TITLE: Increasing Access and Developing Predictors for Colorectal Cancer Screening for Minority and Medicaid Clients

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Principal Investigator:	**Deborah O Erwin, PhD Roswell Park Cancer Institute Elm and Carlton Street Buffalo, New York 14263 716-845-2927 Deborah.erwin@roswellpark.org**
Sponsor:	**NIH/NCI SBIR/STTR**

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1 SYNOPSIS

African Americans have 22% higher incidence and 49% higher death rates from colorectal cancer (CRC) than any other ethnic/racial group. Similarly, lower socioeconomic status (SES) is also associated with higher CRC incidence and mortality. Both of these groups are overrepresented in Medicaid populations. Screening colonoscopy is the "gold standard" for cost-effective cancer prevention and control and several fecal tests (e.g., FIT) are reliable alternatives. However, Medicaid clients have much lower screening rates causing large "gaps in care" – contributing to higher CRC morbidity and mortality—and are major challenges for health insurance companies and clinical practices which are negatively impacted by the lower quality metrics and reduced financial benefits that result from lower screening rates. Improving CRC screening rates is therefore a strategic priority for both health care providers and insurers. The mission of Witness CARES, LLC, is to improve people's lives by facilitating use of health care. The goal of this Phase I STTR proposal is to test the feasibility of providing specialized services (i.e., *WC Services*) to increase CRC screening for Medicaid clients and thereby improve metrics for our health insurance (YourCare and clinical practice (Mercy Comprehensive Care Center) customers. Based on prior research and experience, we will conduct a small pilot effectiveness study combining a broad range of services to educate, activate and navigate these "gaps in care" clients for a broader market (not just a single facility or patients with screening referrals) in order to test the feasibility for future commercialization. In addition, we will evaluate these clients to develop a predictive algorithm for assessing likelihood of CRC screening outcome. We propose the following specific aims: ***Aim 1:*** Test the feasibility of *WC Services* to achieve CRC screening for non-adherent Medicaid clients. **Milestone 1a:** Achieve colonoscopy by a minimum of 60 out of 200 (≥ 30%) patients contacted. **Milestone 1b:** Achieve CRC stool screening for 70 of the 140 colonoscopy non-adherent clients. **Milestone 1c:** *WC Services* will be revised to produce a new prototype to test in a Phase II based on feasibility findings. ***Aim 2:*** Develop an algorithm for predicting CRC screening outcomes following intervention services. **Milestone 2a.** Develop models based on existing R01 data to predict intent and CRC screening behaviors. **Milestone 2b**. Revise this R01 model incorporating new measures collected prospectively with 80% of clients contacted (n=160) to identify variations for likelihood of stool test v. colonoscopy completion. **Milestone 3** will be the Phase I report of these findings. Successful completion of these aims are expected to show the acceptability and feasibility of *WC Services* to improve CRC screening rates for Medicaid patients and develop assessment tool(s) that enable us to evaluate this product in a randomized controlled trial in a Phase II study with a special emphasis on reducing CRC disparities in minority and lower income populations.

2 BACKGROUND

Colorectal cancer (CRC) is the second leading cause of cancer deaths in the U.S.[1] African Americans have 22% higher incidence and 49% higher death rates from CRC than any other ethnic/racial group.[1] Similarly, lower socioeconomic status (SES) is also associated with higher CRC incidence and mortality.[2] Both of these groups are overrepresented in Medicaid populations.[3] Amongst screening options for average-risk individuals, both stool tests (e.g., fecal immunochemical-FIT or DNA-mtsDNA/Cologuard®) and colonoscopy are deemed effective;[4] with colonoscopy being the most effective at reducing CRC incidence.[5,6] Adherence to CRC screening guidelines is poor for African American and low SES groups,[7] even for insured individuals. In New York State (NYS), over 80% of CRC screening non-adherent individuals are insured. Lack of screening in insured adults is a "gap in care" that poses significant challenges for insurers, including reduced quality metrics (i.e., Medicare Star and Healthcare Effectiveness Data & Information Set - HEDIS® scores) which negatively impacts financial bonus payments to these companies. Increased CRC screening is a high value product in the health care market as

well as addressing cancer disparities.

Disparities and low screening rates exist primarily because of a host of structural (e.g., access, transportation) and individual barriers (e.g., fear, negative affective associations, daily life issues) experienced by lower income and minority patients that are generally beyond the scope of clinical practices and health insurance companies to address. Approaches to address these barriers have been proven effective by our team and others for various screening services but have not been tested as a marketable commodity. These proven methods include the use of patient navigation,[8,9] culturally appropriate education,[10,11] and community-based participatory processes.[12,13] However, navigation services are not reimbursable expenses for clinical providers, require specialized expertise and access to multiple ancillary services (e.g., transportation). Health insurers have experimented with monetary incentives, reminders and incentivizing health providers, but these approaches are limited and do not address the basic structural and individual barriers influencing behaviors. But if proven to reduce "gaps in care"—insurance companies *will* outsource and pay for these services (e.g., see Letters; and National Witness Project (NWP) in Facilities and Resources). Effective programs offering multi-level services to optimize screening for non-adherent clients are not readily available for insurers or clinicians to adopt or purchase. Witness CARES, LLC proposes to remedy this gap by offering a full-service resource for educating, activating and navigating clients to screening for insurance companies (e.g.,YourCare, see Letter) and for primary care clinics (e.g., Mercy Comprehensive Care Center, see Letter). Moreover, although there is an extensive body of work examining decision-making predictors of successful CRC screening,[14,15] there are not easily implementable tools for predicting compliance in real time, or to assess for which clients at-home stool testing versus colonoscopy screening is likely to be most achievable. This STTR Phase I study provides an opportunity for Witness CARES, LLC to explore the feasibility of providing these services to Medicaid clientele to satisfy the screening expectations of insurers and primary care providers (Aim 1), and the feasibility of developing a predictive tool(s) (Aim 2) for determining which screening test is most appropriate for clientele.

