Protocol	
Study Title:	A pilot investigation to examine the effect of a multi-media, computer based tool (Talking Touchscreen) on enrollment in adult oncology-specific clinical trials at an academic medical center
Institution Name	The University of Chicago
Principal Investigator Contact Information: - Full address - Phone No. - Fax No. - e-mail address	Blase N. Polite, MD, MPP, Section of Hematology/Oncology Assistant Professor of Medicine Center for Gastrointestinal Oncology Center for Interdisciplinary Health Disparities Research The University of Chicago 5841 S. Maryland Avenue, MC 2115, Suite G109 Chicago, IL 60637 (773) 702-2069 (vm) (773) 834-3834 (Fax) bpolite@medicine.bsd.uchicago.edu
Co-Investigator	Toni M. Cipriano-Steffens, MA, Communications and Research Manager, Section of Hematology/Oncology, The University of Chicago Center for Interdisciplinary Health Disparities Research The University of Chicago 5841 S. Maryland Avenue, MC 2115, Suite G109 Chicago, IL 60637 (773) 702-3902 (vm) (773) 834-3834 (Fax)
Co- Investigator	Elizabeth A. Hahn, Associate Professor Department of Medical Social Sciences Feinberg School of Medicine Northwestern University 633 N. St. Clair St., Suite 1900 Chicago, IL 60611 e-hahn@northwestern.edu (312) 503-9804

Section #2- Core Protocol	
2.1 Objectives & Hypotheses	**i. Objectives/Specific Aims** Clinical trials lead to effective treatments for cancer patients. Hindering the success of these treatments are several factors, of which patients' attitudes play an important role. Low rates of participation have and will continue to inhibit medicine's progress in developing these lifesaving therapies. [1-3] Enrollment in therapeutic cancer trials (CT) is low for minority populations[4-7]. Evidence shows African Americans (AA) are 30% less likely than whites (W) to enroll in clinical trials; a disparity that is worsening over time. Rather than conceptualizing race or ethnicity as a global factor influencing health behavior outcomes, as has been the norm,[8,9] we chose to treat it as a descriptive-level variable through which other psychosocial variables coalesce to produce the perceived race-outcome effect.[10,11] Specifically, our intervention will evaluate changes in patient knowledge and beliefs about clinical trials within the context of the Behavioral Model for Vulnerable Populations [12]. There is an urgent need for hypothesis-driven, quantitative studies with enrollment to trial as the primary outcome variable. [13] Although many interventions have been tested to overcome barriers to improve cancer health outcomes and disparities, they have been met with mixed success[14,15]. Overcoming barriers to positive health outcomes is a priority as established by the Agency for Healthcare Research and Quality (AHRQ), which released an Evidence Report on cancer clinical trials[16]. to the report recommends funding of research that documents and demonstrates promising practices in cancer clinical trial recruitment and retention efforts, and in particular, efforts to involve members of underserved minority, non-English speaking, poor and elderly communities. Specifically, the report's conclusions are that there is 1) substantial uncertainty about effective approaches for cancer clinical trials recruitment, especially among minority populations; and 2) a need for further investigation of effective communication and trust-building strategies, including research on the best approaches for disseminating information about clinical trials, both at community levels and at points of interaction with potential participants. The report also identified increased investigation of effective communication strategies, including investigations on the best approach to deliver information about clinical trials, both at the community level and at the point of interaction with the potential participant. To that end, our focus will be on the use of a proven and effective communication strategy aimed at improving patient knowledge of

