intervention arm, women will have the opportunity to schedule the appropriate screening tests without a prior clinical appointment.

The proposed interventions will target female patients in a family practice-based research network who are 50 to 75 years of age, nonadherent to current CRC screening recommendations, and may or may not be adherent to BC screening. Nonadherence to CRC screening recommendations is defined as not having had one of the recommended screening tests (fecal occult blood test, fecal immunochemical test, sigmoidoscopy, or colonoscopy) in the appropriate timeframe.⁽¹²⁾ A review of records for 180,000 women in the targeted age group and practice plan found that 26% were nonadherent to CRC screening guidelines but were adherent to BC guidelines, 44% were nonadherent to both CRC and BC screening guidelines, 10% were adherent to CRC but

not to BC screening guidelines, and 20% were adherent (currently up-to-date) to both screening guidelines. Because the group that is adherent to CRC but not BC screening is so **small (10%)**, we will not have power to sufficiently test interventions with this group. However, some women who may be at higher risk for CRC because of family history will likely be included in the study because family history data is not readily available in the medical records. At baseline interview and during the intervention, these women will be considered at higher than average risk for CRC and colonoscopy will be recommended.

For women who are nonadherent to CRC screening guidelines but adherent to BC screening (Group A), the TIWeb and the CSC will encourage CRC screening by building on the women's success with regular BC screening. For women who are nonadherent to both CRC and BC screening (**Group B**), the TIWeb and the CSC interventions will promote both CRC and BC screening simultaneously. Research indicates that individuals who undergo one type of cancer screening are more likely to pursue other forms of screening,⁽¹³⁾ making a holistic approach to cancer screening efficient and consistent with what would happen in a routine preventive care visit. In the proposed study, we also will test the cost-effectiveness of each intervention arm and the intervention interactions with demographic and practice variables. Past research^(14, 15) has shown that interventions vary in both cost and efficacy, making the addition of cost-effectiveness analysis important for future translation to practice. We will use a 2X2 factorial design with women randomly assigned to receive one of the following: 1) usual care, 2) a TIWeb, 3) a Cancer Screening Call (CSC), or 4) a TIWeb plus a CSC.

Aim 1: Compare the efficacy (adherence and stage) of four conditions to promote CRC and BC screening among women ages 50 to 75: 1) usual care; 2) a mailed TIDVD; 3) a CSC, and 4) a mailed TIDVD + a CSC. All women will be non adherent to CRC screening and may or may not be adherent to BC screening. 50 **Group A (nonadherent to CRC screening guidelines but adherent to BC screening guidelines)**

Hypothesis 1 (Primary outcome): There will be differences in CRC screening adherence and stage of adoption, when controlling for adherence to BC screening at baseline, among women who are randomized to 1) usual care; 2) a TIWeb; 3) a CSC, and 4) a TIWeb plus a CSC.

Group B (nonadherent to both CRC and BC screening guidelines)

Hypothesis 2 (Secondary outcome): In the group that is nonadherent to both CRC and BC screening at baseline, there will be differences in adherence to both CRC and BC screening and stage of adoption, among women who are randomized to 1) usual care; 2) a TIWeb; 3) a CSC, and 4) a TIWeb plus a CSC.

Aim 2: Compare the cost-effectiveness of four conditions to promote CRC and BC screening among women ages 50 to 75: 1) usual care; 2) a TIWeb; 3) a CSC, and 4) a TIWeb + a CSC. Two groups of women will be included. **Group A** includes women who are nonadherent to CRC screening but adherent to BC screening and **Group B** includes women nonadherent to both CRC and BC screening.

Aim 3: Examine differences in intervention effects by knowledge, cancer screening beliefs, health status, demographic variables (age, race, education, and marital status), screening history, out-of-pocket costs for screening, baseline stage of adoption, health care site, and participant involvement in the intervention.

Hypothesis 1: *Interactions will be observed when intervention effects are examined by knowledge, cancer screening beliefs, health status, demographic variables (age, race, education, and marital status,), provider recommendation, screening history, out-of-pocket costs for screening, baseline stage of adoption, provider recommendation, and participant involvement in the intervention.*

Hypothesis 2: *Women receiving care at primary care practices that have on-site colonoscopy available will have greater CRC adherence than women receiving care at sites where on-site colonoscopy is not available.*

Our intervention approach will include interactive, tailored, and theoretically based interventions to promote appropriate cancer screening based on risk assessment and adherence status. We will use the theoretical model proposed by Noar for multiple health behaviors, which identifies common variables that predict multiple behaviors.⁽¹⁶⁾ If a woman needs only CRC screening, interventions will deliver messages that affirm her prior success with mammography while encouraging participation in CRC screening. For women who are currently nonadherent to CRC and BC screening recommendations, the intervention will address both screening behaviors, reflective of the clinical encounter women would have with their health care provider. We will also test for the effectiveness of the intervention to move women across stages of screening. Exposure to the intervention could move a woman from precontemplation (not thinking about having screening) to contemplation (considering screening). Past research has demonstrated that stage progression is an important outcome that ultimately leads to screening.⁽¹⁷⁾ In today's health care setting, addressing only one type of cancer screening with patients, if more than one is relevant and overdue, would constitute substandard preventive care. Providing a comprehensive and interactive preventive health intervention to motivate cancer screening during a single point of contact may be the most efficacious and cost-effective approach for increasing cancer screening rates.

B. Background and Significance

B.1. Prospective randomized trials have demonstrated that routine screening for both BC and CRC significantly reduce cancer mortality. Mortality and incidence for CRC and BC are higher than for any other cancers among nonsmokers in the United States.⁽¹⁸⁾ In 2009, approximately 24,680 women are expected to die from CRC and 40,170 women are expected to die from BC.⁽¹²⁾ Timely and routine screening is our best weapon against both CRC and BC mortality. Prospective randomized trials have demonstrated the efficacy of screening with fecal occult blood tests (FOBT) in reducing CRC mortality by over 30%.⁽¹⁹⁾ The removal of precancerous (adenomatous) polyps in the colon and rectum at the time of endoscopic screening has been found to decrease CRC incidence by 75% to 90%.⁽²⁰⁾ Additionally, mammography screening has been demonstrated to decrease mortality through early detection in randomized prospective trials conducted over the last 30 years. Eight major randomized controlled studies have collectively included more than 500,000 women in screening studies.⁽²¹⁻³⁴⁾ Women 50 or over who are routinely screened by mammography demonstrate a 30% reduction in mortality.

B.2. Screening for both CRC and BC is recommended for women 50 or older. Current guidelines for CRC screening recommend starting at age 50 and include 7 different test options for average-risk individuals, including: 1) annual FOBT, 2) annual fecal immunochemical test (FIT), 3) stool DNA test (sDNA), 4) flexible sigmoidoscopy every 5 years, 6) colonoscopy every 10 years, 6) double contrast barium enema every 5 years, or 7) CT colonography (virtual colonoscopy) every 5 years.^(1, 35) For persons at increased risk for CRC, screening colonoscopy is recommended.⁽³⁾ Although out-of-pocket cost varies by insurance plan, all insurers of women in this study include colonoscopy coverage for those at average or increased risk.

B.3. Research has identified common variables related to a woman's propensity to be screened for either CRC or BC. A description of these variables will be followed by a review of health promotion interventions that have been efficacious in promoting CRC and BC screening. Additionally, we will review the theoretical support for tailored interventions, including our preliminary studies that demonstrated efficacy in increasing CRC and BC screening. Tailored interventions are defined as "any combination of information and behavior change strategies that are designed to reach one specific person, based on characteristics that are unique to that person." Information is also tailored to the outcome of interest - in this case CRC and BC screening.⁽³⁶⁾ Research supports tailored and interactive CRC and BC screening interventions as a promising strategy for influencing attitudes and behaviors. Research also supports proactive outreach by the health care setting in the form of Cancer Screening Calls (CSC), which have yielded significant increases in mammography adherence.⁽¹¹⁾ Goldstein (2004) has specifically addressed an evidence-based strategy for increasing behaviors that includes arranging or scheduling appointments or providing increased access to care.⁽³⁷⁾ Finally, an important component of screening interventions is the cost of delivery. We will provide support for adding the cost-effectiveness component as well as rationale for comparing the various intervention strategies.

B.4. Common predictors including risk, benefits, barriers, and self efficacy have been identified for both BC and CRC screening. Beeker⁽³⁸⁾ conducted 14 focus groups to identify knowledge, attitudes, and beliefs about CRC screening. Respondents had little knowledge about their own risk or the benefits of screening. Barriers such as embarrassment, inconvenience, physical discomfort, and concern about being able to actually

complete screening tests were cited. Knowledge about cancer and knowing someone with CRC have been related to adherence to both FOBT⁽³⁹⁻⁴¹⁾ and flexible sigmoidoscopy.^(39, 42) Manne⁽⁴³⁾ studied the relationships of the Transtheoretical Model (TTM) and Health Belief Model (HBM) variables to stage of screening and adherence for CRC, finding that perceived risk, benefits, and barriers, among other variables, were related to both stage of screening and adherence. In prospective studies of patient or community populations, the demographic characteristics of being older (over 70 years of age), being male, having less education, and being of low income were consistently negatively associated with FOBT. Adherence was lowest in persons aged 70 or older. However, a gender bias favoring male utilization of endoscopy was suggested when authors found that men are more likely to be screened than women.^(44, 45) Studies have shown the predictive value of higher perceived risk and perceived benefits, and lower perceived barriers for CRC screening for both average-risk individuals and those at increased risk due to family history.^(43, 46, 47)

Descriptive research has identified beliefs such as perceived risk, benefits, and barriers to BC screening, as well as self-efficacy as important in predicting mammography adherence. Younger age and higher education are also reported to predict increased adherence.⁽⁴⁸⁻⁵⁰⁾ The barrier "fear of cancer" has emerged as a salient factor to be considered when evaluating the predictors of BC screening.^(50, 52) The same beliefs - perceived risk, benefits, barriers, and self-efficacy - are related to stage of screening for BC. Skinner⁽⁵³⁾ and Lauver⁽⁵⁴⁾ both found beliefs were significantly different among women in precontemplation (no intent to screen), contemplation (intent to screen) or action. In both studies, higher perceptions of benefits and fewer perceived barriers predicted a more advanced stage of mammography adoption. Finally, recommendation by a health care provider has been consistently linked to screening.^{(55), (56-63)}

B.5. Research has supported the efficacy of tailored interventions for increasing CRC and BC screening.⁽⁶⁴⁻⁶⁶⁾ Tailored interventions can be delivered in several ways. King et al.,⁽⁶⁷⁾ Marcus et al.,⁽⁶⁸⁾ and Rimer et al.,⁽⁶⁹⁾ along with the proposed investigators,⁽⁷⁰⁾ have delivered tailored mammography counseling interventions by telephone and found significant increases in mammography use. A recent innovation is using computer-tailored print materials created specifically for individual recipients based on their responses to particular questions.⁽⁷¹⁻⁷³⁾ Randomized controlled intervention trials comparing tailored and non-tailored print communications have demonstrated that tailoring enhances intervention efficacy in promoting mammography use.^(74, 75) For example, Skinner and colleagues⁽⁷⁵⁾ found that among low-income women nonadherent at baseline but considering a mammogram, those who received tailored print communications were much more likely to have a mammogram than those whose print communications were not tailored (75% vs. 32%). Lipkus et al.,⁽⁶⁴⁾ and Rakowski et al.,⁽⁶⁵⁾ also found an advantage in tailoring mammography interventions. Clark et al.,⁽⁷⁶⁾ demonstrated the advantage of stage-matched tailoring as compared to non-stage-matched tailoring.

Interventions that have been tailored to individuals' beliefs about CRC screening have also been efficacious in increasing CRC behavior. Jerant⁽⁷⁷⁾ found that a tailored interactive computer program significantly increased beliefs and stage of readiness for CRC screening. Studies that have addressed variables theoretically related to CRC screening behavior such as knowledge, health beliefs, and attitudes have yielded high rates of participation in FOBT and sigmoidoscopy.⁽⁷⁸⁻⁸²⁾

B.6. Technology has opened a new paradigm for tailoring health messages to individuals. Interactive computer programs, whether delivered via TIWeb or some other platform, allow linkage of participant responses to individualized messages that are then delivered to the user in real time.⁽⁸³⁾ There is evidence that, regardless of age, education, or socioeconomic status, people like these interactive programs.⁽⁸⁴⁻⁹¹⁾ Advantages of interactive programs include not requiring the presence of an educator or nurse counselor, private and consistent information delivery, and the ability to meet the needs of people with low literacy.

TIWeb allow users to interact with the program using a mouse or keys on the keyboard, which would likely be familiar to those with computers or experience with computers. The number of households with broadband internet is now 67%.