Specialized Interventions. Our team has developed and implemented effective, specialized interventions for over 20 years to reach, educate, activate and navigate African American and low SES clients into cancer screening.[16,17] For example, patient navigation by lay navigators (Consultant, Jandorf) increased adherence to screening colonoscopy to 66.4% among urban minority pateints[18] at a cost of only $29/patient screened. Our sister, not-for-profit, The National Witness Project (NWP) (See Facilities and Resources), has provided specialized services to health insurance companies in western New York (WNY) on a contractual basis (> $600K) for over three years, screening over 3000 women with mammograms and Pap tests, and demonstrating a potential market for CRC screening navigational services. Witness CARES, LLC needs to conduct this Phase I study to determine if we can create a similar group of services and assessments specialized for increasing CRC screening based on findngs about behavioral constructs impacting CRC screening behaviors from our R01 CA171935 study.[19,20] If proven feasible in this Phase I study, this will be a novel set of services to offer health insurance companies and their clinical practices, with the added innovative technology of an algorithm for predicting screening preferences for this Medicaid population. This would be an important service for over 835,000 African American men and women, and 104,752 additional Medicaid clients between the ages of 50 and 79 who have not had a timely colonoscopy and/or other fecal testing for CRC screening in New York State.[1,21,22] Achieving the aims of this STTR feasibility study, *Witness CARES, LLC has a significant opportunity to develop a feasible prototype for WC Services to improve CRC screening by Medicaid clients and initiate the development of predictive measures to determine the most acceptable CRC screening test.*

3 RATIONALE

The National Witness Project (NWP), has provided specialized services to health insurance companies in western New York (WNY) on a contractual basis for over three years, screening over 3000 women with mammograms and Pap tests, and demonstrating a potential market for CRC screening navigational services. Witness CARES, LLC needs to conduct this Phase I study to determine if we can create a similar group of services and assessments specialized for increasing CRC screening based on findngs about behavioral constructs impacting CRC screening behaviors from our R01 CA171935 study.[19,20] If proven feasible in this Phase I study, this will be a novel set of services to offer health insurance companies and their clinical practices, with the added innovative technology of an algorithm for predicting screening preferences for this Medicaid population. This would be an important service for over 835,000 African American men and women, and 104,752 additional Medicaid clients between the ages of 50 and 79 who have not had a timely colonoscopy and/or other fecal testing for CRC screening in New York State.[1,21,22] Achieving the aims of this STTR feasibility study, *Witness CARES, LLC has a significant opportunity to develop a feasible prototype for WC Services to improve CRC screening by*

4 OBJECTIVES

The goal of this Phase I application is to prove the feasibility and small scale pilot efficacy of *WC Services* to increase CRC screening. We propose the following specific aims:
Specific Aim 1: Test the feasibility of *WC Services* to achieve CRC screening for non-adherent Medicaid clients. **Milestone 1a:** Achieve colonoscopy by a minimum of 60 out of 200 (≥ 30%) patients contacted. **Milestone 1b:** Achieve CRC stool screening for 70 of the 140 colonoscopy non-adherent clients. **Milestone 1c:** *WC Services* will be revised to produce a new prototype to test in a Phase II based on findings.
Specific Aim 2: Develop an algorithm for predicting CRC screening outcomes following intervention services. **Milestone 2a.** Develop models based on existing R01 data to predict intent and CRC screening behaviors. **Milestone 2b**. Revise this R01 model incorporating new measures collected prospectively with 80% of clients contacted (n=160) to identify variations for likelihood of stool test v. colonoscopy completion.

Research Questions: **a)** Will Medicaid clientele, health insurers and physicians find *WC Services* usable and valuable for CRC screening? **b)** Will clients accept services and obtain colonoscopy or stool tests? **c)** Will current and/or new measures show predictive potential within Medicaid clientele for colonoscopy and/or stool tests? **d)** Will *WC Services* be able to increase screening enough to demonstrate potential for improving quality metrics for health insurance companies and primary care practices? Answering these research questions and achieving these aims (**Milestone 3**: Phase I Report), position us for a larger randomized controlled evaluation in Phase II while addressing important CRC screening disparities for the community and health care system.

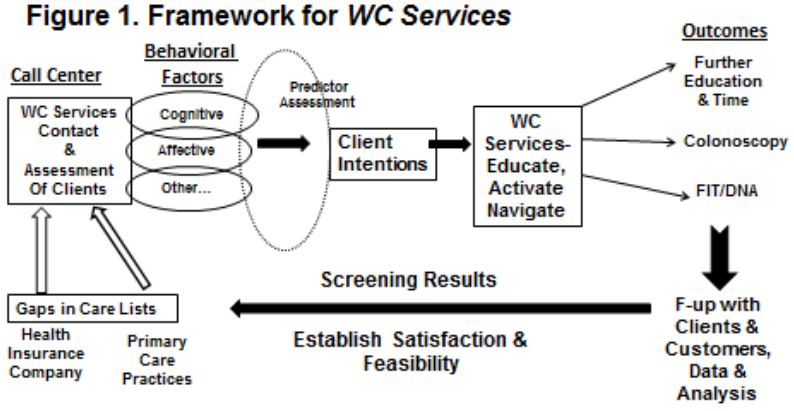
5 METHODOLOGY

Overview. This Phase I small pilot efficacy and feasibility application is built upon the combined passion, persistence, science, expertise and experience from the following: a) Research on navigation for CRC screening (R01 CA 120658, Jandorf, see Bio);[25] b) Years of community-based studies (Erwin, Johnson, Jandorf, see Bios)[10,16,26] resulting in the National Witness Project® (NWP) not-for-profit; c) Ability of the NWP to garner contracts for services from health insurance companies and health care providers (see Facilities and Resources); d) Results from our R01 (CA171935, MPIs: Erwin, Kiviniemi, Jandorf, see Bios);[19,20,23] and e) Training through the NCI SPRINT Supplement (Erwin, Johnson, see Bios).[27] Based on this foundation, we now