	available clinical trials leading to change in behavior to increased enrollment in clinical trials. Electronic health interventions[17,18], including tablet computer-based interventions[19] have shown promise in a variety of settings addressing barriers in health literacy[20,21] and patient-provider communication[22], among others. The Talking Touchscreen (TT) is a multimedia program using text, graphics and audio, that is installed on a tablet computer. It was developed and pilot tested among 410 English- and 414 Spanish-speaking patients, where its acceptability to self-administer health measures was established.[23,24] **We propose the following four specific aims for a TT pilot intervention**: **Specific Aim 1:** To determine whether TT delivery of educational clinical trial information can improve clinical trial knowledge overall and within low literacy populations, in particular. **Specific Aim 2:** To determine the feasibility and acceptability of TT technology in a busy urban academic medical center oncology clinic. **Specific Aim 3:** To evaluate the proportion of patients who sign consent to enroll in a cancer-specific treatment clinical trial when one is offered, compared to historical data. **Specific Aim 4:** To evaluate the associations between socio-demographics, health literacy, patient-reported outcomes (anxiety, depression, social support) and clinical trial enrollment, using the Behavioral Model for Vulnerable Populations.[25] ***We hypothesize that the TT educational tool will increase patient awareness and knowledge of clinical trials through the use of patient friendly technology in the immediate pre-visit period and will thereby increase clinical trial enrollment both by making patients more receptive to a clinical trial when discussed by their provider and increasing the likelihood that they will raise the issue of clinical trials with their provider. The effect will be most robust among those with low health literacy.***
2.2 Background & Rationale, Significance of Selected Topic & Preliminary Data	**ii. Significance and Background** ***Clinical Trial Participation-General*** Cancer is the second leading cause of death in the United States [US]. Over the past 15 years, the overall incidence of new malignancies has remained relatively stable; however the mortality rates over that time period have declined markedly.[26] Although the reasons for this success are manifold a significant portion of the credit belongs to the development

of novel therapeutic agents, which are brought to the market through patient participation in clinical trials. Clinical cancer research continues to be robust: a recent search of clinicaltrials.gov showed 127,886 registered clinical trials, of which 34,689 were related to cancer care [27.1%]. However, the pace of new drug development has continued to be slow. The US Food and Drug Administration approved four anti-cancer agents in 2010 and seven in 2011.

As can be inferred from the high number of clinical trials to approved drug ratio, there are many logistical problems related to clinical trial administration that are becoming more prominent. Over the past 50 years, the length of time that it takes to bring a new drug to the market has lengthened from 8 years to nearly 15.[27] This is partially due to increased regulations and safety monitoring, although death due to toxicity has not decreased during this time period.[27] The cost of bringing a new drug to the market has increased dramatically over the past few decades and now tops one billion US dollars, leading to increased market prices and healthcare costs.[28] Phase III trials can often take a decade to complete and a significant portion of National Cancer Institute [NCI] sponsored adult oncology Phase III trials are unable to meet their accrual goals.[29]

Improving the efficiency of clinical trial design and boosting enrollment in therapeutic adult oncology trials is a major initiative of the NCI. To this effect in recent years they have introduced the Community Clinical Oncology Program, the NCI Community Cancer Centers Program and the Minority-Based Community Clinical Oncology Program in an attempt to broaden the reach of clinical trials. However, despite the estimation that 20% of adult cancer patients are eligible to participate in a clinical trial, only 3-5% of patients nationwide are enrolled in a trial.[30] Lessons can certainly be learned from colleagues in pediatric oncology, where data from the national pediatric cancer clinical trials groups in the US show that more than half of children with cancer in the US are enrolled in a clinical trial and the cure rate for children with cancer in the US now exceeds 80%.[31]

Clinical Trial Participation-Race/Ethnicity

Enrollment in therapeutic clinical trials is low, particularly so for minorities[4-7]. In a cross-sectional population-based study of over 37,000 patients participating in NCI-sponsored clinical trials in multiple cancer-sites over a 2 year period, only 1.3% of African-Americans enrolled in a clinical trial. Overall, African-Americans (AA) were 30% less likely than whites (W) to enroll (OR 0.71; 95%CI:0.68-0.74).[7] Additional retrospective chart-based work in lung cancer suggests that even among those deemed eligible for a clinical trial, AA patients are 50% less likely to enroll in clinical trials[32], a worsening trend for which the reasons are not clear.