B.7. Intervention messages can be tailored in real time through a proactive counseling call from a health care provider and have been used with both CRC and BC screening.^(56-63, 94, 95) Stone found that use of a designated staff member to focus on patient reminders increased CRC screening by an odds ratio of 2.75.⁽⁹⁵⁾ Many studies have tested the effect of telephone interventions among both healthy community-residing adults and cancer survivors and found telephone counseling to be as effective as face-to-face encounters.⁽⁹⁶⁾ Taplin

found that a brief reminder call from a health care staff member that included an opportunity to schedule a mammogram significantly increased mammography adherence over a simple reminder postcard.⁽¹¹⁾

B.8. Cost-effectiveness analysis of screening interventions is necessary to guide decision-makers toward the most efficient means to achieve important health behaviors and outcomes and the costs of providing the interventions. Population screening for CRC has been shown to compare favorably to other expenditures in the health care field.⁽⁹⁷⁻⁹⁹⁾ Another important issue is the cost-effectiveness of interventions to increase CRC screening. Cost-effectiveness analysis for intervention delivery is defined as the cost per individual screened.⁽¹⁰⁰⁾ Abrams (1999) identifies cost per incremental gain in outcome as one of the key factors in translating research. Unfortunately, almost a decade later, we still lack data on the cost-effectiveness of tailored interventions as compared to other more commonly used practice interventions.⁽¹⁰¹⁾

An important component of this proposal is the estimation of the efficacy and cost-effectiveness of interactive interventions tailored to beliefs and stage of adoption alone and together. Similar to other studies, the outcome to be compared in the cost-effectiveness analysis is the proportion of participants in each of the intervention arms who have had recommended CRC or BC screening tests during the six-month period following initial intervention. Using this design, we will be able to determine if aTIWeb, a CSC, or a TIWeb+ CSC will significantly increase adherence for CRC and/or BC screening and at what costs. If efficacy and cost effectiveness relative to other interventions are demonstrated with the TIWeb program, it could be promoted at health care visits. If the CSC increases screening at an acceptable incremental cost when added to the TIWeb, office staff could make telephone counseling calls to participants from the health care setting after the TIWeb.

B.9. Researchers have tested the effectiveness of intervening simultaneously for multiple health behaviors. In 2005, Emmons et al. reported that a telephone-delivered intervention which focused on six behavioral risk variables for colorectal cancer was effective in promoting change.⁽¹⁰²⁾ In a different research study, a home-based intervention to change smoking, high fat diet, and sun exposure produced significant changes as compared to a control.⁽¹⁰³⁾ Recently, a series of articles addressed multiple behavior research.⁽⁵⁾ Behaviors included weight management, smoking, exercise, and fruit and vegetable intake.⁽¹⁰⁴⁻¹⁰⁶⁾ All interventions that addressed multiple behavior change were effective.

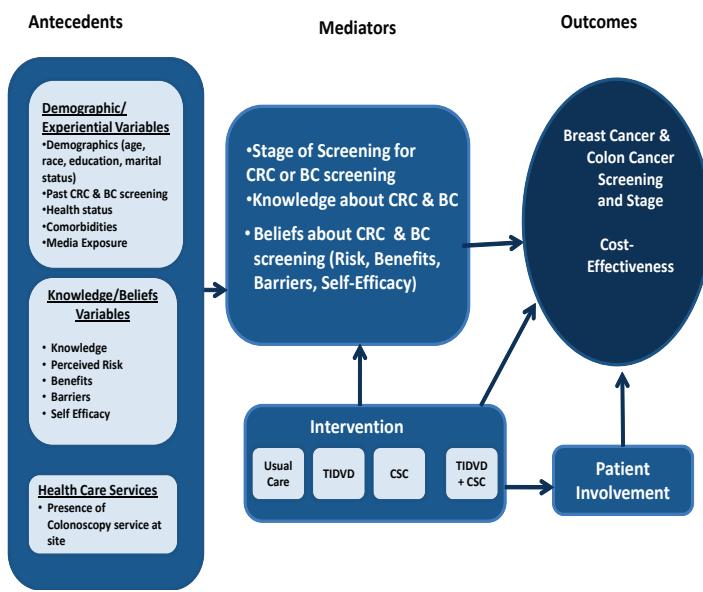
Theoretical considerations for multiple behavior change have been presented by Noar et al. (2007).⁽⁶⁶⁾ A key theoretical consideration is to identify common principles or variables that have been found to predict behaviors. An example includes the variables of benefits and barriers (pros and cons) that are common to many theories. Health behavior theories have driven many interventions to change single behaviors.⁽¹⁶⁾ Most theories, however, include a common set of variables that determine behaviors as is the case with BC and CRC screening. If similar variables do predict multiple behaviors, interventions that address several behaviors can be effectively combined. Additionally, research has demonstrated the superiority of simultaneous interventions over sequential interventions when addressing multiple behavior change.⁽¹⁰⁷⁾

The use of a multiple behavior theoretical approach is especially appealing when addressing behaviors that are conceptually similar-such as cancer screening behaviors. For women, guidelines support population screening for both BC and CRC. Screening for BC and CRC have many commonalities and the behaviors have been found to be correlated.⁽⁶⁾ Additionally, common variables are known to predict both screenings. These variables include perceived risk, benefits and barriers to screening, as well as self-efficacy. Risk for both cancers is driven by age and family history, and routine screening is supported for both starting at 50 years of age. Both screening behaviors include benefits of finding cancer early, thus decreasing the need for aggressive treatment and saving the individual's life. Barriers, or cons to each behavior, are strongly related to action but vary depending on the screening behavior.

The common variables that will be used to deliver simultaneous messages originate in the Health Belief Model (HBM) and the Transtheoretical Model of Behavior Change (TTM)-both of which have demonstrated efficacy with single behaviors. The multiple behavior theoretical approach will build on this previous work by identifying the common variables that have predicted behavior change and applying these tailoring of these variables simultaneously to CRC and BC screening. The variables have been integrated into a conceptual framework that will guide the proposed study (see **Figure 1**) and include: perceived risk, perceived benefits and barriers to a health behavior and self-efficacy to accomplish the behavior.^{(108, 109), (110)} The belief variables of perceived risk, perceived benefits and barriers, and perceived self-efficacy have been used in previous interventions and found

to predict both CRC and BC screening behavior.^(14, 38, 40, 43, 50, 111) Antecedent variables are identified in the HBM and include knowledge, age, education, and marital status, all of which have been related to both CRC and BC screening.^(1, 53, 112-114) Race has been included as a demographic variable given the relatively greater mortality from both cancers in African American women. Although research has focused only on the most recent history of a behavior, we will also incorporate the lifetime screening behavior for CRC and BC. Changing or initiating a health action involves a gradual change in decisional balance between the pros (benefits) and cons (barriers). In our proposed interventions, decisional balance will be addressed through communication directed toward the perceived benefits and barriers for the specific screening tests needed by each individual recipient. (See **Appendix A**)

Figure 1. Theoretical Framework



Tailoring messages to individuals' stage of readiness has been found to have important cost-effectiveness implications.^(15, 115) Several research studies have used the TTM to develop interventions to increase mammography screening,^(10, 14, 116) including intervention trials conducted by the investigators.^(14, 117, 118) More recently, the TTM has also been supported in the context of CRC screening.⁽⁴⁷⁾ The definitions and validation of mammography stage of adoption have been consistent across several studies.^(65, 119, 120) Criteria for defining stage of screening adoption for BC screening are consistent with the NCI consortium stage definitions and were used to develop CRC stage definitions (see **Table 6**). Previous research has indicated that barriers, such as fear of radiation, differ between women in the contemplation stage and those in other stages. For instance, women who are in the precontemplation stage may not initially be

concerned about barriers because they have not yet developed perceptions of risks or benefits to mammography or CRC screening, whereas women who are in the contemplation stage have begun to think about their barriers to having the tests.⁽⁴⁹⁾ Risk and benefits messages are programmed before barriers. If women are in precontemplation, the program will address risks and benefits of screening before barriers. If women are in contemplation, their messages about the risk and benefits constructs will be brief and the program will focus on barriers.

B.10. Communication theory will inform intervention delivery. Common variables guide the development of messages that participants receive in the TIWeb. Persuasive delivery of these messages has been informed by well established and previously tested communication theories. Several factors determine whether the message content is relevant to the belief system of the message recipient.⁽¹²¹⁾ Petty and Cacioppo⁽¹²²⁾ identified the five key components that influence persuasion. Person Factors include the characteristics of the individuals who are the targets of the behavior change intervention. Characteristics of the audience relevant for this application include age, race, marital status, and education as well as beliefs and past screening history. Message Factors include the content of tailored messages that are theoretically driven. Source Factors include the person or mechanism through which the message content is delivered. Channel Factors are the mechanism through which messages are delivered. These include the TIWeb platform to be used for delivering the interactive program, chosen because it enables us to deliver health messages in a variety of ways, including graphs, video clips, and storytelling. We will also test the addition of a CSC to determine additive effect. Finally, Participant Involvement in Message Processing is an important prerequisite for attitude and behavior change. The key components that enhance participant involvement include relevance of the messages, engagement, receptivity, and integration of new information with old.

C. Preliminary Studies

Dr. Champion has a strong history of developing and demonstrating the efficacy of tailored mammography interventions and of collaborating with Drs. Rawl, Springston, Zollinger, and Monahan. Dr. Rawl, the study Co-I, conducted several CRC studies and collaborated with Dr. Champion on both BC and CRC screening studies. *Preliminary data presented below support tailored interventions significantly improving adherence to both BC and CRC.*

The efficacy of a computer-tailored printed physician recommendation letter plus information packets versus tailored telephone counseling for mammography adherence was tested with women accrued from two managed care sites (R01NR04081, 1996-2000).⁽⁷⁰⁾ At two months post-intervention, percentages of participants in the action stage (i.e., recently screened) differed across groups; 1) usual care- 26%, 2) tailored letter- 38%, 3) tailored telephone- 36%, and 4) tailored letter plus telephone counseling-40%. Compared to usual care, all intervention groups significantly increased mammography adherence (odds ratios 1.60 to 1.91). We also considered stage movement by intervention. That is, baseline precontemplators could move one stage to contemplation or two stages to action post-intervention. Contemplators could move forward one stage and become adherent, or women could remain in their current baseline stage. Analyses controlling for covariates showed that all intervention groups moved women forward in stage. For contemplators, the combination of telephone and print was clearly the most effective intervention for promoting both 2-month stage movement (OR = 2.5, p < .0005) and 4-month adherence (OR = 2.1, p = .0003). It appeared that adding printed material to the phone messaging had an additive effect and that it may be a useful intervention to move women forward in stage even if adherence is not the outcome.

The investigators developed and tested a tailored interactive computer program for low-income African American women who were clients of a multi-service community center in Indianapolis (R01CA77736, 1999-2005). The program content addressed perceived breast cancer risk and perceived mammography benefits, barriers, and self-efficacy. Using a randomized trial design, we compared women receiving: 1) a tailored interactive computer program, 2) a targeted, culturally appropriate videotape promoting mammography specifically for African American women, and 3) usual care. The results showed that the odds of adherence were twice as great (OR = 2.0) for the interactive computer program compared to the targeted video.⁽¹²³⁾ The interactive computer program was significantly better than either pamphlet or video in moving a woman forward in mammography adoption stage.

We are currently testing the efficacy of a tailored DVD mailed to a woman's home against an interactive tailored phone intervention for women aged 50 to 75 who are nonadherent to BC screening. Preliminary data from the study indicated that there was a significant difference (p<0.05) in mammography adherence at 1 month between women receiving a DVD (18%) or a phone counseling session (20%) as compared to usual care (10%). At six months, the adherence levels were 61% for the DVD group, 56% for the phone counseling group, and 45% for the usual care group. Additionally, we found that 83% of women who received a mailed DVD completed the interactive DVD and reported it to be highly usable (Mean of 4.79 on a 5 point scale). Although data are preliminary, it can be concluded that women used the DVD when mailed to their homes and that both the mailed DVD and phone counseling session were significantly more effective than usual care.

Finally, Drs. Rawl, Champion, and Springston are testing a tailored interactive computer program designed to promote CRC screening among African Americans in a primary care setting through a current intervention trial funded by the National Cancer Institute (1R01 CA115983, 2006-2011). Prior to this trial, Drs. Rawl, Champion, and Skinner, with support from the Walther Cancer Institute, collaborated on the development of an interactive computer intervention designed to increase CRC screening among African Americans. Variables that are being assessed and used to generate tailored messages include health beliefs such as perceived risk of CRC, perceived benefits and perceived barriers to screening, self-efficacy, and stage of adoption. Preliminary results from this ongoing pilot study showed that, among persons who were noncompliant with FOBT at baseline, participation increased to 43% in the interactive computer group compared to no change in the control group. Satisfaction with the program was very high; of 36 African Americans who evaluated the program, 100% indicated they found the program interesting, easy to use, easy to understand, and that it provided important information.

This proposal builds on over a decade of intervention research by study investigators, who have found that interactive tailored interventions and telephone counseling increase both CRC and BC screening behaviors. Our current work has demonstrated that both a mailed DVD and a counseling call are more effective than usual care, but we have yet to compare the interventions against each other or considered the additive effect of these two interventions compared to each other or usual care. Because we are also assessing important covariates such as stage of screening, race, age, and out-of-pocket costs, we will be able to determine which intervention is more effective for subgroups of women. This proposal is unique in that it compares the efficacy of interventions that include either CRC screening alone or both CRC and BC screening combined based on the individual needs of the participant. Screening research, however, has not tested promotion of more than one behavior at a time nor has research compared an interactiveTIWeb, a CSC, or the combination against each other or usual care.⁽⁶⁾

The proposed research is innovative in two important ways. First the interventions being tested will provide the opportunity for participants to receive or schedule screening tests by phone. We are including an access-enhancing component in both interventions to simplify the screening process. Women in all groups can request a mailed FOBT card or can schedule appointments for colonoscopy and mammograms, as needed, on the phone.^(14, 15) Second, we will examine both the efficacy and the cost-effectiveness of these interventions. Lairson⁽¹²⁴⁾ has emphasized the importance of defining the costs attributable to both intervention development and personnel costs. This information will be key to translating the intervention to practice if found to be efficacious.