are in a position to determine if we can combine this experience, data and expertise into a deliverable product (*WC Services*) that provides acceptable and appropriate services to non-adherent Medicaid clients resulting in effective CRC screening rates to meet the various requirements of health insurers (i.e., YourCare), primary care practices (Mercy Comprehensive Care Center- MCCC) and gastrointestinal endoscopy providers.

Product Concept. The proposed framework for services based on previous research[19,28] is displayed in Figure 1. Encrypted lists of eligible clientele will be given to racially-concordant, call-center staff, including experienced navigators, according to established procedures by NWP. Scripts, based on Jandorf's CRC screening protocol, will be used by navigators and call-center staff, including messaging and information that promotes positive affective associations with colonoscopy. From initial assessments and client responses, navigators will determine next steps following cues and flow chart experience (see Figure 1). Based on assessments in real time, navigators will offer to send appropriate materials, messages and videos to clientele electronically and or by mail as requested to assist with clients' decision-making if they are not prepared for either colonoscopy or stool tests, and will be followed up by phone within two weeks. For clients desiring colonoscopy, navigators will assess client capacity to obtain this screening (e.g., Rx, GI doctor, scheduling appointment, prep materials and process, transportation, escort) and offer assistance as needed. For clients desiring to use a stool test, navigators will facilitate FIT tests or mtsDNA (Medicare eligible only and Exact Sciences provide navigation). Telephone follow-up will be conducted on a prescribed schedule for clients planning to be screened. Including primary care clients (MCCC) as well as insurer clients (YourCare) gives us an opportunity to test the acceptability of *WC Services* for both customers and their clientele to determine variations in services, needs and outcomes for the two sources.

Figure 1. Framework for *WC Services*



Phase I Goals, Timetable and Milestones: The goal of this Phase I STTR study is to determine the feasibility and small scale pilot efficacy of *WC Services* to increase CRC screening, determine appeal and satisfaction with services by clients and company partners, and based on client variables, predict the CRC screening test most acceptable and likely to be

Table 2. Phase I Timeline, Tasks, Milestones	Jul	Aug	Sep	Oct	Nov	Dec*	Jan	Feb	Mar	Apr	May	Jun
1)Test ability to increase CRC screening												
-Finalize *WC Services* process flow chart	X	X										
-Conduct pilot for colonoscopy (Milestone 1a)			X X	X X	X X		X X	X X	X X			
-Conduct pilot for stool screens (Milestone 1b)			X	X	X	X	X	X	X	X	X	X
-Conduct satisfaction & prediction surveys												
-Produce prototype for RCT (Milestone 1c)												
2) Develop algorithm for predicting CRC												
-Analyze R01 variables (Milestone 2a)	X	X	X	X								
-Assess new measures with clients			X	X	X		X	X	X			
-Analyze new variables for new Screening Engagement Model (Milestone 2b)						X	X	X	X	X	X	
-Prepare Phase I Report (Milestone 3)											X	X

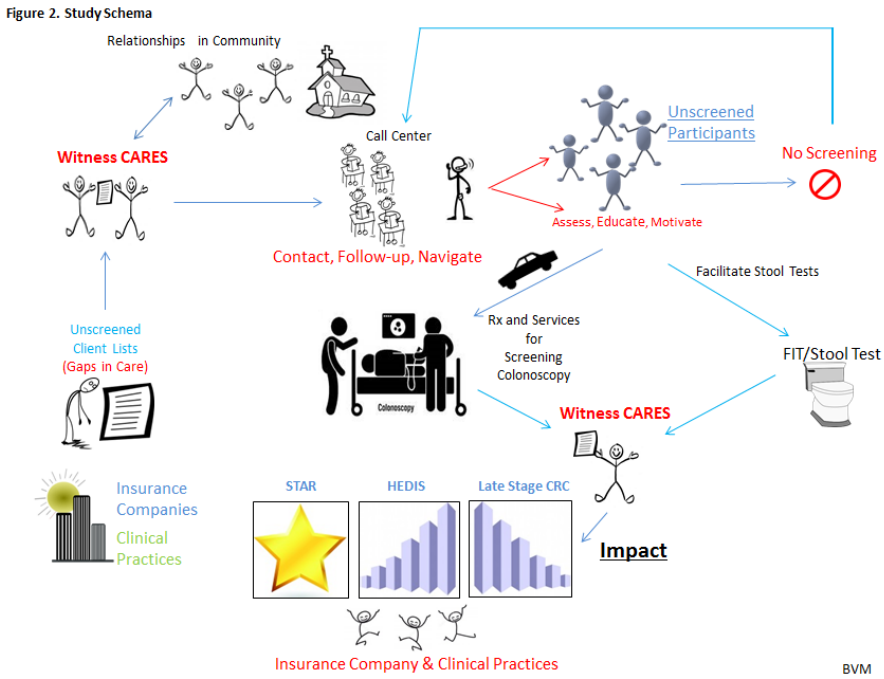
successfully completed. Table 2 presents the timeline (*Dec. is not an ineffective month for scheduling screenings based on our experiences, so we resume the pilot in Jan.)
Study Team: Dr. Deborah Erwin (RPCI subcontract) and Ms. Detric Johnson will manage the science and *WC Services* activities, respectfully, as MPIs. The *WC Services* to Medicaid clients will be conducted by experienced team members contracted from the NWP (see Budget Justification). The pilot efficacy study benefits from the expertise of assembled colleagues Drs. Kris Attwood (Statistician), Marc Kiviniemi (Consultant) and Ms. Jandorf (Consultant). The entire process and especially the feasibility assessments will be reviewed under the guidance of a five-member advisory board designed to offer expertise and counsel regarding 1) Technology transfer and potential commercialization issues (RPCI, Dr. Emmerling); 2) Needs and concerns of the health insurance industry (YourCare, Ms. O'Donnell); 3) Needs and concerns of primary care clinical practices (MCCC, Ms. O'Hara/Gomlak); and 4) Science and clinical issues of colonoscopy and CRC screening (RPCI, Dr. Bain).