Previous physician survey-based research in breast cancer suggests that African-Americans are over 60% less likely to be offered a clinical trial.[33] This is mainly due to physician determined ineligibility based on patients' comorbidities and overall performance status. When patients were offered clinical trials, there were no differences in enrollment by race; however, only 33% of all patients offered a trial agreed to participate with patient refusal listed as the main reason[33]. A similar analysis at Howard University Medical center also suggested that patient comorbidities rendered a large portion of their African-American cancer population ineligible for clinical trials[34]. Additional retrospective chart-based work in lung cancer suggests that even among those deemed eligible for a clinical trial, African-American patients are 50% less likely to enroll in clinical trials[32]. When racial and ethnic minority populations do enroll in clinical trials, disparities in cancer outcome disappear. [35-39]

Barriers to Clinical Trial Enrollment:

A survey of African-American physician members of the Cook County Physicians Association found that they perceive the major barriers to clinical trial enrollment among African-American patients to be: (1) Lack of patient awareness of trials, (2) patient mistrust, (3) patient burden from clinical trial enrollment, and (4) blind drug assignment.[40] A recent systematic review found several barriers related to participating in clinical trials including feeling uninformed or inadequately informed, loss of decision-making control, and general feelings of uncertainty about trials. [41] Interesting too are the findings from a frequently cited study investigating factors influencing enrollment in clinical trials with 40% of new cancer patients with access to a CT declining participation, which according to these authors, points to the need for continued efforts to educate both physicians and the public as to the value of clinical trials. [42] Lending support to this need for increased knowledge about and awareness of clinical trials, our preliminary work showed the number one reason that patients did not consent to a trial if offered was that they felt *overwhelmed by the information* (56%).[43]

Clinical Trial Accrual Interventions

A systematic review published in 2006, which focused on recruitment of patients into randomized controlled cancer trials, found no studies that showed an improvement in clinical trial participation.[44] These studies included easy to read versus standard consent form documents, and a study by Paskett and colleagues utilizing a multi-component, system level intervention which included lay and professional health educators providing community-based interventions. [45]A more recent UK trial compared DVD-based information versus standard written information. There was a significant increase in clinical trial knowledge (p=0.007) and decrease in anxiety (p=0.011) in the intervention arm, but no difference in clinical trial participation which was quite high in both

arms (72% versus 76%). [46] In a recent randomized trial by Jacobsen and colleagues, intervention patients received a DVD which provided standard clinical trial information and also addressed common misperceptions and concerns about trials. The control group received the 16-page NCI booklet I. Those in the DVD group showed a more positive attitude to clinical trials (p=0.016) and greater willingness to participate (p=0.011). [3] In this trial, 9% of the patients were non-white and 66% were college educated.

Less is known about interventions directed at underrepresented populations. A systematic review of published studies, which focused on effectiveness of different strategies for recruitment of underrepresented populations into cancer trials, identified only 5 such studies (including the one by Paskett above). [47]Only three found that interventions such as media campaigns and church-based project sessions improved accrual to cancer trials. One of the studies, which looked at the rate of enrollment of African-American men to the prostate, lung, colorectal and ovarian (PLCO) cancer screening trial, showed the greatest increase (3.9%) in participation in the most intensive, church-based intervention arm, which had the highest rate of face-to-face contact . The commonly shared characteristic between these studies was that they increased interaction time with participants through targeted messaging. The problem remains that few studies have investigated the effectiveness of strategies to recruit minority and ethnic populations to clinical trials.

In light of the above, we agree completely with the following conclusions from the Agency for Healthcare Research and Quality technology report on Recruitment of Underrepresented Populations to Cancer Clinical Trials: 1) There is substantial uncertainty about effective approaches for cancer clinical trials recruitment, especially among minority populations. 2) There is a need for well-designed, controlled studies of strategies to improve accrual to cancer prevention and treatment trials. These studies should be hypothesis-driven, and include defined measures of success. 3) There is a need for further investigation of effective communication strategies, including investigations on the best approach to deliver information about clinical trials, both at the community level and at the point of interaction with the potential participant.[16]

An estimated 35% of new patients who seek care in medical oncology clinics at the University of Chicago are African-American. This statistic, along with one of the robust cancer clinical trial programs in the country, make us uniquely suited to meet the challenge put forth by the AHRQ and does so in a way that if successful, is exportable to other cancer centers around the country treating underrepresented populations. .