Rationale for Combining BC and CRC Screening. There are several arguments for simultaneously promoting BC and CRC screening. It makes little sense and could be argued that it is negligent to promote CRC screening without recommending BC screening if both are needed. The focus on comprehensive screening for cancer is emerging as the model for health care. In a supplement to the American Journal of Preventive Medicine, a series of health care policy experts provided a comprehensive overview of the need to address multiple behavioral risk factors in primary care, yet research on implementing interventions that promote multiple screening behaviors is limited.⁽¹²⁵⁾

Three arguments support this trial which combines BC and CRC screening into one intervention. First, in a supplement to the American Journal of Preventive Medicine, health care policy experts provided a comprehensive overview of the need to address multiple behavioral risk factors in primary care especially in relation to cancer screening.⁽¹²⁶⁾ Prochaska argues that the burden of health care and the importance of preventive medicine demand that interventions be more efficient and cost-effective.⁽⁵⁾ A more integrated approach to preventive care can lead to better outcomes with less provider burden and lower costs for our health care system.

Secondly, research has demonstrated that similar variables drive adherence to both BC and CRC screening. The principal investigators have found that tailored interventions targeting perceived risk, benefits (pros), cons (barriers), and self-efficacy have been effective in increasing both BC and CRC screening behaviors. In a meta-analysis Hall and Rossi, (2008) described 48 target behaviors, including mammography and colonoscopy, that were driven by the theoretical concepts of pros and cons.^(43, 127, 128) Thus similar variables drive both behaviors. Research also has demonstrated a strong relationship between participation in mammography and CRC screening.⁽¹²⁹⁾

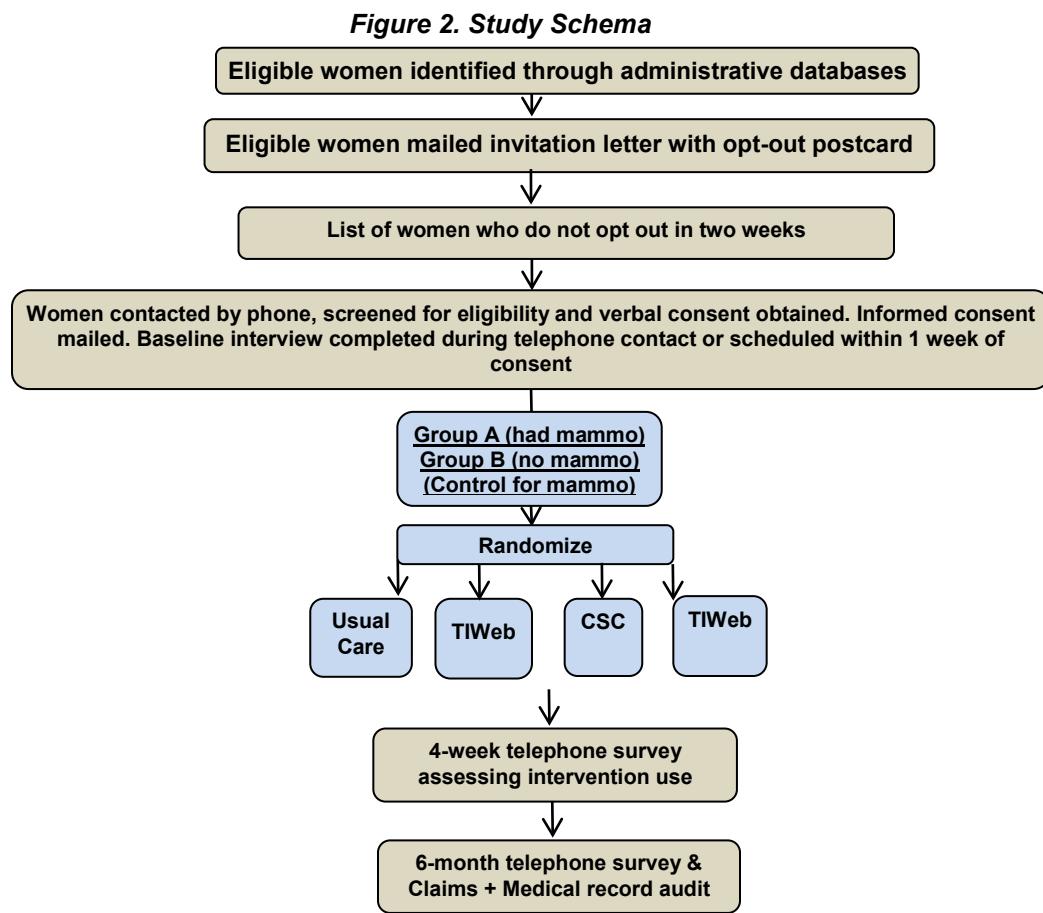
Third, it is possible that co-variation does occur and would be demonstrated if the uptake of one screening behavior increases the odds of uptake for another. Noar (2007) discussed a multiple behavior approach that would identify behaviors that might be expected to change together. Combining an intervention to increase screening for both BC and CRC has the potential to be synergistic as well as additive.

D. Research Design and Methods

D.1. Research Design. We propose a prospective randomized 2X2 factorial design: 1) usual care; 2) aTIWeb; 3) a Cancer Screening Call (CSC), and 4) a TIWeb + a Cancer Screening Call (CSC). The intervention will be tested in two groups of women. **Group A** will include women who are nonadherent to CRC but adherent to BC screening guidelines. **Group B** will include women who are nonadherent to both CRC and BC screening guidelines. Random assignment to intervention

arms will be performed within both **Group A and Group B**. A periodic list of eligible women will be pulled from databases and sent to the research study office at IUSON. The list will then be forwarded to the co-investigator in charge of recruitment (Dr. Deborah Allen, Executive Director for the Indiana Family Practice Research Network) and the physicians for the opportunity to review their own patient list. This information will consist of name, DOB/age, address, and phone number. An additional field will include mammogram status, indicating whether the individual has a documented mammogram in the past 15 months. Then a letter, brochure, and refusal postcard will be sent to potentially eligible women. A parsed list of women who don't opt out by returning the refusal post card, calling a toll free number, or emailing the project manager (number and email provided on brochure) will be scheduled for a recruitment phone call. Participants in the TIWeb Intervention Arm will be given access to a TIWeb that is programmed to provide an intervention that is interactive and tailored to the participant's individual beliefs and demographics. Individuals receiving the TIWeb will be given information that allows them to call and receive an FOBT kit in the mail or schedule an appropriate CRC test and/or mammogram. The physicians at the recruitment sites will have reviewed the list of potential participants before recruitment to ensure they are candidates for screening tests.

Figure 2. Study Schema



Women randomized to CSC will receive a telephone counseling call during which the opportunity to complete CRC screening (FOBT or a colonoscopy) and/or mammography will be offered. The CSC will include tailored counseling as well as the ability to schedule BC and CRC screening tests. The combined TIWeb + CSC group will receive a mailed TIWeb followed in four weeks by a CSC with the same opportunity to receive FOBT kits or schedule a colonoscopy and/or mammogram. The nurse counselor, knowing the participant is a good candidate for screening tests, will be trained to schedule CRC or BC screening appointments or to mail FOBT kits to individuals in the intervention groups even if they have not had a recent clinic visit. The usual care group will receive usual care that varies dependent upon the practice setting. Participants will have a baseline telephone or electronic survey prior to randomization that assesses beliefs, knowledge, self-reported CRC & BC screening, and other study variables. Four weeks following intervention, participants will be surveyed via

telephone or electronic survey on CRC & BC beliefs, knowledge, and participant involvement in and satisfaction with the intervention. Again at 6 months, a final telephone or electronic survey will be done and claims data collected. (See Figure 2) A Community Advisory Board will be involved in design and review of interventions, accrual, and intervention delivery.

In order to tell whether or not the two week opt out period is sufficient time for women to opt out, the PI and project manager will monitor a spreadsheet that will be developed for tracking calls made by study staff to women who indicate that they did opt out of the study by returning the refusal postcard, calling the toll free number, or emailing the project manager. If a woman indicates that she did opt out the study staff will apologize and indicate to the project manager or PI that this has happened. The project manager will then make sure her documentation is destroyed. Once this occurrence has happened a total of ten times, the PI will reevaluate the opt out time period and consider revising. Any occurrences will be reported to the IRB at continuing review.

D.2. Eligibility Criteria. Women will be considered eligible if they: 1) have been a patient of any of the participating physicians 2) ages 50 to 75; and 3) nonadherent to CRC screening guidelines and 4) have high speed Internet access. Exclusion criteria are: 1) having a personal history of colorectal cancer, colorectal polyps, or inflammatory bowel disease, and 2) having any medical conditions that would prohibit a mammogram or CRC screening. We are excluding women at high risk due to the exclusion criteria above which can be obtained through medical records. However, there will be women at higher than average risk for CRC due to family history that will likely be entered into the study. We will obtain the information about family history during the baseline interview and it will be considered through the intervention. Women at higher than average risk because of family history will be encouraged to have a colonoscopy.

Nonadherence to CRC screening guidelines will be defined as having had neither: 1) a fecal occult blood test in the last 12 months; or 2) a fecal immunochemical test in the past 12 months; or 3) a sigmoidoscopy more than 5 years ago; or 4) a colonoscopy more than 10 years ago. The algorithm for training research assistants to determine eligibility/adherence at baseline for CRC is included in **Appendix A**.

Table 1. Timeline

Activity	Year 1				Year 2				Year 3				Year 4				Year 5			
	Q1	Q2	Q3	Q4																
Intervention Development	X	X	X	X																
Refinement of process and outcome measures		X	X																	
Development/testing of study databases		X	X																	
Training research staff	X	X	X																	
Intervention pre-testing	X	X																		
Participant Enrollment		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Baseline data collection & intervention delivery		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
4-week follow-up interview		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
6-month follow-up interviewed med record audit			X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Data cleaning and analyses													X	X	X	X	X	X	X	X
Analysis, write-up, dissemination																	X	X	X	X
Quality Assurance			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			

months will be in **Group B**. Although there is a small group of women who could be adherent to CRC screening but not to BC screening (10%), the numbers are too small to have adequate power for testing hypotheses. In practice, however, the program can be easily modified to also accommodate women who are adherent to CRC but not to BC screening. Because administrative data may not include complete screening history information, adherence to CRC and BC screening guidelines will be verbally verified with each woman prior to consent to

determine eligibility. This will allow us to screen out women who are ineligible because they have received CRC or BC screening within the appropriate timeframe. The study timeline is illustrated in **Table 1**.

A minimum age of 50 was selected to allow women time for screening after they turned 50. If a woman develops CRC or BC during the study, she will no longer be a candidate for routine screening and her data will be deleted from final analysis. In our past work, this occurred only 2-4 times over the course of any given project. Claims data will verify initial eligibility regarding age and CRC and/or BC screening status followed by verbal confirmation at time of enrollment.

D.3. Sample. In the *Power Analyses* section, we show that inclusion of **397** participants in each of the four intervention groups - usual care, TIWeb, CSC, and TIWeb plus CSC - will yield adequate power to detect clinically significant effects at 6 months. The sample size also takes into account the average rollover of women to different health care plans that may occur during the course of this study. Women members are approximately 81% Caucasian and 19% African American. Letters of support for all sites are included in the consortium agreement section.

We will use a total of eight practice sites of which four have colonoscopy available on site and four that must schedule colonoscopy at other locations. The first four sites with colonoscopy facilities have approximately **8,500** women patients who are between the ages of 50 and 75. The second four sites without colonoscopy have **8,700** potentially eligible women patients for a total of **17,200** women. According to our prior data approximately 26% are nonadherent to CRC but adherent to BC (**n=4472**) and 44% are nonadherent to both (**n=7568**). Our study requires **1588** women for **Group A** (nonadherent to CRC) and **Group B** (nonadherent to both CRC and BC screening) total (**see Section D.1.2**). Assuming a 50% acceptance rate, we will contact **3176** total for both groups. Although there will be some participants who cannot be contacted because of recent moves or change in telephone numbers, our past work (**Preliminary Studies**) has shown that fewer than 13% would be lost to follow-up or because of change in insurance. In a current ongoing study, we have found that up to 30% of phone numbers are incorrect, reflecting increased use of cell phones. Assuming the worst case scenario of 30% incorrect numbers, we will have more than adequate numbers to enroll the total of **1588** women.

D.4. Recruitment/Accrual Procedures. Recruitment and other study procedures are depicted in **Figure 2**. Our recruitment procedures have been determined to be Health Insurance Portability and Accountability Act (HIPAA) compliant. A periodic list of eligible women will be derived from the Indiana Network for Patient Care (INPC), Community Health Network, or may be provided by the participating physicians or their designee and sent to the research study office at IUSON. The list will then be forwarded to the co-investigator in charge of recruitment (Dr. Deborah Allen, Executive Director for the Indiana Family Practice Research Network), and the participating physician will have the opportunity to review. The lists will include contact information (name, address, DOB/age, and phone number) as well as mammogram status (y/n) indicating whether the subject has a record of mammogram in the past 15 months. Each potentially eligible woman will be mailed an informational letter about the study (**Appendix B**) and brochure. A postage-paid postcard will be included for women to return should they not wish to be contacted. Women may opt out by mailing back the refusal postcard, calling a toll free number, or emailing the project manager (number and email provided on the letter and the brochure). In order to tell whether or not the two week opt out period is sufficient time for women to opt out, the PI and project manager will monitor a spreadsheet that will be developed for tracking calls made by study staff to women who indicate that they did opt out of the study by returning the refusal postcard, calling the toll free number, or emailing the project manager. If a woman indicates that she did opt out the study staff will apologize and indicate to the project manager or PI that this has happened. The project manager will then make sure her documentation is destroyed. Once this occurrence has happened a total of ten times, the PI will reevaluate the opt out time period and consider revising. Any occurrences will be reported to the IRB at continuing review. Once the two-week opt-out period has passed, research assistants (RAs) at the Center for Survey Research will call each woman using a "call sheet" with the woman's name, address, and telephone number and with spaces for recording information about each call attempt, including the date, time, disposition (e.g., busy, no answer, answering machine), and callback preference. If the woman is not reached initially, RAs will make up to 10 call attempts at different times. Ten calls allows the staff to have adequate attempts to reach the woman. The calls will be made at different times of day and different days of the week. After reaching an eligible woman, the RA will verify eligibility and explain the study. (**See Appendix A**). Eligibility based on nonadherence to CRC screening guidelines will be determined first as defined in **section D.2**. Women then will be asked about their last mammogram. Women who have had a mammogram in the past 15 months will be in **Group A** and those

who have not in **Group B**. The RA will also review the entire study verbally with the potential participant. Women will be referred to the introductory letter that indicates what study involvement includes. If a woman agrees to participate, the RA will obtain verbal consent for the study and conduct a baseline telephone interview immediately or schedule a more convenient time within one week. If she would like to complete the baseline interview electronically, she will be given instructions on how to do that. HIPAA documentation for release of medical records will be accessed and signed electronically at the time of the second online questionnaire. The woman will be able to review the electronic forms before indicating her signature. She will be able to print off the form as well. If a woman declines participation, she will be thanked for her time. We will need a cohort of approximately 45 women consented each month for 36 months to accrue a total of 1588 women. Assuming 50% will agree to participate, we will actually contact approximately 90 women each month.