Aim 1*: Test the feasibility of WC Services to achieve CRC screening for non-adherent Medicaid clients.* Based on previous experience and research (see Bios, Facilities), we hypothesize that we will be able to combine multi-level services to effectively assist ≥ 65% of Medicaid clients from health insurer and clinical partners to obtain CRC screening in a 6-month trial during this Phase I. Achieving the milestones and benchmarks in Aim 1 will provide proof that we can improve screening metrics and meet the needs for our potential customers.

Partners, Recruitment and Participants. Witness CARES, LLC has established relationships with Mercy Comprehensive Care Center (MCCC), a local primary care practice serving a high proportion of Medicaid patients, and YourCare Health Plan, a Medicaid Managed health insurance company serving Buffalo, NY (see Facilities and Resources) to conduct this Phase I study (see Letters), and we will rely upon our Scientific Advisory Board (see Letters) to guide the conduct of the study, assuring that we are meeting the needs of customers, providing optimal services for clients/patients and truly achieving our feasibility measures in this study to effectively move forward into Phase II.

WC Services Flow Chart. To finalize details of the decision flow chart for contacting and providing services for CRC screening, Dr. Erwin and Ms. Johnson will work with the NWP navigators and call center staff to modify activity flow charts from current mammography screening, adding all details for CRC screening actions. We will also notify physicians including gastroenterologists and private and hospital colonoscopy facilities serving MCCC and YourCare patients that we are piloting new services for patients in the area, explain the services and obtain preferred colonoscopy prep instructions. MCCC and YourCare will assist with this process.

Pilot Study. Study participants will originate from MCCC and YourCare "gaps in care" lists of Medicaid/Medicare patients who are ages 50-75, have not had a stool test within 11 months, colonoscopy within 9 years and live in the Buffalo/Niagara Falls area. YourCare currently has a CRC gaps in care list of approximately 2500 clients and MCCC has 1599 patients for this study. From the NWP experience with insurers, we expect up to 48% of clients to be excluded (e.g., incorrect phone numbers, no longer insured, already screened). Therefore, we anticipate having a working list of at least 1,968 clients from which to contact over the approximately 26-week enrollment period (see Timeline Table 2). Based on prior experience with mammography screening for gaps in care clients, we know we can successfully contact ≥ eight new clients per week (within the STTR budget) for a potential sample size of N=200 from the two sources (MCCC ~100 clients; YourCare~100 clients), which is expected to provide 80% power (at α=0.05) (see Analysis of Aim 2 below). (Also See Figure 2. Study Schema).



Aim 2: *Develop an algorithm for predicting CRC screening outcomes from intervention services.* We hypothesize that we will be able to identify a set of predictive measures, applicable for Medicaid clients and feasibly implementable, that will allow us to effectively predict which clients would be most likely to "convert" from not intending to screen to intending to screen following the receipt of *WC Services* and which clients would be most likely to translate that intention to screen into actual engagement in specific screening behavior.

Data Sources and Participants: Specific Aim 2 will rely on a two pronged approach. First, we will leverage a rich, existing data resource collected as part of our recently completed community trial R01 of the WitnessCARES intervention for CRC screening (See Measures Table in Human Subjects). The data available from this study includes pre-intervention measures on a variety of psychosocial determinants of screening behavior, relevant demographic characteristics, intentions to screen both before and after the intervention, and, for a subset of participants, a 6 month follow-up report of actual screening behavior. The dataset contains 516 individuals who were: over age 50, self-identified as Black/African American, and either never screened or currently screening noncompliant. In addition to this secondary data analysis, we will collect and analyze new measures as a part of the methods described in Aim 1.