Low Health Literacy and Its Effect on Participation

An estimated 90 million Americans have literacy rates below the high school level, implications of which are far reaching, and key to understanding poorer health outcomes in those populations most affected. Low health literacy too, is a potential explanation for poor clinical trial participation, which is linked to patients' health knowledge and outcomes.[21] Health literacy is "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions." This involves using a range of skills (e.g., reading, listening, speaking, writing) to perform health-related tasks. According to the National Adult Literacy Survey, 21% of Americans have low literacy skills and another 27% have marginal literacy skills.[52] Low health literacy has been correlated with lower rates of adherence with breast,[53] colon,[54] and cervical[55] cancer screening and women with low health literacy were less likely to follow through on abnormal mammography results.[55] In men with prostate cancer, low health literacy has also been correlated with diagnosis at a later stage[56] and may limit understanding of complex information and patient participation in the shared decision making process.[57]

Low health literacy affects physician-patient communication as doctors are often unable to communicate effectively with this population, due to a mismatch in the way physicians provide information and the way patients process information.[22] Patients who are deficient in literacy skills may receive insufficient information for treatment decision-making and are often excluded from outcome evaluation in a clinical practice setting where patient-reported data are collected on forms.[58-60] Several national organizations have recognized that low literacy creates barriers to healthcare,[59,61] yet literacy skills are rarely assessed by healthcare providers and low literate patients are often uncomfortable disclosing their reading deficiencies.

Although investigations of the effects of low literacy rates on participation in clinical trials is sparse [62], studies do suggest that the risk of poor health outcomes increased as low health literacy is often exacerbated by the inadequate and poorly communicated information about clinical trials [63-66] including a doctor's reluctance to broach the subject of clinical trials with the patient. [67,68] Doctors also fail to recognize low literacy in patients as it is not usually apparent during casual visits to the doctor [69], and so when complications caused by cancer arise, low health literacy makes effective communication ever more tenuous.

Using Proven Communication Strategies to Improve Low Health Literacy

Work in the Health Communication field has identified the complexity of the exchange of messages within the medical field as a primary barrier to achieving positive patient health outcomes [66] as the physician-patient

encounter creates meaning subject to the perceptions and interpretation of each participant - patient and doctor.[70] Understanding that information is power and that when some have access to facts others do not, inequality exists. The result: ineffective communication between patients and physicians leading to poorer health outcomes. Studies have demonstrated that patients recall and comprehend as little as 50% of what was said by their physician.[60] This puts patients with low health literacy at an increased risk of misunderstanding.

One area effective in improving issues related to cancer care in patients across literacy levels, including increasing adherence to screening guidelines and understanding of the informed consent process, are multimedia interventions. [20,71]Patients frequently seek information about their disease and treatment; [72-76] about 85% of patients identify information needs as important.[74] Although use of the Internet is increasing, printed materials remain the most common source of information.[77-80] Despite the importance of cancer information, research has consistently shown that patients and family members are dissatisfied with cancer education.[75]

Improved quality of communication between patients and healthcare providers can have a positive effect on patient outcomes, including improved information recall,[81] satisfaction,[82-85] biological status,[86] overall health-related quality of life (HRQL)[87,88] and adherence to doctors' recommendations.[85] In breast cancer patients, satisfaction with communication increases when patients take a structured approach to preparing for the interaction with their doctor.[89] A previous study showed that when oncologists addressed issues on a "question prompt sheet," it promoted patient confidence to ask about prognosis, alleviated patient anxiety and reduced visit length.[90] In addition, implementations of personal health records have shown that patients feel more empowered when they have access to this information.[91] Interventions are needed to target important issues regarding patients' willingness to engage in information seeking, such as cultural factors, knowledge about illness and disease, ability to prepare questions in advance and the ability to ask questions spontaneously.[92]