Summary:

- 1) A list of eligible women will be pulled from databases and sent to the research study office at IUSON. The list will then be forwarded to the co-investigator in charge of recruitment (Dr. Deborah Allen, Executive Director for the Indiana Family Practice Research Network), and the physician at each recruitment site will have the opportunity to review the list. Data will include name, address, DOB/age, and phone number as well as mammogram status. Each woman mailed an informational letter about the study and brochure. If the woman has not declined in two weeks, the woman's name will be added to the recruitment call list.
- 2) Trained RAs at the Center for Survey Research will begin call attempts to those women who had not opted out of the study.

- a. The RA will attempt 10 calls
- b. The call attempts will be logged on a call sheet.

If the woman is reached, the RA will verify eligibility using the screening questionnaire.

- 3) The RA will also review the entire study by reading the study information sheet over the phone, ask if she is interested in participating, and conduct a baseline interview at that time (or within 1 week if it's not a convenient time) if she agrees to participate in the study and gives verbal consent for the study.
 - a. If she does not want to participate, she will be thanked for her time and her information will be destroyed.
- 4) After a woman provides verbal consent over the phone, she will be prompted to do the electronic HIPAA form at the time of the second online survey.
- 5) Once the consent and authorization are given, the woman is eligible for the rest of the study.
 - a. A reminder call will be made if the first online survey is not completed within 2 weeks. A refusal postcard will be sent if she cannot be reached.
- 6) Depending on the randomization of group:
 - a. Those receiving TIWeb only, the TIWeb information will be mailed and emailed out within 1 week of receiving the consent and authorization.
 - b. Those receiving the cancer screening call, the RA will begin attempting 1 week after receiving the consent and authorization.
 - c. Those receiving the TIWeb and call, the TIWeb information will be mailed and emailed within 1 week of receiving the consent and authorization. The call will then be attempted 1 week after the mailing of the TIWeb information.
- 7) Data collection calls or electronic communications will be placed at 4 weeks and 6 months following the intervention by the Center for Survey Research in Bloomington.
- 8) Information will be stored in locked file cabinets in a locked research office and data stored on a database that is password protected. This database will be used for this study only.

D.5. Data Collection. The baseline interview by phone or electronic communication, which will occur during the verbal consent call or within 1 week if the women needs a more convenient time, will include questions about CRC and BC screening as well as questions for perceived risk, benefits, barriers, and self-efficacy. Sociocultural/demographic variables will be measured for subgroup comparisons. The computer program used to conduct telephone surveys will have the randomization scheme integrated into the program. When a baseline survey is completed, the computer program will provide the randomized group assignment to the research assistant. The research assistant will then provide instructions to the participant based on her randomized group assignment.

Those randomized to the TIWeb or CSC intervention group will be told they will receive a TIWeb or CSC in the next week followed by data collection calls at four weeks and six months. Women randomized to the TIWeb plus CSC will be told they will receive access to TIWeb in the next week followed by the CSC about CRC or BC screening as well as data collection calls or electronic communication at 4 weeks and six months. The usual care group will be told they will receive telephone calls or electronic communication for data collection at 4 weeks and six months. At the 4-week interview, women will be queried about their receipt, recall, and use of the TIWeb and their recall of the CSC. At six months, women will be asked about their screening behaviors. Participants will be offered a \$20 gift certificate for each telephone survey they complete, for a total of \$60 per participant across the entire study. This small incentive compensates women for their time. **Table 1** contains a timeline of project activities.

D.6. Tailored Interactive Website (TIWeb).

The interactive program will operate from a computer. The specific

graphic design will be determined after Community Advisory Board (CAB) preference testing, but be similar to the sample screens provided in Appendix C. Control buttons will be large enough to be easily seen and will be clearly labeled for easy identification. The narrator will walk the viewer through every aspect of the program so that each woman can easily respond to data queries. The program will also be designed to allow a woman to stop the program at any given point and return later to that place in the program.

D.6.1. ITWeb Development:

Message libraries, tailoring algorithms, and the majority of the content that will be included in the proposed TIWeb and CSC have been

Figure 3. Flow of TIWeb Content for Group A (Non adherent to both CRC and BC)

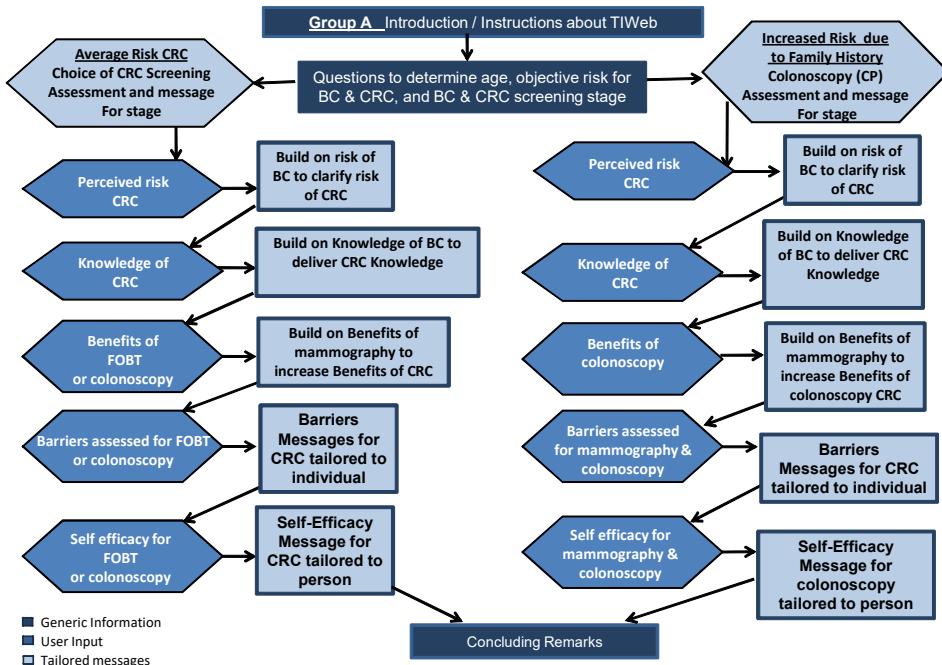


Table 2. Messages for Screening by Stage

developed in our preliminary studies. The development of TIWeb programs will begin by convening all key stakeholders: (1) content experts, Drs. Champion and Rawl; (2) Dr. Kathy Russell, head of the Community Advisory Board; and (3) the design team from the University of Georgia led by Dr. Jeff Springston. First, we will conduct scientific review and content inventory of Dr. Champion and Rawl's existing interactive programs and identify the components that will be used for each TIWeb program. Next, we will engage the **Community Advisory Board** by eliciting feedback on the user interface and navigation of the existing programs in meetings facilitated by Dr. Russell. The primary outcome of the meetings with the **Community Advisory Board** will be to clearly identify the goal of the TIWeb programs from the users' and stakeholders' perspectives. We will also elicit information from our community advisors about user characteristics and preferences for the "look and feel" of programs, including users' expectations of how the interactive products should work in the home setting, that is, contextual factors.

Based on the results of the CAB session and scientific review, co-investigators Rawl and Champion will develop a content matrix document, incorporating theoretical constructs. The document will identify theoretical constructs, user input, core content, health messages, and media assets (e.g., video clips, audio files, animations) in a hierarchical classification that will determine the information flow. Although the matrix document will continue to be refined in subsequent iterative design phases, the design team will use the matrix to identify the number and type of media assets to be created as well as the basis for algorithms that will determine navigation pathways.

Stage	Precontemplation Both BC and CRC	Contemplation BC and Precontemplation CRC	Precontemplation BC and Contemplation CRC	Contemplation for both BC and CRC	D.6.2. TIWeb Program Intervention Pretesting:
Message	Although you haven't thought about having breast or colon cancer screening in the next six months, there are very good reasons why you should consider both of these tests. As we grow older, both breast and colon cancer incidence increases but both cancers can be detected early and cured 95% of the time. This program will tell you more about both of these cancers including your risk and the benefits of getting screened.	Although you have thought about having a mammogram, you haven't really considered colon cancer screening. Actually, the need for both types of tests is important. This program will help you take the next step for breast cancer screening-scheduling a mammogram-and also help you think about the need for colorectal cancer screening.	You have thought about having colon cancer screening but not considered having a mammogram. Actually, the need for both types of tests is important. This program will help you take the next step for colon cancer screening-deciding what test is right for you and answering questions about what is holding you back. We will also help you think about the need for a mammogram	It is great that you have thought about having screening tests for both breast cancer and colon cancer. Your willingness to consider both these tests probably means that you know the occurrence of both cancers increases as we get older. Also, both cancers have tests that can detect the cancer early when there is a 95% chance of being cured. There are many things that keep us from taking the next step-actually scheduling a mammogram and colon cancer screening. This program will help you with concerns about both breast and colon cancer screening so you can take the final step-scheduling an appointment and getting screened. In fact, you can call the number given in this program to schedule both tests.	To validate narrative content, literacy level, and ease of use, 10 women who meet the eligibility criteria for the study will participate in one of up to four Community Advisory Board (CAB) meetings.

Women for the CAB will be selected in the same way as those who participate in the larger study but will be ineligible for the larger study. Selected participants will be representative of women in the target populations with regard to age and race.⁽¹³⁰⁾ Other qualitative methodologists^(131, 132) indicate that three to five sessions are sufficient to achieve redundancy or "saturation" of information. The program's usability will be evaluated by assessing ease of use, content (leveling and appropriateness), aesthetic appeal, and cultural relevance. The program will also branch women dependent on whether answers to risk factors identify them as average or high risk for CRC due to family history. Women at average risk will be offered options of FOBT or colonoscopy. For women at increased CRC risk due to family history, colonoscopy will be recommended as the most appropriate test. If a woman at increased risk is not interested in colonoscopy, FOBT will be offered. The interactive programming allows users to receive feedback after each question or short series of questions. For individuals in **Group A (Figure 3)**, the program will provide messages to increase CRC screening that build on the success with BC screening using the common principles identified in the theoretical framework. The program will begin with risk messages that include age and stage of adherence. For women who are non-adherent to both cancer screenings (**Group B**), the program will branch to messages designed to promote both CRC and BC screening behaviors simultaneously. (**Figure 4**) For both groups of women, benefits and barriers to screening will be individually tailored. For barriers, each individual item will be listed so that all perceived barriers can be included. For women who have never had previous CRC or BC screenings or for those whose answers indicate low self-efficacy, the TIWeb will include a video of the procedures. Women receiving TIWeb will be able to observe video demonstrations of mammography and CRC screening tests as appropriate, and to listen to testimonials from health providers and survivors. Animated graphics and charts will be included. *For example, for women in Group A, message tailoring will target CRC screening because they are already adherent to BC screening. However, the message will incorporate illustrations that relate back to their adherence to BC screening.*

Table 3. Differences in Benefits Messages between Women in Group A and Group B

<u>Colorectal Cancer Screening Benefit Question</u>	<u>Common Principle Content for Benefits.</u>	<u>Group A (Yes-BC& No CRC)</u>	<u>Group B (No-BC&No CRC)</u>
Having regular colon cancer screening tests would help me find colorectal cancer early when it can be successfully treated.	Cancer starts as a single cell that grows more quickly than other cells.	You already understand the benefit of mammography but might not know that colon cancer starts as a single cell just like Breast Cancer. And it can grow and divide for a long time before you would be aware you had cancer. Just like breast cancer, if colon cancer isn't found early, it can spread to a woman's brain, liver or bones and when it does, it is hard to treat. Also just like Breast Cancer, if Colorectal Cancer is found early before it has spread, 95% of women are cured.	Many women don't realize it but both breast cancer and colon cancer start as a single cell that is so small it can't be seen. It can grow and divide for a long time before you would be aware you had cancer. If either of these cancers isn't found early, they can spread to a woman's brain, liver or bones and when it does, it is hard to treat. The good news is that both breast cancer and colon cancer can be found early – before they spread and when 95% of women are completely cured. That's why it is so important to be regularly screened for both breast and colon cancer.
<u>Breast Cancer Screening Benefit Question</u>	Having a mammogram will help me find BC early when it can be successfully treated.	Almost 95% of early stage colon cancer and breast cancers can be cured	

a benefits question, a variation of messaging combinations could be delivered as illustrated in **Table 3**. Further examples are given in **Appendix C**. Examples of pain barriers messages for women in **Group B** are illustrated in **Table 4**.