Proposed Secondary Data Analysis (Milestone 2a). The dataset from the WitnessCARES intervention study will provide us the ability to develop an initial iteration of a predictive tool to effectively identify two types of potential clients: a) individuals who, if they receive the intervention, are most likely to change from not intending to screen for CRC to intending to screen for CRC; b) individuals who intend to screen following the intervention but do not successfully convert that intention to actual engagement in screening behavior. To do so, we will use the individual items in the psychosocial and demographic measures collected pre-intervention to identify a subset of items that can successfully distinguish the types of potential clients described above. The analysis will proceed in 3 phases: variable reduction, screening intent model, and screening engagement model. *Variable Reduction:* Standard variable reduction techniques (such as principle components, missing values ratios, low variance filter, etc.) will be used to combine or exclude individual items (or sub-scales) for the candidate list of variables for model development. *Screening Intent Model:* Model development will proceed in two steps and will be based on available subjects. First, using a multivariable logistic regression model, main effects will be selected using a bootstrap backwards selection method (BBSM; alpha exit = 0.01). Second, potential two-way interactions between the selected main effects will

be identified using the BBSM (alpha exit = 0.001). The final model estimates for predicting screening engagement will be obtained using standard bootstrap methods. *Screening Engagement Model:* The model development will proceed as described for the screening intendent model, except only subjects intending to be screened will utilized. *Model Performance:* The screening intent and engagement models will produce predicted probabilities of intent and engagement based on subject characteristics. These probabilities are relatively subjective, so the Youden's index criterion will be used to identify a cut-off for both models that identifies which clients should be identified as "intending to screen" and "screening engaged". Model performance will be summarized using the receiver operating characteristic (ROC) curve and corresponding area under the ROC curve (AUC), and the sensitivity and specificity corresponding to the Youden's index cut-offs. *Alternative Approaches:* Classification and Regression Tree (CART) or other machine learning methods may be employed for the development of a classification model. In the presence of multiple models, models will be ranked by the specified performance measures.

Proposed Data Collection (Milestone 2b). For this secondary data analysis, as a part of the Aim 1 methods described above, navigators will invite all clients contacted to complete assessment items via telephone. Based on prior research and navigation experience, we know that clients are willing to complete health assessments and surveys of up to ~130 questions by phone if incentivized. This telephone assessment includes 118 self-report questions all of which have been used by the current team members with African American and Medicaid clients. However, we have never combined all of these items, and expect this to increase our capacity to identify impactful predictors. Based on prior experience, we are adding a Patient Activation Measure (PAM),[29-32] Process of Change (POC)[33,34] for CRC screening and a 3-item unpublished, Navigator Subjective Assessment/Predictor (NSAP) by the navigator at the completion of the other questions (based on recent experiences by Jandorf and Erwin). A similar data analysis strategy will be applied here. The 118 items will be used to predict differentiation of screeners from non-screeners as well as, among screeners, those who chose FIT versus colonoscopy (COL). Together, these are expected to significantly increase our predictive capacity for colonoscopy outcomes. We anticipate (Milestone 2b) being able to complete the survey with at least 160 clients during this Phase I.

6 TARGET ACCRUAL AND STUDY DURATION

From a list of approximately 2000 unscreened individuals from insurer and primary care patient lists (acquired through a Business Association Agreement), we will contact and enroll a maximum of 200 participants. Accrual is expected to take up to 2 years.

7 SUBJECT SELECTION

Recruitment and Informed Consent. Witness CARES, LLC staff members will work with our customer clients (YourCare and MCCC) to obtain Business Association Agreements in order to call, recruit and consent clients from their "gaps in care" lists. Information sheets and oral consent over the phone will be used in order to conduct the telephone survey that collects information to contribute to the outcomes and predictor tool development. The Business Agreements will provide coverage for offering the navigational services.

The key elements of the informed consent procedure which will be explained to the participants are: 1) the research status of the study- particularly the survey; 2) the prospect of psychological risk and the provisions for it; 3) the lack of guarantee of benefit from participation in the survey, 4) the confidentiality of subjects responses to all study measures; 5) the voluntary nature of the study; 6) the lack of consequences to medical care of the decision to consent or to refuse to participate in the survey (all participants will be offered CRC screening regardless of the

decision to complete the telephone survey); 7) the receipt of the gift card for participating in the survey interview, and 8) the freedom to withdraw from the study or to refuse to answer specific questions at any time.

Before the survey is conducted, staff members will explain: 1) the nature and purpose of the research endeavor, 2) that participation in the research component is completely voluntary, and 3) that data collected from participants will be confidential and assessed, evaluated and reported as aggregate data, as well as precautions taken in the storage of the data. The study staff member will verify that the women and men who wish to participate meet the study's eligibility criteria as described below. The staff member will solicit and respond to any and all inquiries.

For the colonoscopy procedures, individual, hospital/facility/physician specific consents will be signed and this is beyond the scope or responsibility of Witness CARES, LLC or the study staff.

7.1 Inclusion Criteria

Witness CARES, LLC will develop and obtain business agreements with YourCare and Mercy Comprehensive Care Center (MCCC) as required by these businesses to allow them to provide lists of their clients who are ages 50 and over and are non-adherent to CRC screening over the past year (i.e., no stool testing in past 11 months or colonoscopy for over 9 years). The clients will be Medicaid or Medicaid/Medicare subscribers. Uninsured patients may be included from MCCC, but will only be eligible for services to obtain FIT tests through the NYS Cancer Services Program.

7.2 Exclusion Criteria

Any participants from the lists of gaps in care clients from insurance or primary care practices who report having had a colonoscopy in the past 9 years (or having positive findings such as polyps, 5 years) or having completed some type of fecal test for CRC will be excluded. Participants under 50 will be excluded unless they have been deemed high risk by their physician, and have a prescription for CRC screening. Participants symptomatic for CRC will be excluded from the study, but will be referred for follow-up and colonoscopy.

7.3 Inclusion of Women and Minorities

The research outlined in this proposal will involve lower socioeconomic and African American clients as CRC screening is lowest in these groups. We will enroll up to 200 men and women in this study (including any race/ethnicity). We hope to enroll equal numbers of men and women.