Interactive health communication has the potential to reduce disease risk, improve HRQL, influence health services use and improve adherence.[93] Computer-based education programs are acceptable to people of different ages, education levels, SES and ethnicity, and outcomes studies have demonstrated improvements in knowledge, HRQL, reduced hospitalizations, improved functional status, reduced pain, confidence in asking questions and self-efficacy.[93] Visual and graphic presentations of cancer information have been shown to increase patient knowledge and satisfaction in a randomized clinical trial.[94] Multimedia interventions have proven effective in improving issues

related to cancer care in patients with low literacy including adhering to screening guidelines and the informed consent process.[20] Computer-assisted patient education is increasingly being implemented in clinical settings. In a small pilot study at an urban community health center, the handheld multimedia computer was well-received by patients, and was rated as more helpful than their previous education. [95]

Multimedia platforms appear promising for patient educational activities by offering better consistency and quality control of the message, and at the same time overcoming literacy and language barriers.[96-98] A recent review identified 30 studies to compare multimedia and print health materials, with 56 outcomes evaluated.[97] Multimedia led to better outcomes vs. print in 21 (38%) comparisons, with the remainder showing no differences (54%) or an advantage for print (9%). The authors of this review also noted that the types of multimedia varied widely and that there is a need for studies to compare "message-equivalent" tools (same content, different format). Our proposed study will provide important information about the use of the TT for clinical trial education in clinical settings. The results will inform a future study to compare equivalent tools (paper vs. TT).

The use of new information technologies has been recommended as a strategy for improving access to health information and for enhancing the quality of communication in healthcare delivery.[99] The proposed study plans to use an interactive health communication tool as an intervention to target improvement in clinical trial enrollment in adult cancer patients and to study its use among patients with low health literacy through increasing patient knowledge of and changing beliefs about clinical trials within the context of the Behavioral Model for Vulnerable Populations.[25]

Theoretical Framework: The Behavioral Model for Vulnerable Populations

The Behavioral Model was developed to understand why people use health services, and to assist in developing policies to promote equitable access to healthcare.[10, 11] The model is illustrated in ***Appendix 1***, and the specific domains to be measured in this proposed project are listed below the figure. Use of health services is a function of a predisposition to use health services, factors that enable or impede use, and the need for care. Health outcomes were added to the model in recognition that improved patient outcomes are explicit goals of effective health services delivery. Feedback loops were also added to emphasize the model's dynamic and recursive nature. The model was recently revised to include domains (such as literacy) that are relevant to understanding health and health-seeking behavior of vulnerable populations.[25]

The adapted model for vulnerable populations has been successfully

used to evaluate utilization and patient outcomes among homeless adults,[12] to evaluate patients' perceptions of their relationships with primary care practitioners,[86] and to examine adherence to cervical cancer screening among publicly housed African American and Latino women.[87] **The model is consistent with approaches to enhance patient-centered care and improve patient outcomes through the use of interactive health communication strategies.**[62] *Please see the Behavioral Model for Vulnerable Populations in* ***Appendix 1***.

iii. Rationale

a. Cancer Relevance

More than ever before, we are entering an era of "personalized medicine". New oncology drugs are targeting patients whose tumors have specific mutations or other molecular abnormalities, often with highly effective results. Patients with breast or gastric cancer whose tumors over-express Her-2/neu receive trastuzumab. Patients with lung cancer who have a specific mutation in the gene for the epidermal growth factor receptor (EGFR) receive erlotinib, and those with a rearrangement of the anaplastic lymphoma kinase (ALK) gene receive crizotinib. These are but a few of the recent additions to the cancer therapeutic armamentarium that have generated such enthusiasm about the possibility of personalized therapeutics. However, unless we include a diverse patient population in our trials, we will likely miss important signatures that lead to important future therapies that reflect our diverse patient population. By specifically targeting more vulnerable patient populations, this proposal, if successful, can lead to increased cancer therapeutic clinical trial enrollment and be used as a model for other researchers around the country including those in charge of the NCI Cancer Cooperative Groups.