D.6.4. Intervention Content: Our tailored interventions will require a short initial query to obtain information that classifies the individual as average or higher than average risk because of family history for CRC so that the appropriate CRC screening test can be recommended. Mammography screening recommendations are uniform regardless of risk. Therefore, the telephone nurse counselors placing the CSCs must have knowledge about

each individual's CRC family history and ability to undergo colonoscopy prior to making scheduling appointments. The nurse counselor will be trained with an appropriate algorithm by our co-investigator, Dr. Allen, to review participants' records prior to calls to determine if participants should be excluded from a colonoscopy recommendation because of their health history.

An experienced professional multimedia development firm, used in our prior studies, will edit and revise the program under the direction of the study investigators. Production of the TIWeb will include layout and design of navigation elements, background,

Table 4. Tailoring Barriers Messaging for Women in Group B

Target Question	Barrier BC (Group B)	Barrier CRC (Group B)	Barriers Message for Pain
<u>Colorectal Cancer Screening Barrier Question</u> Having a colonoscopy would be painful	No	No	No message
	No	Yes	Many people are concerned that colonoscopy may be painful. Most of the time, you can be put to sleep so that you don't even know what is happening. This is why you will have someone come with you for the test. The medicine may make you sleepy
<u>Breast Cancer Screening Barrier Question</u> Having a mammogram will be painful.	Yes	No	Most women do not find mammography painful but if you are worried there are several things you can do. Take Tylenol before coming for an appointment. Also-talk with the technician who does your mammogram. Tell her that you are concerned and she will do her best to only do what is absolutely necessary.
	Yes	Yes	A lot of women put off having both a mammogram and colonoscopy because they have heard about how painful it is. Most women do not find mammography painful but if you are worried there are several things you can do. Take Tylenol before coming for an appointment.. Also-talk with the technician who does your mammogram. Tell her that you are concerned and she will do her best to only do what is absolutely necessary. As far as a colonoscopy-almost everyone is put to sleep so you shouldn't have any pain at all. This is why they ask you to bring another person to drive you home.

color schemes, and layout of content including video, graphics, text, and animation as appropriate to this family practice patient population. These refined prototype interfaces will appear as complete designs. They will be reviewed within CAB of women in the target population (discussed in more detail below), after which the

D.6.3. Tailored

Messages: The tailoring for each construct occurs when a woman's answer to a key question prompts delivery of the appropriate message. For **Group B**, several scenarios might present depending on a woman's staging answers for BC and CRC screening. **Table 2** illustrates how messaging could be combined depending on these categories. Additionally, depending on answers to

prototypes will be finalized. We estimate that approximately 800 unique photographs will be acquired through on-site photography/ videography and digital imaging libraries. Full-motion video clips (500) will be used to show mammography and CRC screening procedures and to present key testimonials and other material as media space allows. Illustrations will be multimedia firm and, if appropriate, obtained from stock illustration libraries. Graphics will be integrated within the interface to ensure consistency of themes(s) and user experience. A visual animation will demonstrate how cancer that is not detected early can grow and spread through the body. Animation will also be used within charts or graphs to emphasize important elements, and animated icons and sound designed by the will be incorporated throughout the program to enhance the look, feel, consistency, and usability of the program. All pages will have spoken (audio) dialogue with the same information repeated in the form of written text, allowing women with low literacy to use the program. Our goal is to create a tailored

Table 5. CSC Intervention Objectives, Constructs and Content

Construct	Objective	Telephone Counseling Content	Time Mins
Intro	Establish rapport	<ul style="list-style-type: none"> • Identification of Counselor as nurse • Verify participant identification • Review purpose of call • Identify adherence and stage with BC and CRC 	1
Objective risk	Identify objective risk	<ul style="list-style-type: none"> • Assess family hx • Information about individual risk 	3
Knowledge	Increase knowledge of CRC & BC screening options depending on individual risk and choice	<ul style="list-style-type: none"> • Assess knowledge of options • Clarify misconceptions • Answer questions • Provide options of FOBT or colonoscopy and mammography for Average Risk individuals and colonoscopy and mammography information for High Risk individuals 	5
Benefits	Increase benefits of CRC & BC screening	<ul style="list-style-type: none"> • Information about benefits • Clarifying misconceptions • Answer questions 	2
Barriers to selected CRC screening option	Reduce perceived barriers to colonoscopy, mammography or FOBT	<ul style="list-style-type: none"> • Assess barriers • Counsel on barriers identified 	5
Access	Enhance access to selected CRC & BC screening option	<ul style="list-style-type: none"> • Mail FOBT • Assist with scheduling colonoscopy 	2
Conclude	Summary for patient activation of CRC & BC screening guidelines		

TIWeb program that is narratively rich and applicable to women at all levels of education.

D.7. Cancer Screening Call. (CSC) A computer interface will act as a counseling guide, but nurse counselors will have flexibility in responding to individuals' questions based on the conversation flow. Our team is experienced in training counselors to use these guides without seeming "rote" or "stiff" in presentation. The conversational tone of messages in the program, combined with flexibility of counselors to paraphrase and answer questions, has assured a pleasing presentation. The telephone nurse counselor will call individuals randomized to the CSC alone to schedule the telephone counseling call after they have been consented and baseline data collected. The call will be placed within 1 week of randomization. For individuals who are randomized to the TIWeb+ CSC, the TIWeb will be mailed after randomization and the telephone nurse counselor will call 1 week after this mailing. *The follow up data collection will occur at 4 weeks post intervention.*

Interpersonal communication interventions using telephone counseling have demonstrated

significant increases in cancer screening compared to usual care. Telephone counseling is interactive and provides a mechanism to provide conversation between a trained nurse counselor and a recipient. *The Cancer Screening Call (CSC) intervention in this proposal will use the same theoretical constructs present in the TIWeb- perceived risk, benefits, barriers, and self-efficacy. Although intervention content is similar in both the TIWeb and CSC, the delivery varies. Both use an interactive format in which women are queried about content and then messages delivered specific to that content. The TIWeb allows use of video, graphs and other media not available in the CSC. The CSC, however, allows individual message clarification in real time. Both the TIWeb and the CSC will offer scheduling of the screening tests without a prior visit. In the TIWeb program, a dedicated number will allow participants to call for scheduling appointments. In the CSC arm, nurse counselors*

will offer to mail FOBT cards and schedule colonoscopies and mammograms at the end of the CSC. The objectives and content related to each common theoretical variable are listed in **Table 5**.

D.8. Intervention Delivery. Women randomized to any of the four groups will receive a baseline call and a call at 4 weeks and 6 months for data collection. Women randomized to the TIWeb alone group will receive a letter and an email with information that will detail how to enter the TIWeb within one week after completing the baseline survey. Women randomized to the CSC call will be scheduled to receive the CSC call within one week of baseline survey. For women randomized to the combination group (TIWeb + CSC), the a letter and an email that details how to enter the TIWeb within the next week. One week after mailing and emailing the information on entering the TIWeb, the CSC will be placed. Individuals will first be asked if they received the letter and/or email detailing how to enter the TIWeb and if they viewed the TIWeb. Prior to delivering the scripted CSC, women will also be given the opportunity to ask any questions that have arisen from watching the TIWeb. The TIWeb will contain both programs for women who are adherent to BC screening but not to CRC (**Group A**) or nonadherent to both (**Group B**). A trained research assistant will be available by phone to provide technical assistance to any women who needs help using the TIWeb. Because CRC screening recommendations vary depending on risk factors, a risk algorithm will be incorporated into the TIWeb and CSC to identify women at average risk or at increased risk due to family history. Women at increased risk will be reminded that colonoscopy is the best test for them, if it is not contraindicated. If their risk is average, a choice of either FOBT or colonoscopy will be presented. If women are uncertain about which method would be best for them, they will be encouraged to schedule an appointment with their primary health care provider to discuss options for screening. Scheduling of colonoscopy or mammography via telephone will be offered to all women in the intervention groups. Women receiving only the TIWeb will have a dedicated number to call and schedule colonoscopy or mammography, or to receive an FOBT kit in the mail. If the woman is an appropriate participant and wants to schedule an appointment for CRC or BC screening, it can be completed while on the call. If the patient requests an FOBT kit, it will be mailed immediately following the call. BC screening recommendations do not vary; therefore, a message will encourage yearly mammography for all women. Within the family practice research network, usual care consists of preventive services for women performed during the physical including regular Pap and pelvic exams. As part of the annual exam, the primary care physician reviews the current age-appropriate screening guidelines for the patient and suggests that these be done. Most hospital systems or radiology clinics also notify the patient when a mammogram is due.

D.9. Training for Interviewers and CSC Nurse Counselors. Graduate nurses will be hired and trained as counselors to complete the CSCs. The nurse counselors will have an initial training session consisting of the following elements: 1) project rationale and overview, 2) detailed information about each intervention, 3) delivery practice, 4) a detailed training manual, 5) an extensive question-and-answer period, and 6) breakout for individual training roles and training to use an algorithm developed by Dr. Allen to determine eligibility for colonoscopy. Nurse counselors will be trained to appropriately answer spontaneous questions that occur either during telephone interviews or during telephone counseling. Nurse counselors who conduct telephone counseling calls will have all calls recorded. Responding to impromptu questions will be an important part of training so that standardization can be achieved. Role play will be especially important in learning to respond to questions. We will have four hours of role play in which mock participants will challenge nurse counselors with extraneous questions. The nurse counselors for the CSCs will be continuously recorded for quality assurance. The role-playing and taped interviews will be evaluated based on a checklist contained in the **Appendix A**. Initial training will be conducted during a two-day session. The first day will consist of presentations including the following: 1) overview of grant objectives and rationale; 2) detailed demonstration of intervention arms; 3) protection of human subjects and confidentiality issues; and 4) practice in answering impromptu questions.

The Center for Survey Research in Bloomington, by phone or electronically survey, will collect T1, T2, and T3 data and provide any technical assistance needed with the TIWeb. Participants who have questions about the TIWeb will be able to call a toll free number and a research assistant will call them back. The additional contact will be recorded for length of time and content and added as a covariate to final analysis. Extensive training will be required for all research assistants who collect data and provide technical help with the TIWeb. Research assistants who provide the CSC will be different individuals than those who do telephone interviews so that bias will not be introduced during data collection. Research assistants will be graduate students who will have an initial training session consisting of the following elements: 1) project rationale and overview, 2) detailed information about each intervention, 3) information about assisting women with the TIWeb, 4) delivery practice,

5) a detailed training manual, 6) an extensive question-and-answer period, and 7) breakout sessions for individualized role training. Although interviewers won't be blind to assignment, training will include extensive focus on standardizing the interviews.

D.10. Process Evaluation. Process evaluation for accrual will be determined by randomly selecting 25% of all accrual calls and rating callers using the evaluation checklist in **Appendix A**. Research assistants that receive below average on any criteria will be given additional training.

*Consistency in intervention delivery is assured through the standardized programming used in the computer-assisted CSC and through taping and review of CSCs. The TIWeb guide the participant through all sections. The CSCs will be continuously recorded for quality assurance. Monthly taping of at least one TIWeb technical assistance session and T1, T2, and T3 interview for each interviewer will allow checks on consistency of performance. Taped interviews and CSC calls will be evaluated based on a checklist contained in **Appendix A**. Research assistants who are not delivering calls as instructed will be given additional training. Research assistants will address any unusual happenings during biweekly meetings. Decisions to modify procedures will be made jointly and documented. The research team will meet monthly to discuss any concerns with implementation of the protocol or collection of interview data. The principal investigators will meet weekly to refine the protocol and training procedures and to discuss ongoing issues.*

Table 6. Measurement of Outcomes: Stage and Adherence for BC and CRC

Stage	CRC Screening Average risk woman	CRC screening At higher risk because of family history	BC Screening
Precontemplation	Is nonadherent to national guidelines and does <u>not intend</u> to have one of the test options in next 6 months	Never had a colonoscopy or had one > 10 years ago and does <u>not intend</u> to have one in next 6 months	Never had a mammogram or had one \geq 15 mo. ago and does not intend to have one in next 6 months
Contemplation	Is nonadherent to national guidelines but intends to have one of the test options in next 6 months	Never had a colonoscopy or had one > 10 years ago and intends to have one in next 6 months	Never had or had mammogram more than 15 months ago but intends to have one in next 6 months
Action (Adherence to any CRC screening)	Had one of the test options since intervention	Had one of the test options since intervention	Had a mammogram since intervention
Action (Adherence to risk appropriate CRC screening)	Had one of the test options since intervention	Had a colonoscopy since intervention	Had a mammogram since intervention

site for other reasons. Therefore, use of self report in addition to claims data, and medical record audits will provide necessary outcome data. Participant involvement and beliefs will be assessed at 4 weeks post-intervention. As described previously, we may have women in the study who are at increased risk for CRC due to family history. For these women, colonoscopy is the most appropriate CRC screening test. However, some of these increased-risk women may decide to do FOBT instead of colonoscopy. In order to identify all behaviors, we will divide adherence to CRC screening into two categories-Risks Appropriate, and Any CRC screening after intervention. For most women who are at average risk, these classifications will be the same. However, for women with a family history of CRC, Risk-Appropriate CRC screening would be colonoscopy. **Table 6** defines each outcome. Data assessment times are specified in **Table 7**. Data collected for cost-effectiveness are described under the cost-effectiveness section.

Table 7: Data Assessment

Variable	Baseline	4 Weeks	6 Months
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D.11. Measurement. Major outcome variables, delineated in Specific Aims, include: 1) Adherence and staging for CRC and BC, and 2) Cost-effectiveness.

The adherence to screening recommendations outcome will be assessed at 4 weeks and 6 months after intervention. As indicated in **Table 7**, the 4 week data collection will only be self report. Mammography and CRC screening and diagnostic tests at 6 months are the primary outcome and will include using claims data that identifies both screening and diagnostic codes in medical records as some test may be labeled diagnostic.