8 STATISTICAL ANALYSIS METHODOLOGY

AIM 1: Assessment and Evaluation. After Navigators have contacted and assessed client CRC screening needs by phone for providing *WC Services*, they will invite and consent clients to complete the study survey to collect prospective predictor assessment measures for which participants will be incentivized with a $20 retail gift card, a method we have found successful in previous studies. A process and system for contacting, monitoring and then assessing satisfaction of clients with services will be conducted based on current mammography services. Witness CARES,LLC will be establishing a new and more comprehensive appointment scheduling monitoring system for this feasibility study to enhance measures currently used by NWP in order to improve the ability to track and document all CRC screening services and outcomes for future development. We currently have metrics for navigation and screening that will be revised for colonoscopy and stool test navigation and colonoscopy appointment

scheduling. We will use current tracking measures for accruals and outcomes and assess these weekly and monthly. We will closely monitor number of client contacts and time requirements to determine potential cost effectiveness and feasibility measures. Colonoscopy and FIT completion will be monitored and then validated by YourCare and MCCC. Basic frequencies and descriptive statistics will be used for this analysis. We will compare outcomes from YourCare and MCCC clients. Upon completion of CRC screening, satisfaction surveys will be conducted by Call Center staff for at least 60% of clients in order to assess *WC Services* acceptability, merit and suggestions for revisions. If clients prefer, these satisfaction surveys can be sent via Survey Monkey and completed on Smartphones. The Call Center will also obtain brief satisfaction and assessment surveys from GI practices and Primary Care Physicians treating Medicaid clients referred through *WC Services*.

Expected outcomes of Aim 1 will prove whether or not *WC Services* can achieve ≥ 65% CRC screening of clients reached. **Milestone 1a:** Achieve colonoscopy by a minimum of 60 out of 200 (≥ 30%) patients contacted. **Milestone 1b:** Achieve CRC stool screening for 70 of the 140 colonoscopy non-adherent clients (50% of clients refusing/ineligible for colonoscopy). Beyond these milestones, additional **feasibility benchmarks** include: a) Acceptance/satisfaction by clients per client satisfaction phone surveys; b) Acceptance/satisfaction by YourCare and MCCC per self-report and any screening metrics improvement; c) Navigation services, number of screening tests per week/month, hours spent for cost analysis; d) Acceptance/satisfaction by GI physicians and facilities per self-report, number and quality of bowel preps and no-shows; e) Process evaluation of all. **Milestone 1c:** *WC Services* will be revised based on outcomes and benchmark measures from Aim 1, to produce a new prototype to test in a larger randomized study in Phase II.

AIM 2: Proposed Data Analysis (Milestone 2b). *Update the Screening Engagement Model:* Utilizing standard Bayesian methods, the data collected in Aim 1 from the (expected) n=160 intent-to-screen clients will be used to: A) update the coefficients of the Screening Engagement Model; and B) determine whether PAM, POC and NSAP measures should be incorporated. The performance of the updated model will be assessed using the AUC, sensitively, and specificity (with 95% confidence intervals as appropriate). If the AUC of the resulting model is 0.8 (or 0.9), indicating reasonable performance, then the corresponding 95% confidence interval width would be 0.14 (or 0.10). *FIT versus COL:* Within the sub-set of subjects that were screened, measures will be compared between those who chose FIT versus COL using the Mann-Whitney U test. In Aim 1 we expect 60 COL and 70 FIT subjects, which provides 80% power (at α=0.05) to detect a 0.5 standard deviation difference. Additionally, a multi-variable logistic regression model may be considered to identify potential independent factors associated with screening choice.

Expected Outcomes. **Milestone 2a:** Develop models based on R01 data to predict intent and CRC screening behaviors. **Milestone 2b**: Revise this R01 model incorporating new measures collected prospectively with 80% of clients contacted (n=160) to identify variations for likelihood of FIT v. COL completion. From these analyses we will produce a new prototype of a Screening Engagement Model to test in a larger trial for a Phase II study. **Milestone 3:** Phase I Report will be prepared to include all Milestones and feasibility benchmarks.

9 INFORMED CONSENT

Human Subjects Involvement and Characteristics. Witness CARES, LLC will develop and obtain business agreements with YourCare and Mercy Comprehensive Care Center (MCCC) as required by these businesses to allow them to provide lists of their clients who are ages 50 and over and are non-adherent to CRC screening over the past year (i.e., no stool testing in past 11

months or colonoscopy for over 9 years). The clients will be Medicaid or Medicaid/Medicare subscribers. Uninsured patients may be included from MCCC, but will only be eligible for services to obtain FIT tests through the NYS Cancer Services Program.

Once Witness CARES, LLC receives these lists they will do the following:

1) Begin calling clients and explaining that they are working collaboratively with their insurer or clinic to provide additional services for clients needing CRC screening. This initial call will allow *WC Services* to determine working/accurate telephone numbers and confirm that clients have not obtained CRC screening. We anticipate calling clients from the list (expected to be up to 2000 clients) until we successfully reach at least 200 clients. Witness CARES, LLC will send insurer and health clinic the lists with results of non-working numbers, patients no longer at numbers, etc.
2) Use an existing CRC navigation assessment to inquire about the client's knowledge and understanding of CRC screening. Depending on the results of this assessment, the navigator may a) determine some basic information about potential services the client will need to obtain screening (stool or colonoscopy), and establish a plan with the client to provide these services with a timeline; or b) send the client additional information by mail, email or text for a smart phone for the client to review, and establish a call-back appointment time.
3) For clients planning to be screened, the navigators will begin the process of working through the services needed by the client (for either completion of the stool test) or the colonoscopy to include some or all of the following: a) delivery of a FIT or Cologuard test (dependent on Medicare coverage); b) telephone followup and assurances that stool test is completed, mailed and results are received; c) assistance to obtain the Rx for colonoscopy; d) determination of acceptable GI physician and screening location for colonoscopy; e) appointment for colonscopy is made; f) education for and assistance with the prep materials and telephone followup for assurance that the materials are purchased (or we deliver them), the client understands the procedure; questions are answered; g) transportation plans are secured if needed, including escort or family member to accompany client; h) telephone followup the day before scheduled colonoscopy to assure prep is/will be completed; i) assistance as needed to transport the client for the colonoscopy appointment; j) telephone followup to assess client satisfaction with the procedure and understanding of results.
4) For clients reluctant to be screened, or who do not complete stool tests or colonoscopy appointments, navigators will conduct additional follow-up and motivational interviewing to encourage completion. After 3 attempts, the navigator will obtain permission from the client to mail them additional information and how to contact the navigator for future assistance, and then the client will be removed from the active list for navigation.
5) All clients reached will be invited to complete a ~130-item survey (based on measures from our R01 CRC study plus two new measures – see Table 1) to obtain answers to questions that will be analyzed to study how to more accurately predict CRC screening compliance. Clients will be offered a $20 gift card as an incentive for completing this survey by the navigator over the phone.
6) Following successful CRC screening (fecal test or colonoscopy), clients will be contacted by telephone to assess qualitative measures of satisfaction with the navigational services as well as the screening services received. These findings will be used to refine and revise the *WC Services*.

Sources of Materials. During the telephone calls, and specifically the survey assessment, survey data will include responses to questions on CRC knowledge, fear of colonoscopy, questions about CRC screening referrals (e.g. regular relationship with PCP physicians, having

had discussion or referral for CRC screening, personal experience or knowledge of individuals in the health care system), Process of Change, Patient Activation Measure and demographic (e.g. age, gender, education level, insurance status) and prior CRC screening (see Table 1). Educational materials will include printed brochures and evidence-based videos about CRC screening.

Table 1. Study Measures

R01 Measure for Milestones 2a & 2b	**Source**	**Reliability**	**Use in Previous Studies**
Benefits/Barriers (Both FIT and Colonoscopy)	Rawl et al 2001	αs > 0.65 Rawl et al 2001	Janz et al 2007 & 2003; Madlensky et al 2004; Menon et al 2003
Affective Associations with screening (including Fear of Colonoscopy)	Crites et al 1994; items selected based on pilot study above	αs > 0.88 Kiviniemi et al 2009; Pilot study described above	Kiviniemi et al 2007 & 2009; Simons et al 1998
Cognitive/Affective Risk Perceptions	Weinstein et al 1995; Zajac et al 2006	Single item measures	Moser et al 2007; Waters et al 2011; Kiviniemi 2010 & 2009
Cancer Worry	Lerman et al 1991		Lerman 1991
Screening Behavior/Intentions	Vernon et al 2004	Test-retest > 90% Vernon et al 2008 Concordance > 0.80 Partin et al 2008	Emmons et al 2009; Janz et al 2007; Nelson et al 2004
Demographics (e.g.,SES, Insurance, PCP, PCP visits, screening referrals)	Erwin et al 2011; Jandorf et al 2010	Single item measure	Erwin et al 2011; Jandorf et al 2010
Prospective New Measures for Milestone 2b only			
Patient Activation Measure®	Hibbard et al. 2005	Reliabiity coeffecients (with ethnic minorities) = ≥.70	Alexander, Hearld and Mittler 2014; Serper et al. 2014; Greene, Hibbard 2012
Process of Change for CRC Screening	Manne et al. 2002	CFI=0.785	Duhamel et al 2011

Potential Risks. There are no physical risks posed by this study. The types of questions asked in the surveys and the types of information presented in the interventions are not different from those that might be asked or presented by a health care provider and thus do not pose greater than minimal risk. Although the chances of psychological distress are minimal, any psychological distress will be monitored by the staff and if appropriate, participants will be offered a referral to Psychology/Psychiatry Staff, if warranted. Potential benefits include increased knowledge about colorectal cancer and screening as well as information about how to get screened and/or assistance and services to successfully complete screening. Although we cannot guarantee that participants may benefit directly from study participation, especially those completing the survey alone, but those clients obtaining colonoscopy may prevent CRC cancer or find it earlier. Study participants in our prior studies have reported they enjoyed providing researchers with greater knowledge of their experience in hopes of facilitating cancer prevention and in possibly benefiting others. Given the potential gains to participants the ratio of risk to benefits is quite low and reasonable.

2. ADEQUACY OF PROTECTION AGAINST RISKS

Recruitment and Informed Consent. Witness CARES, LLC staff members will work with our customer clients (YourCare and MCCC) to obtain and recruit clients from their “gaps in care” lists. Information sheets and oral consent over the phone will be used for the telephone survey. The Business Agreements will provide coverage for offering the navigational services.

The key elements of the informed consent procedure which will be explained to the participants are: 1) the research status of the study; 2) the prospect of psychological risk and the provisions for it; 3) the lack of guarantee of benefit from participation, 4) the confidentiality of subjects responses to all study measures; 5) the voluntary nature of the study; 6) the lack of consequences to medical care of the decision to consent or to refuse to participate; 7) the receipt of the gift card for participating, and 8) the freedom to withdraw from the study or to refuse to answer specific questions at any time.