b. National Funding

If successful, this project has tremendous opportunity for RO1 level or Program Level National Funding. As we point out in the text, the specific areas we are targeting were the very ones identified by AHRQ in their 2005 report "Knowledge and Access to Information on Recruitment of Underrepresented Populations to Cancer Clinical Trials." In addition, we have purposely designed this trial to utilize standardized resources (the NCI pamphlet, the PROMIS measures) so that it is readily exportable to other cancer centers across the country. In our opinion, the use of "home grown" messaging and measurements while methodologically appealing, limits the ability to export the intervention to other settings quickly. Finally the PI and Co-PI of this study are well situated to move the findings from this study to a more National level. Dr. Polite serves as Chair of the ASCO Health Disparities Advisory group and is a cadre member of the Alliance cooperative group (formerly CALGB, NCTTG, and ACOSOG) health disparities committee. Dr. Hahn has served in a leadership role on numerous AHRQ-, NIH- and foundation-funded projects and has

received funding from multiple National bodies including ACS, AHRQ, NCI, and NHLBI. This funding includes the use of the Talking Touchscreen technology which indicates that it has already been well received by National Funders.

IV. Preliminary Studies

A. University of Chicago Clinical Trial Study

General Findings: Clinical Trial Participation at the University of Chicago

Funding from an ACS-IRG (Polite BN) and an ASCO Young Investigator Award (Ray M) allowed us to perform a paired survey of physicians and 375 new patients (57% white and 34% African American) seen in the cancer clinics at the University of Chicago Medical Center from September 2008-May 2010 to determine oncologist and patient attitudes toward enrollment in therapeutic cancer clinical trials. [43]Of the 375 patients approached, 338 (90%) agreed to participate and returned their survey forms.

In terms of health literacy (using one question health literacy screener[100] with those "quite" and "extremely confident" filling out medical forms classified as having high health literacy) 63% of the sample had high health literacy and 37% low health literacy. Whites were more likely than AA to have high health literacy (79% vs. 57%; p<0.0001)

Knowledge of clinical trials in general, differed significantly by both race and health literacy status.

- High vs. Low HL: 77% vs. 48% (p<0.0001)
- White vs. AA: 83% vs. 56% (p<0.0001)

Clinical Trial Participation

As shown in ***Table 1*** below, overall 10% of our patients signed consent for a therapeutic clinical trial with African American patients more likely to sign consent. When a trial is available and offered, 41% of all patients and 63% of our African American patients sign consent. Those with higher health literacy are more likely to sign consent and to sign when offered.

Table 1: Clinical Trial Participation

	All	W	AA	*p*-value	HHL	LHL	*p*-value
Signed Consent	10%	10%	18%	0.07	12%	7%	0.2
Clinical Trial Available	57%	61%	46%	0.06	58%	54%	0.69
Offered if Available	35%	36%	31%	0.7	37%	30%	0.47
Signed if Offered	41%	37%	63%	0.2	42%	33%	0.6

W-White; AA-African American; HHH-High Health Literacy; LHL-Low Health Literacy

To better understand the findings regarding African American race and health literacy, we ran a multivariable logistic regression model that controlled for both variables. As displayed in ***Table 2***, when controlling for health literacy, AA are 2 times more likely than whites to enroll in a clinical trial. Similarly, those with high health literacy are 2.5 times as likely to enroll as those with low health literacy, controlling for race.

Table 2-Signed Consent: Logistic Regression Models

	OR (bivariate)	95% CI	OR (multivariable)	95% CI
AA:White	1.9	0.9-3.7	2.1	0.8-5.2
HHL:LHL	1.8	0.6-4.9	2.5	0.8-7.8

These data are consistent with our hypothesis that low health literacy is a potential barrier to trial participation. These results also suggest that the impact may be particularly helpful for our African American patients since low health literacy is an intervenable factor which may be dampening what appears to otherwise be enthusiastic support for trial participation in our patient population.

Barriers to Participation

The number one reason that patients did not consent to a trial if offered was that they felt *overwhelmed by the information* (56%). Measured barriers which correlated with not signing consent if offered were lack of social support (*p*=0.05), lack of emotional support (*p*=0.01), high levels of anxiety (OR 0.51; 95% CI 0.13-1.87) and high levels of depression (OR 0.45;95% CI 0.09-2.08). Despite our *a priori* hypothesis that physician trust would play an important role, no measure of physician/institution trust predicted clinical trial enrollment at the University of Chicago.