FOBT is not always charged to the patient. Therefore, verification of FOBT will require medical chart audit. A woman may not have a screening reported in her claims data because she is new to the health plan and received screening elsewhere. It is also possible that women may switch health plans or use another

Self Report CRCS and BCS	X	X	X
Screening Record verification	X		X
Knowledge and Beliefs	X	X	
Participant Involvement		X	
Demographic Variables	X		

Stage of Adoption for CRC and BC Screening:
Stage will be identified using measures of Prochaska and DiClemente's Transtheoretical Model developed for mammography by Rakowski and colleagues⁽¹¹⁹⁾,

¹²⁸⁾ and consistent with our previous research.^(9, 10) Construct validation for these stage measures was established via principal components analyses in an original and a replication study (involving 142 and 676 women, respectively).^(119, 128) Items for CRC and BC screening will determine whether participants: 1) have ever had a mammogram, FOBT, sigmoidoscopy, or colonoscopy; 2) have thought about having a mammogram, FOBT, sigmoidoscopy, or colonoscopy; or 3) intend to have any of these tests in the next six months. We will also ask participants if CRC or BC screening tests were for screening or diagnostic purposes and use their responses as a covariate. Screening and diagnostic procedures have different CPT codes.

Mammography and colonoscopy scheduling will be based on the location of the participating physician. The study team will be given a preferred list of sites to be scheduled as well as alternative sites if the patient chooses. Results of screenings will be sent immediately to the participant's primary health care provider as part of her routine care.

Past Screening History will be measured by self-reported items that assess CRC and BC screening tests women have had in the past 20 years or since the individual turned 50. Self-report will be the most feasible method to assess screening history since claims data may not accurately reflect all screening tests done in other health care settings or while they were covered by a different health insurance plan.

Participant Involvement: will be measured for the TIWeb and for the CSC. The participant involvement scale for TIWeb has 19 items that address interest and engagement in the program and its content. The items, piloted with 36 people (see Preliminary Studies), address ease of use, relevancy, information content, barriers, and general satisfaction. The Cronbach's alpha was 0.89 and 100% of people indicated that they found the program interesting, easy to use, easy to understand, and containing information that was important to them. The survey instrument can be found in **Appendix E**. There are 15 items that measure participant involvement in the CSC. Participants will be called within 4 weeks following intervention to obtain data on involvement with the intervention.

Beliefs about CRC or BC Screening

Perceived risk, benefits, barriers, and self-efficacy measures for BC screening have been extensively tested and refined since 1984.⁽¹³³⁻¹³⁵⁾ Validity was tested using confirmatory and exploratory factor analysis and known groups' technique. Internal consistency (0.87) and test-retest reliability (.60) were also computed.⁽¹³⁴⁾ Parallel scales to measure CRC screening have been tested for validity and reliability and results recently published.⁽¹³⁶⁾

Perceived Risk (BC & CRC): Perceived risk for BC includes four items with a reported internal consistency coefficient of 0.87 and test-retest reliability of .67.⁽¹³⁴⁾ The items measure beliefs about the participant's perceived risk of getting BC in the future. Perceived risk for CRC includes four items, a 3-item scale developed by Dr. Champion and a single-item measure designed to assess perceived age-adjusted risk. The summated risk scale was originally developed for BC⁽¹³⁵⁾ and adapted to CRC.⁽¹³⁷⁾ Validity and reliability have been extensively tested with diverse population groups. Internal consistency reliability analyses from previous studies yielded Cronbach's alphas ranging from 0.75 to 0.77.

Benefits (BC & CRC screening) Dr. Champion has developed a four-item "Benefits to Mammography" scale that assesses women's perceptions of mammography's ability to find BC early and avert death. In a past study,⁽¹³⁴⁾ the scale showed an internal consistency alpha of .75 and test-retest reliability of .59. Benefits of FOBT (3 items) and colonoscopy (4 items) will be measured separately using summated Likert scales modified from those previously developed to measure BC screening benefits.⁽¹³⁵⁾ Items specific to CRC screening have been identified in the literature and through focus group discussions and were psychometrically tested.⁽¹³⁶⁾ The Cronbach's alpha coefficients obtained in a preliminary study for 5-item scales measuring benefits of FOBT and colonoscopy were 0.65 and 0.70, respectively.

Barriers (BC & CRC screening): Barriers to mammography are measured on a 12-item scale developed by Dr. Champion.⁽¹³³⁻¹³⁵⁾ The internal consistency coefficient was 0.88 and test-retest coefficient was 0.72. Information Version date 1.24.2014 IRB Protocol #1009001808

on all items will be collected, although tailoring will be based on barriers found to be most relevant in prior work. Barriers to FOBT and colonoscopy will be measured by separate summated Likert scales modified from those previously developed to measure BC screening barriers.⁽¹³⁵⁾ Items specific to CRC screening have been identified in the literature and through focus group discussions and were psychometrically tested in preliminary studies.⁽¹³⁸⁾ Barriers to FOBT are assessed using a 9-item scale and barriers to colonoscopy with a 15-item scale, all with the same 5 Likert response options. Internal consistency reliability (alpha) coefficients of the barriers scales for FOBT and colonoscopy were 0.72 and 0.77, respectively.

Self-efficacy (BC & CRC screening): Self-efficacy for mammography is measured on a 10-item scale developed by Dr. Champion and has been tested for reliability and validity.⁽¹²³⁾ The internal consistency reliability was 0.91, and all items loaded at 0.60 or above in a unidimensional factor structure. Significant differences on scale scores emerged between adherent (mean=42.74) and nonadherent (mean=40.74, $t=3.07$, $p<.003$) women. Further validity and reliability testing will be conducted in the proposed study. Self-efficacy for FOBT and colonoscopy will be measured independently using 12-item scales that use a Likert response scale. Self-efficacy scores for FOBT and colonoscopy scales had internal consistency reliabilities of 0.90 and 0.92, respectively, in a previous study.⁽¹³⁹⁾

Knowledge (BC & CRC): BC knowledge will be measured using a scale developed by Dr. Champion in preliminary studies. The scale had an internal consistency reliability of 0.77. Knowledge about CRC will be measured using a multidimensional scale that has been tested in preliminary studies and found to have content and construct validity. Several aspects of knowledge about CRC will be assessed, including risk factors, screening, and treatment.

Demographic/Medical History/Insurance Variables/Personal Experience/Media Exposure: will be assessed using the form in **Appendix F**. Questions will assess age, race, education, and marital status. These items have been used for descriptive reporting in our previous research without interpretation or scoring difficulties. In the proposed study, questions about personal experience will relate to previous information about mammography screening experiences or to information gathered during the grant period. Women will also be asked about experiences with close friends or relatives with cancer. Participants will be queried regarding any CRC or BC screening recommendations or counseling outside of the study protocol. *Women will also be queried about out-of-pocket cost for any BC and CRC screening.* Cost-effectiveness will be measured and calculated as described under the Data Analysis section.

Overall Functioning: will be assessed using the Medical Outcomes Study - Short Form 12 (SF-12[®]), a 12-item scale that yields summary physical and mental health outcome scores that are interchangeable with those from the SF-36[®]. The SF-12[®], published in early 1995, is one of the most widely used instruments that reproduces the SF-36[®] physical and mental health summary scales (PCS and MCS) as well as the eight subscales of the original SF-36. Reliability and validity have been well supported; test-retest reliabilities of 0.89 and Cronbach alphas of 0.76 are reported.⁽¹⁴⁰⁾

Cost-effectiveness will be measured and calculated as described under the *Data Analysis* section.

D.12. Sample Size and Power Analysis: The *primary efficacy hypothesis in this area of research is adherence to screening. Therefore, adherence to CRC and BC screening at 6 months has driven our choice of sample size.* Originally, we proposed conducting analysis with two separate groups based on initial mammography status: 1) women who were adherent to mammography but not to colorectal cancer (CRC) screening, and 2) women who were adherent to neither mammography nor CRC screening. By testing these groups separately, we required a sample size of 2616 to achieve 80% power between both the control and intervention groups and between any combinations of groups. In re-considering this approach, we realized that since the outcome of CRC screening was common across both groups A and B, this was not the most efficient design to test our outcomes. We are proposing analyses using one group of women, all of whom will be non-adherent to CRC screening at baseline. In this group, some women will be adherent to mammography guidelines (i.e., had a mammogram in the past 15 months) and others will be non adherent. For Aim 1, when we examine intervention effects on the outcome of CRC screening, we will control for baseline adherence to mammography. For Aim 2, we will use only the sub-group of women who were not adherent to either breast or CRC screening at baseline. Using this approach will reduce the sample size needed and reduce the overall costs of the study, more closely aligning the budget with the amount awarded. Most importantly, revising our analytical approach will enable us to achieve our initial Aims despite the reduced sample size.

Specifically, for the outcome of CRC screening adherence, we had justified sample size in the original proposal to achieve 80% power to detect differences between intervention groups, *separately* for two groups of women depending on their baseline breast cancer screening adherence status.

Group A includes women who were nonadherent to CRC screening but adherent to BC screening, and **Group B** includes women nonadherent to both CRC and BC screening.

We realize now that it is unnecessary to perform the analysis of CRC adherence separately for the two groups (A and B). Instead the Group variable (A vs B) can be entered in the model using baseline mammography screening as a covariate.

In Table 8 of the original application (see appendix), we proposed enrolling 327 for each of 8 combinations of 4 arms and 2 groups (A and B) for a study total of 2616. However, using this alternative approach will require only 1308 (327 in each of the 4 arms) women to test the primary outcome of CRC adherence. However, new studies, including our own, indicate 15-20% adherence to CRC screening in control conditions. Our initial proposal anticipated on 10% adherence in the control arm. Thus, although the new design decreases the sample size by combining the groups, a more realistic estimate of the adherence in the control group will actually increase the sample size compared to our estimate in Group A for the initial proposal. Specifically, we propose to increase our estimate of CRC adherence in all four arms, to accommodate a change in the proposed adherence in the control group from 10% to 20%. This will require 397 instead of 327 per arm (see Table 1). Thus, a sample of 397 per group at baseline (357 per group at 6 months after 10% estimated attrition) will provide 80% power to detect differences between any pair of the four randomized arms for Aim 1 (Table 1).

Revised Sample size and Power analysis for primary efficacy hypothesis of estimated CRC screening adherence rates in the combined groups of those adherent (Group A) and non-adherent (Group B) at baseline to breast cancer screening (Aim 1, primary outcome of CRC adherence)

GROUPS A and B combined

Time	Usual Care (1)	TIDVD (2)	CSC (3)	TIDVD+CSC (4)	Power
Baseline adherence	0%	0%	0%	0%	NA
Total sample size (N):	(n = 397)	(n = 397)	(n = 397)	(n = 397)	
N by baseline strata, Adherent to BC (A) Non-adherent to BC (B)	(n = 119) (n = 278)				
6 months adherence	20%	30%	40%	55%	Power for 357/arm (Groups A and B combined)
Total sample size (N):	(n = 357)	(n = 357)	(n = 357)	(n = 357)	1v2 .87 1v3 .99 1v4 .99 2v3 .80 2v4 .99 3v4 .98
N by baseline strata, Adherent to BC (A) Non-adherent to BC (B)	(n = 107) (n = 250)				

Enrollment will be stratified by women adherent to breast but not CRC screening and those adherent to neither in a 30%/70% ratio so that we will have an adequate sample to detect an 80% power for Aim 2. Aim 2 will use only the subgroup of women who are not adherent to either breast or CRC screening. This will provide at least 80% power for Group B for comparing each pair of randomized arms, when testing the secondary outcome (adherence to both CRC and BC screening) (Table 2).

Thus, the hypotheses for Aim 1 can now be conceptualized as

Aim 1:

Hypothesis 1 (Primary outcome): There will be differences in CRC screening adherence and stage of adoption, when controlling for adherence to BC screening at baseline, among women who are randomized to 1) usual care; 2) a TIDVD; 3) a CSC, and 4) a TIDVD plus a CSC.

Aim 2:

Hypothesis 2 (Secondary outcome): In the group that is nonadherent to both CRC and BC screening at baseline, there will be differences in adherence to both CRC and BC screening and stage of adoption, among women who are randomized to 1) usual care; 2) a TIDVD; 3) a CSC, and 4) a TIDVD plus a CSC.

D.13. Analyses. Descriptive statistics will be computed for all variables, using stem-and-leaf plots, central tendency indices, variability indices, and frequency distributions. We will compare demographic information at baseline across the four randomized groups (usual care, TIWeb, CSC, and TIWeb + CSC), using the analysis of variance (ANOVA) for continuous variables (describing with means and standard deviations) and using the Pearson chi-square test for categorical variables (describing with cross-classification tables). If the ANOVA parametric assumptions of normality and equal variances are not met, we will perform the nonparametric Kruskal-Wallis test for the continuous variables. If there are significant baseline differences between the two intervention groups at a liberal significance level of 0.20, we will adjust for those characteristics in subsequent logistic regression analyses.