Before the survey is conducted, staff member will explain: 1) the nature and purpose of the research endeavor, 2) that participation in the research component is completely voluntary, and 3) that data collected from participants will be confidential and assessed, evaluated and reported as aggregate data, as well as precautions taken in the storage of the data. The study staff member will verify that the women and men who wish to participate meet the study's eligibility criteria as described above. The staff member will solicit and respond to any and all inquiries.

For the colonoscopy procedures, individual, hospital/facility/physician specific consents will be signed and this is beyond the scope or responsibility of Witness CARES, LLC or the study staff.

Protection Against Risk. Oral consent will be received from participants prior to their completion of study questions for the telephone survey. These include questions on CRC knowledge, fear of colonoscopy, cancer worry, perceived risk, questions about regular relationship with physicians and having had discussion or referral for CRC screening), affective and cognitive associations with CRC and questions about demographics (e.g. age, gender, education level, insurance status) and prior CRC screening. The data will be recorded on the phone and on a pen and paper survey form (to be developed into an electronic record). The survey data will be identified with a coded ID in order to add CRC screening outcomes to the record for analysis. Reporting of the data is completely anonymous and de-identified.

Participants may refuse to participate without penalty. Participant records and responses are identified by an assigned identification code of the client and the client list will be kept locked and separated from the interview data.

10 SUBJECT CONFIDENTIALITY AND DATA SECURITY

All study staff members will comply with federal regulations to ensure participant confidentiality is maintained. Information gathered from participants will be protected and kept in encrypted programs and locked file cabinets. There will be no reference by name to any participant in any data capture for the surveys or satisfaction assessments. All study records will be kept in a locked, secured cabinet in the study offices. All data collected will be stored on password protected computers and encrypted USBs. Data transfers among collaborators (clinics, insurers, RPCCC UB and Mt. Sinai and Witness CARES, LLC) will be done via encrypted files. All procedures will be monitored by the PIs.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

Potential benefits include learning about CRC screening, cancer risks, and cancer prevention efforts and receiving information and assistance to participate in screening activities. For participating in the additional survey participants will receive gift cards to local stores.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

As stated in the text of this proposal, the proposed research aims to improve CRC screening in Medicaid and African American clients in the Buffalo area. Findings from this study are expected to contribute to the knowledge about the effectiveness of Witness CARES services to increase CRC screening.

5. DATA SAFETY AND MONITORING PLAN

The following plan addresses the four essential elements noted in NCI's 2001 outline: "Essential Elements of a Data and Safety Monitoring Plan for Clinical Trials Funded by the National Cancer Institute."

1. Monitoring the progress of trials and the safety of participants.

The proposed program is an educational and navigation to screening study and is low-risk. This program will be submitted to the Roswell Park Comprehensive Cancer Center IRB as the IRB of record in order to establish exemption.

Per Roswell Park IRB policies, all Roswell Park trials receive some form of data and safety monitoring. Study investigators and clinical trials staff forward all adverse event reports to the Roswell Park Office of Clinical Research Services. On a monthly basis, the IRB reviews all adverse events for all clinical trials active at Roswell Park and makes recommendations to address concerns of patient safety. Roswell Park also has in place a rigorous compliance monitoring program that addresses the investigators' adherence to the precise implementation of our IRB approved protocols. External adverse event reports (those that are reported to Roswell Park but take place on studies done outside of the institute) are reviewed on an annual basis, and more frequently if needed.

While these activities have been a vital and important role for our clinical trials, the NIH guidelines require a more comprehensive and detailed data and safety monitoring plan. Thus, the Roswell Park Data and Safety Monitoring Plan has been developed to coordinate and provide oversight for data and safety monitoring for all therapeutic trials consistent with the National Institutes of Health Policy for Data and Safety Monitoring dated June 10, 1998, with further guidance issued on June 5, 2000. The National Cancer Institute issued a policy on June 22, 1999 for data and safety monitoring of all trials with special emphasis on randomized phase III trials by Data and Safety Monitoring Boards [DSMB's].

Data and Safety Monitoring Board

The Data and Safety Monitoring Board (DSMB) meets at least quarterly to review the results of adverse event reporting, protocol deviations, protocol audits and the conduct of the study. Each Roswell Park study not otherwise overseen by an external DSMB is reviewed at least annually. The DSMB reports the analysis of their review to Sr. Vice President for Research and to the IRB. To avoid conflicts of interest, members of the DSMB are not involved in the oversight of studies for which they serve as principal investigator or co-investigator / biostatistician.

2. Plans for assuring adherence with requirements regarding the reporting of adverse events (AEs).

All serious AEs (e.g., medical occurrences resulting in death) that occur during the study defined by the given protocol, regardless of the relation to the research, must be reported to the IRB by telephone, e-mail or FAX within 24 hours of the investigator's awareness of the occurrence of the event. The MPIs will report SAEs to the Roswell Park IRB and will disseminate information to other agencies as necessary. These initial reports are followed by a safety report which is a written account of a serious AE determined by a sponsor/investigator to be both related to the treatment under investigation and unexpected in nature. Serious AEs will be summarized annually in the IRB application for continuation or termination of research.

All expected non-serious AEs that occur at a greater frequency or severity than anticipated and all unexpected non-serious AEs will be reported to the IRB within 15 working days of the investigator becoming aware of the event. These AEs are also summarized annually in the IRB application for continuation or termination of the research.

3. Plans for assuring that any action resulting in a temporary or permanent suspension of an NCI funded clinical trial is reported to the NCI grant program director responsible for the grant.

Don Handley, Administrative Director of Research Subject Protection at Roswell Park Comprehensiv Cancer Center, will provide prompt written notification of any action resulting in a temporary or permanent suspension of this protocol to the NCI grant program director responsible for the grant.

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12 APPENDICES