Aim 1: Analysis for intervention efficacy: Women in **Group A women** are nonadherent to CRC screening but adherent to BC screening at baseline and thus could become adherent to *CRC screening*. *Depending on whether a woman is at increased risk (due to family history) or average risk, we will code each participant as risk-appropriate adherence or adherence to any CRC screening. For women at average risk, these categories will be identical. For women at high risk, completion of a colonoscopy is needed to classify them as adherent to the risk-appropriate test. Thus, two outcomes will be tested in relation to CRC adherence: 1) adherence to any CRC test; and 2) adherence to a risk-appropriate test. Women in Group B will be nonadherent to both CRC and BC screening at baseline and thus could remain nonadherent to both, become adherent to one, or become adherent to both screenings.*

Group A (nonadherent to CRC but adherent to BC screening guidelines)

Hypothesis 1- Efficacy Analysis: The differences in binary adherence across the four randomized arms will be tested initially with the chi-square test for a 2x4 cross-classification table (adherence by randomized intervention groups). Binary logistic regression analysis, with three dummy variables using usual care as the reference category, will be computed to study the effects of each intervention (TIWeb, CSC, TIWeb +CSC) versus usual care on adherence, while adjusting for any potentially confounding covariates. In addition, model contrasts will be specified to statistically compare each of the three intervention arms to the others. Since the intervention is delivered to the patient and not the provider, analysis of variation in CRC screening by practitioners will be limited. Outcomes of patients who share the same providers may be slightly more correlated than outcomes of patients from different providers. Thus, the within-provider correlation among patients will be assessed with variance components, and if necessary generalized estimating equations (GEE) will be used with logistic regression to account for the within-provider correlation. We will enter as independent variables into logistic models the following: randomized group membership and any demographic covariate (age, race, education, marital status, screening history, baseline stage of adoption, SF12 mental health component, SF12 physical health component) for which the randomized groups differ significantly at baseline using a liberal significance level of 0.20. We will also measure whether subjects report that their physicians have recommended the screening test in the past and the amount of out-of-pocket expense for screening and enter these as covariates. In addition to demographic variables, other potential covariates will be location of TIWeb intervention (use of a computer at home or elsewhere), and whether women in the TIWeb group needed technical help from the research assistant to use the TIWeb program. We plan to include screening history as a covariate in our analysis by using the total number of past screenings for each test since the participant turned 50. For analysis with mammography screening, one covariate will be included (total number of mammograms since age 50). For the analysis of CRC screening, two covariates will be included simultaneously in the models (total number of FOBTs since age 50, and "any previous endoscopic test" [yes/no]). The CRC screening analysis requires two covariates because a history of five FOBTs, for example, is not equivalent to one previous FOBT and one previous colonoscopy or sigmoidoscopy. All variables in the

logistic regression models will be tested using the likelihood ratio test.⁽¹⁴¹⁾ Adjusted odds ratios and profile-likelihood-estimated 95% confidence intervals for those odds ratios will be provided.

Analyses of stage of screening will be the same as analyses above for adherence, except that the binary outcome is advancement (from baseline) in stage of adoption for CRC screening guidelines. There are two possible stages of adoption at baseline (precontemplation and contemplation) and three possible stages at 6 months (precontemplation, contemplation, and action). Thus, there are four possible stage movements from baseline to 6 months (fall back one stage, remain the same, advance one stage, or advance two stages). However, data on a large sample in the Preliminary Studies demonstrated that, of 904 women followed to 9 months post-baseline, only 4% of women fell back one stage and only 6% advanced two stages; the majority either advanced one stage (50%) or remained the same (39%). Therefore, we will implement the outcome of stage change as a dichotomous variable: improvement (advance one or two stages) versus no improvement (remain the same or fall back one stage).

Group B (nonadherent to both CRC and BC screening guidelines)

Hypothesis 1- Efficacy Analysis: Similar to the approach in Hypothesis 1 for **Group A**, screening adherence across the four randomized arms will be tested initially with the chi-square test for a 2x4 cross-classification table and then adjusting for covariates in logistic regression models. However, the statistical procedures will be generalized versions (Mantel chi-square and ordinal logistic regression) to accommodate an ordinal outcome. The three possible ordinal responses for the outcome are: 1) no adherence, 2) adherence to either CRC or BC screening, and 3) adherence to both CRC and BC screening. Specifically, we will perform: a) the Mantel chi-square test of linear trend and the Liu-Agresti ordinal odds ratio (the latter is a contingency-table-based statistic but assumes proportional odds) on a 2 x 3 cross-classification table (intervention group by ordinal adherence), and b) ordinal, instead of binary, logistic regression models. If the assumption of proportional odds is not satisfied, a more general logistic regression model, the generalized logit model, will be employed, and two odds ratios, instead of a single Liu-Agresti odds ratio, will be reported for the classification tables. Analyses of stage will be the same as for adherence, except the three possible ordinal responses would be based on improvement (from baseline) in stage of adoption: 1) no improvement in stage, 2) improvement in stage of either CRC or BC screening, and 3) improvement in stage of both CRC and BC screening. The Preliminary Studies show we have a great deal of experience analyzing outcomes of screening adherence and stage improvement, for both BC and CRC outcomes.

Aim 2: Analyses for cost effectiveness is described next. To conduct cost-effectiveness (CE) analysis of a cancer screening program, it is necessary to determine both the effectiveness of a given intervention (as measured by the achieved outcomes) and the costs of providing the intervention to both groups A and B. The cost-effectiveness analysis will be conducted from the perspective of both the provider and the participants.

Program Effectiveness: The main effect is screening compliance at 6 months from the baseline measure as determined by the randomized trial. For those in **Group A**, CRC screening is the outcome. For **Group B**, there are three outcome groups: CRC screening adherence, BC screening adherence, and adherence to CRC and BC screening. Outcomes will be determined with an “intent-to-treat” analysis by analyzing data from all women who originally consented and were randomly assigned to a research arm regardless of deviations from the protocol, the degree of treatment they received (e.g., regardless of whether TIWeb was viewed or CSC was made), or withdrawal from treatment or loss to follow-up. The use of claims data and medical records data for the main outcome of adherence will make it possible to analyze adherence at 6 months even for women who dropped out, as long as claims data for those women can be obtained.

Program Costs: To calculate the costs of the interventions, we will consider delivery costs only. Costs associated with research and development (R&D) activity or costs of screening tests are excluded. The cost of developing the TIWeb is expected to be a major pre-intervention R&D cost. Researchers have debated how to handle these “first-copy” costs and there is no universally accepted “correct” answer. First-copy costs, defined as costs incurred in establishing a regimen or intervention, are considered quasi-fixed costs independent of the number of units produced, once production is started. Generally, first-copy costs are excluded when they involve situations in which much of the intervention is already in existence and only modification is needed to adapt it for implementation. While R&D costs can be high, they are “sunk cost” from a societal perspective, in any future decision to implement the interventions. The final product developed for this study could be made available to

other organizations. We expect managed care organizations would not develop their own TIWeb, but would rely on public access or licensing arrangements to secure such educational material. However, the cost of developing the TIWeb will be calculated to inform future developers of the approximate cost of developing this type of interactive technology for health promotion interventions and to test CE analysis with and without these costs.

The total costs of an intervention include both direct and indirect costs. Direct costs are those directly related to services provided to the participants and include such inputs as personnel time, supplies, postage, and capital equipment. The total cost of a specific intervention will be based on several inputs including: the cost of personnel (time needed to provide the intervention multiplied by the salary and benefit cost); the cost of nondurable, consumable supplies (quantity consumed times the unit price); and the cost of durable capital equipment (depreciated over the expected life of the asset, to reflect annual costs). Postage will be a non-trivial cost in this study since some of the correspondence with participants will be by mail. Ancillary miscellaneous costs (printing, workstation design, space rental, phone charges, etc.) will be obtained from the project's monthly expenditures. Incentives used in this study to secure cooperation of the participants will not be considered a cost of the intervention since these are considered research costs and not a necessary ingredient of the interventions. Incentives are provided for data collection and not for participation in an intervention. Overhead costs, including housekeeping, administration costs, rent, building and equipment depreciation, insurance expenses, and utilities are very difficult to allocate to the appropriate intervention without developing a detailed accounting procedure, which is beyond the scope of this project. Therefore, overhead costs will be estimated by a percent of direct cost, based on previous health promotion studies. The base case indirect cost rate will be 30 percent of direct cost.⁽¹⁴²⁾ Participant time costs (the time a woman spends participating in the intervention) will be included in the cost figures since participant time has value from a societal perspective. Participant time will be valued by the national median wage rate (<http://www.bls.gov/bls/blswage.htm>) Participant time cost will be excluded when computing costs from the provider perspective.

Direct costs (labor, supplies, postage, and equipment) will be determined for each of the two interventions through resource utilization monitoring of daily consumable materials, travel expenses, labor/time activity logs, and equipment expenses to track individual intervention costs. An on-going accounting of the work effort and materials required to complete an intervention will be determined from daily activity logs kept by project staff (see Appendix E). The total cost of a specific intervention will be based on the cost of labor (labor time needed to provide the intervention multiplied by the salary and benefit cost), plus the cost of the consumable supplies and ancillary costs (printing, phone charges, etc). The resulting amount will be the estimated cost of providing each intervention. We expect that the TIWeb + CSC costs will be higher than the TIWeb or CSCs alone costs, since different labor costs will be incurred with the two interventions. Costs will not be discounted to a present value because we are attempting to determine the relative efficiency of operating the alternative interventions on an ongoing basis. Substantial capital equipment will be amortized over the expected life based on a 3 percent rate of interest.

Bundling screening promotion services to promote multiple screening tests for women in group B presents a special cost problem due to the difficulty of allocating cost to specific outcomes. The main difference in cost between participants in **Group A** and those in **Group B** will be participant time and telephone counseling time required to communicate information about two versus one type of screening. These costs will be directly allocated to the screening interventions by tracking time for each participant. Other implementation costs will be the same for subjects eligible for either one test or two screening tests (e.g., recruitment). For group B, we follow methods employed by Chirikos et al. (2004)⁽¹⁴³⁾ to adjust the cost estimate for subjects eligible for two screening tests. In their study of an office-based primary care tracking system to increase screening for breast, cervical, and colorectal cancer, they apportioned the cost to subjects based on the number of tests they were eligible for. If a participant was eligible for two screening tests, they were assigned ½ of the intervention cost and the full intervention cost if they were eligible for only one test. Thus, cost for participants in group B will consist of directly allocated cost for their time and nurse counselor time and other costs apportioned by the number of tests for which they are eligible (see equations below).

Cost-effectiveness Analysis: The cost-effectiveness evaluation is examined from the societal perspective and from the more limited perspective of the provider to inform future decision-makers about the relative efficiency of the alternative interventions. The analysis focuses on the incremental cost per additional individual who is adherent (i.e., has a CRC, BC, or both screening tests during the observation period) for each alternative intervention. The intervention costs will include participant time costs and resource costs and be

valued in 2010 constant U.S. dollars. This focus is consistent with the recommendations of the Report of the Expert Panel on Cost-Effectiveness in Health and Medicine.⁽¹⁴⁴⁾ The base case will be defined as the estimate of costs and effects derived from the best point estimate of intervention parameters. Planning, implementation, and participant costs will be tracked for the interventions.

The primary cost-effectiveness measures will be the incremental cost-effectiveness ratios (ICERs) obtained by dividing the additional per target individual cost by the additional percent of target individuals who are screened by the end of the follow-up period, comparing the control group to the TIWeb group, to the CSC group, to the TIWeb+CSC group moving from the least resource-intensive to the most resource-intensive interventions (equations 1,2,3). These measures will be based on intention to treat methods and correspond to the observation period of the study.⁽¹⁴⁵⁾

Group A (cost fully allocated to BCS intervention)

- 1) $ICER_1 = (Cost_{TIWeb} - Cost_{UC}) \div (\%BCS_{TIWeb} - \%BCS_{UC})$
- 2) $ICER_2 = (Cost_{CSC} - Cost_{TIWeb}) \div (\%BCS_{CSC} - \%BCS_{TIWeb})$
- 3) $ICER_3 = (Cost_{TIWeb+CSC} - Cost_{CSC}) \div (\%BCS_{TIWeb+CSC} - \%BCS_{CSC})$

Group B (cost adjusted for joint production)

BCS: (directly allocated plus 1/2 of non directly allocated cost applied to BCS intervention)

- 1) $ICER_1 = (Cost_{TIWeb} - Cost_{UC}) \div (\%BCS_{TIWeb} - \%BCS_{UC})$
- 2) $ICER_2 = (Cost_{CSC} - Cost_{TIWeb}) \div (\%BCS_{CSC} - \%BCS_{TIWeb})$
- 3) $ICER_3 = (Cost_{TIWeb+CSC} - Cost_{CSC}) \div (\%BCS_{TIWeb+CSC} - \%BCS_{CSC})$

CRC: (directly allocated plus 1/2 of non directly allocated cost assigned to CRCS intervention)

- 1) $ICER_1 = (Cost_{TIWeb} - Cost_{UC}) \div (\%CRCS_{TIWeb} - \%CRCS_{UC})$
- 2) $ICER_2 = (Cost_{CSC} - Cost_{TIWeb}) \div (\%CRCS_{CSC} - \%CRCS_{TIWeb})$
- 3) $ICER_3 = (Cost_{TIWeb+CSC} - Cost_{CSC}) \div (\%CRCS_{TIWeb+CSC} - \%CRCS_{CSC})$

BCS & CRCS: (all costs allocated to joint BCS & CRCS intervention)

- 1) $ICER_1 = (Cost_{TIWeb} - Cost_{UC}) \div (\%BCS \& CRCS_{TIWeb} - \%BCS \& CRCS_{UC})$
- 2) $ICER_2 = (Cost_{CSC} - Cost_{TIWeb}) \div (\%BCS \& CRCS_{CSC} - \%BCS \& CRCS_{TIWeb})$
- 3) $ICER_3 = (Cost_{TIWeb+CSC} - Cost_{CSC}) \div (\%BCS \& CRCS_{TIWeb+CSC} - \%BCS \& CRCS_{CSC})$

The effects on the ICERs of methods and parameter uncertainty will be assessed by one-way and/or multi-way sensitivity analysis. For example, ICERs may be sensitive to wage rates of key personnel and the overhead rates. Statistical uncertainty in the cost-effectiveness ratios will be assessed with 1,000 bootstrap samples. The outcome of each bootstrap sample will be expressed as a point on a scatter plot of incremental costs and percent screened and reflects the uncertainty arising from the model parameters. Scatter plots of the incremental costs and effects will be used to define the 95% confidence limits around the cost-effectiveness ratios.⁽¹⁴⁶⁾

Aim 3: Interaction analysis.

Hypothesis 1 Interactions: We will use interaction terms in the logistic regression models, developed above for analyses of Aim 1, to test whether intervention effects depend on knowledge, cancer screening beliefs, health status, demographic variables (age, race, education, and marital status), screening history, out-of-pocket costs for screening, baseline stage of adoption, provider recommendation, and participant involvement in the intervention. We will also test the interaction between each intervention and whether participants sought help through additional contact(s) with the research assistants. If an interaction is significant, we will use parameter estimates from the logistic regression model to estimate odds ratios for intervention effects at various levels or scores of the interacting covariates (e.g., within each race or site, or at various values, for example quartiles, of perceived barriers). Because many interactions will be tested, we will adjust for multiple comparisons (see below).

Hypothesis 2 Site Differences: We will compare screening adherence between the group of women who receive care in sites that have colonoscopy available with those who are not in such sites using logistic regression after adjusting for randomized group (usual care, TIWeb, CSC, and TIWeb + CSC).

Adjustment for multiple comparisons: Because many tests will be performed in Exploratory Aim 3, we will report p-values adjusted for multiple comparisons in the analyses, using the resampling step-down adjustment method of Westfall and Young,⁽¹⁴⁷⁾ which accounts for the dependence structure between related tests.

Analysis Issues: *SPSS Data Entry*⁽¹⁴⁸⁾ will be used as the data management system for the project's telephone interviews. A computer-assisted telephone interview (CATI) program will be developed by an experienced programmer from the Indiana University School of Medicine Division of Biostatistics. For each field of entry, ranges will be set to accept only legitimate responses, and skip patterns will be programmed to make the interviews more accurate.

Limitations of This Study and Analyses to Address Limitations: The proposed study is designed to achieve the specific aims and test the hypotheses. However, several limitations are listed below along with explanations of our efforts to minimize the limitations.

- **Loss to follow-up:** Although we will attempt to retain subjects who complete the baseline telephone interview through the 6-month follow-up interview, there will be attrition because of participant dropout, death, and moving. We are conservatively estimating a 10% loss to follow-up although we expect it to be closer to our previous studies of 5% over a 6-month period. When analyses are performed to examine criterion variables at any given time point, all subjects who have data at that point will be included, minimizing the effects of loss of subjects because of later drop-out. In addition, the primary outcome variables, mammography and CRC cancer screening adherence, will be available through electronic records audit. As long as women drop out at a similar rate in both intervention groups, the threat to internal validity of dropout bias will be minimal (in addition, see Missing Data below). Additionally, we expect a low drop-out rate. It should be noted that attrition was accounted for in the sample size determination and power analysis.

- **Missing data and methods for handling in analyses:** Missing data should be minimized by the use of telephone data collection and through interviewer training. Based on our previous work, we expect no more than 1-2% missing data for any single variable. Missing data for the major variables of CRC and breast cancer screening adherence (claims data) will be of concern if a woman changes health insurance plans. If a woman changes plans, we will still collect 6-month self-report data and inquire as to whether she has received either CRC or BC screening at another location. Because enrolled women will have signed informed consent to access claims data, we will be able to obtain CRC screening mammography records even in the event that health care plans have changed. We will examine reasons for drop-out and compare baseline characteristics of those with complete data versus those with missing data. If data are 'missing at random' (MAR) estimates will be biased and if 'missing completely at random' (MCAR) estimates will be inefficient if models are not adjusted for missingness. Therefore, we will use multiple imputation to perform adjustment for missingness. We will also perform sensitivity analyses to see how the results might have been affected under various assumptions had the data been available. The sensitivity analysis will also include estimating models while stratifying on the categories of missing data patterns,⁽¹⁴⁹⁾ although the multiple imputation method will be considered the more authoritative adjustment. Because patients will be randomized after they receive their baseline assessment, there are three possible missing data patterns (i.e., missing 2-week assessment, missing 6-month assessment, or missing both 2-week and 6-month). Furthermore, claims data will make it

possible to analyze adherence at 6 months even for women who dropped out, as long as claims data for those women can be obtained.

- **Sample bias:** We conservatively estimate that about 50% of contacted women will consent to participate, and women who are interested in CRC or BC screening may self-select into the study. Contacting only nonadherent women will minimize this bias.
- **Feasibility/Clinical Relevance:** Either of the intervention strategies tested in the proposed project could easily be adapted into routine practice, if found effective. Previous studies have tailored interventions on a large number of variables necessitating lengthy interviews (Preliminary Studies). In contrast, the proposed interventions will be tailored on fewer variables and in an interactive format, thus facilitating data collection at baseline and “batch processing” the intervention. The TIWeb could even be distributed during routine care visits if a recent mammogram or CRC screening is not recorded on the chart. The addition of a CSC call from the provider’s office could also be incorporated into practice if found to have an additive value to the TIWeb.

E. Human Subjects

1. Risks to Subjects

Human Subjects Involvement and Characteristics. Participants in this study will be eligible if they have ever been a patient of any of the participating physicians; are age 50 to 75; are nonadherent to CRC or CRC and BC screening; and are able to complete telephone surveys and, depending on intervention, view a TIWeb, view a TIWeb and receive a counseling call, or receive usual care. Women will not be eligible if they have a history of adenomatous polyps, a personal history of CRC, inflammatory bowel disease or an hereditary syndrome (HNPCC\FAP). Eligibility criteria will be determined from both database records and self-report. Because this project involves mammography utilization, only women will be included.

Source of Materials: Data will be obtained from self-report at baseline and at 4-week and 6-month follow-up. Mammography status and CRC screening will be obtained from medical record data as well as self-report. Cost data will be obtained from the study administrative records.

Potential Risks: The proposed investigation does not present physical risk. Emotional or psychological risks, if they occur, would be slight. Possible fear or anxiety may be elicited when asking questions about BC,mammography, and/or colon cancer screening.

2. Adequacy of Protection against Risks

Recruitment and Informed Consent: Recruitment of subjects follows a plan that complies with the HIPAA requirements. Eligible women will be identified by the INPC, Community Health Network, any of the participating physicians, or their designee. The research office will send each potentially eligible woman a letter explaining the study and including a brochure and refusal postcard. Women will also receive a refusal postcard to send back if they choose not to be contacted. They can also refuse by calling a toll free number or emailing the project manager (this information found on the brochure). They can also call the toll-free telephone number provided on the brochure to call should they have questions. If women have not returned the refusal postcard, called, or emailed to decline within two weeks, they will be put on the schedule for a recruitment call. In order to tell whether or not the two week opt out period is sufficient time for women to opt out, the PI and project manager will monitor a spreadsheet that will be developed for tracking calls made by study staff to women who indicate that they did opt out of the study by returning the refusal postcard, calling the toll free number, or emailing the project manager. If a woman indicates that she did opt out the study staff will apologize and indicate to the project manager or PI that this has happened. The project manager will then make sure her documentation is destroyed. Once this occurrence has happened a total of ten times, the PI will reevaluate the opt out time period and consider revising. Any occurrences will be reported to the IRB at continuing review. Research assistants will attempt to contact each woman by phone to further explain the study. If a woman indicates that she does not want to participate, she will be thanked for her time and no further contact will be made. If a woman agrees to participate, we will obtain verbal consent for a baseline telephone or electronic interview that will be conducted at the time of contact if convenient or within one week. The components of consent are listed on the brochure and include the right to terminate the study at any time without changes in health care. An authorization form to access medical records will be available for the

participant to sign electronically. The entire process of the study will be explained including the possibility of being assigned to one of two groups, the 4-week and 6-month telephone interviews, and the need to obtain mammography records.

Protection against Risk: Interviewers and research assistants delivering the CSD will be graduate research assistants in a health-related field who will be trained to detect unwarranted anxiety or fear. Precautions will be taken to minimize anxiety, fear, and embarrassment. Women will be informed about the study prior to entry. Women will understand that they may terminate participation in this study at any time during the interview. They will also have the opportunity to decline to answer questions that are objectionable to them.

The proposed research may present possible risk to confidentiality because follow-up interviews require monitoring of the participant's address and telephone number. Participants will be given an identification code to separate identifying information from responses. Personnel involved with the interviewing will be educated about the importance of confidentiality. All identifying information will be destroyed following the final interview. Analyses will include only summaries of data and datasets with personal identifiers removed.

The proposed research does involve slight emotional or psychological risk. Precautions will be taken to minimize these risks through: 1) thoroughly explaining the study initially, 2) emphasizing that participation is voluntary, 3) allowing the participant to stop at any time during the interview, 4) using well-trained female interviewers and nurse counselors, and 5) coding data for confidentiality.

Indiana University has procedures in place to fulfill the NIH requirement for education in the Protection of Human Research Subjects. All grant personnel involved in the design or conduct of research involving human subjects on this project have or will complete this required education prior to the initiation of this project.

3. Potential Benefits of the Proposed Research to Subjects and Others

All participants will benefit monetarily because each will receive \$60 in gift cards for fully completing the study (\$20 for baseline and each of two telephone or electronic data collection interviews). In addition, participants may benefit from gaining knowledge about CRC and mammography screening. We will utilize the gift card service offered by Hallmark Business Connections.

4. Importance of knowledge to be gained: The research will indirectly benefit all women by testing interventions that may be related to BC and CRC screening behaviors in the population at greatest risk for CRC and BC, those 50 or older. Study findings may be used by health professionals to deliver new, more effective interventions to increase both CRC and BC screening.

Women and Minority Inclusion in Clinical Research:

By virtue of the nature of this study, all study participants will be women. Women will be recruited through their physician's medical records. Of these we estimate we will need to contact 5232 to yield 2616 participants who will be randomized, after consent, to one of three intervention groups and a usual care group. A letter of support is included in this application.

Inclusion of Children

The research topic to be studied is not relevant to children.

Data Safety and Monitoring Plan

Graduate research assistants will be extensively trained and monitored throughout the project to conduct computer-assisted telephone interventions (interviewers) and deliver assistance with the group completing the TIWeb program. Initial training will be conducted during a two-day session. The first day will consist of presentations including the following: 1) overview of grant objectives and rationale; 2) detailed demonstration of two intervention arms; 3) background and training on collecting data free from bias; 4) basic information on scale and item response issues; 5) protection of human subjects and confidentiality issues; and 6) data and intervention monitoring and quality assurance procedures. The second day will begin with a demonstration of

data collection using computer-assisted telephone interviewing. Following this initial demonstration, interviewers will role-play with videotaped feedback until they have reached 100% compliance with guidelines for data collection integrity. Research assistants who provide technical assistance to women needing help to use the TIWeb in their homes will be trained to assist with use of the TIWeb without providing additional education or information. They will practice and role-play until they have reached 100% compliance with guidelines for intervention delivery.

Quality Assurance for Intervention Delivery

Quality assurance and monitoring for integrity of intervention delivery are described in the previous section and in the Process Evaluation section of the proposal. Procedures for monitoring outcome data collection are described below. Dr. Susan Rawl will be responsible for oversight of monitoring quality assurance for intervention delivery, outcome data collection, and technical support.

Quality Assurance for Outcome Data Collection

After data collection begins, data collectors/interviewers will be part of the biweekly research team meetings that include the investigators, project managers, and research assistants to discuss project implementation and address questions or concerns that have arisen in the previous two weeks. All interviewers will be required to record one telephone interview each month; these interviews will be reviewed by the project manager and the investigators for quality assurance purposes. An evaluation checklist has been developed to assess the quality of data collection interviews and adherence to study protocol. Interviewers will be trained to query participants who have reported an abnormal mammogram to ensure prompt medical follow-up.

Quality Assurance for Data Managers

Data management will be handled by biostatisticians in the Indiana University, School of Medicine, Department of Medicine, Division of Biostatistics. Data monitoring will occur weekly as data from each interviewer are merged with the larger data set. Biostatisticians will handle all data merging. Backup data files will be kept in the Principal Investigator's office as well as the office of the biostatisticians. Interviewers will complete a form each week when sending data to be merged. The form will alert the biostatisticians to any abnormalities in the data set. All computers that will be used to collect and send data during implementation of the study or to store data at the central secured location will be password-protected.

Data integrity and security

IUPUI-Clarian Institutional Review Board approvals and related documents as well as all signed informed consent forms will be kept at Indiana University, School of Nursing in a locked location. All computers will be password-protected. Only trained grant personnel will have access to data. Once all data have been linked together for individuals, identifiers will be deleted from the data base that includes interview and mammography data. Identifiers will be kept in separate locked files from the collected data and used only for follow-up data collection. At the end of the study all identifiers will be deleted.

Identification of Adverse Effects

The principal investigators will monitor adverse events. First, adverse events will be monitored through the interviewers. Any concern will be brought to the attention of the principal investigators and, if immediate action is necessary, it will be undertaken and later discussed at team meetings. Adverse events will also be immediately reported to the IUPUI-Clarian Institutional Review Board. Participants will have a phone number to call if problems occur. Indiana University has a process in place whereby random monitoring for data integrity will occur by a committee external to the grant staff.

Data Sharing Plan

Results of the trial will be disseminated through presentations at professional meetings and publications. The final dataset, with necessary identifiers (excluding those prohibited by HIPAA), will be made available to qualified investigators within 6 months of acceptance of the manuscript describing major outcomes. Investigators who request to use the dataset will be required to obtain IRB approval and sign a data use agreement before data will be released.

F. Vertebrate Animals

None

G. Literature Cited

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