B. General Findings: Talking Touchscreen Technology in Vulnerable Populations

The Talking Touchscreen [TT] is a multimedia program using text, graphics and audio that is installed on a tablet computer. It was developed and pilot tested among 410 English- and 414 Spanish-speaking cancer patients, where its acceptability to self-administer health measures was established.[23,24] Its utility for self-administration of a health literacy measure was then tested among 610 patients in four separate primary care clinics in the Chicago area.[101] The internal consistency reliability coefficients for each of the six health literacy item subsets were all high [range 0.83-0.91]. The tool was well accepted by the participants; 92.5% of participants reported no difficulty using the TT; 96.7% of participants required no help or a little help from study personnel to use the TT; >95% of participants rated the design elements of the TT as good, very good or excellent; >95% of the participants rated their experience as the same or better than expected and would recommend participation to other people.[102] The TT is well accepted among individuals who are computer naïve and have low literacy.[102] It can be adapted to provide complex information about diseases and treatments in simple and easy to understand terms using text, pictures, and audio, and has broad research potential in clinical cancer care. Below is a list of completed and ongoing studies from our group utilizing this technology.

Multimedia Health Information Technology (HIT) Programs for Vulnerable Patients (R01-HS010333, ACS #TURSG-02-069: Hahn, PI). In response to national initiatives, we received funding to improve outcomes measurement in low literacy patients and to validate an innovative HIT (to be used in this proposal). We developed the "Talking Touchscreen" (TT), a bilingual multimedia program that allows patients with varying literacy, language and computer skills to self-administer questionnaires.[58,103] Patients reported that the TT was easy to use, and commented on the usefulness of the multimedia approach. [23,103] Over 60% of both low and high literacy patients preferred the TT over other alternatives (interviewer or no preference) [23]. The majority (87%) said they would be willing to complete TT surveys when they visit the doctor in the future. **This multimedia program maximizes opportunities to assess patient-reported outcomes.**

CancerHelp® Patient Education Software (Muench and Miller, PIs). The CancerHelp Institute's (www.cancerhelp.org/) mission is to provide patient education information, especially to minorities and those with low literacy skills, with its user-friendly, interactive touchscreen software. The Institute collaborates with the NCI through a license agreement to distribute NCI material. Users rated the software very highly in ease of use and quality of information. Among 57 cancer patients in an ongoing study (R18-HS017300; see below), all reported that they were able to

find the information they wanted in the software, and that it helped them better understand their disease and treatment "somewhat" (47%) or "a lot" (51%) (manuscript in preparation). It has been used by more than 230 hospitals, clinics and oncology practices in 40 states.

Implementing a low-literacy, multimedia IT system to enhance patient-centered cancer care (R18-HS017300: Hahn, PI). The objective of this randomized trial is to test whether a low literacy, multimedia information and assessment system used in daily clinical practice enhances patient-centered care and improves patient outcomes. CancerHelp-Talking Touchscreen (TT) delivers user-friendly patient education information and enables low literacy patients to self-administer questionnaires. A similar approach will be used in the proposed study.

Literacy Assessment Benefits and Patient Preferences (Coleman Foundation: Hahn, PI). This study evaluated patient attitudes and preferences regarding literacy screening. We enrolled 97 cancer patients (67% African American); 42 were reading at or below the 7th grade level. Most (96%) agreed that "It is important for doctors and nurses to know about their patients' reading abilities," and 84% would be willing to have their literacy level provided to their doctors and nurses [104]. **This suggests that literacy assessment is acceptable to patients, and they consider it important for clinicians to be aware of their patients' reading abilities.**

C. Current Trials in University of Chicago Lung Cancer Clinic

The Thoracic oncology clinic at the University of Chicago currently has over 20 active therapeutic cancer clinical trials for patients with Small Cell and Non- Small Cell Lung cancer. These trials cover every stage and line of therapy including phase I trials for multi-treated patients. They also include trials for patients with poor performance status. This situation is unparalleled by almost any other cancer center in the United States and makes the University of Chicago the ideal place to perform the study laid out in this grant. *A list of current and pending clinical trials is included in* ***Appendix 5****.*

Additional Cancer Site Added to Study:

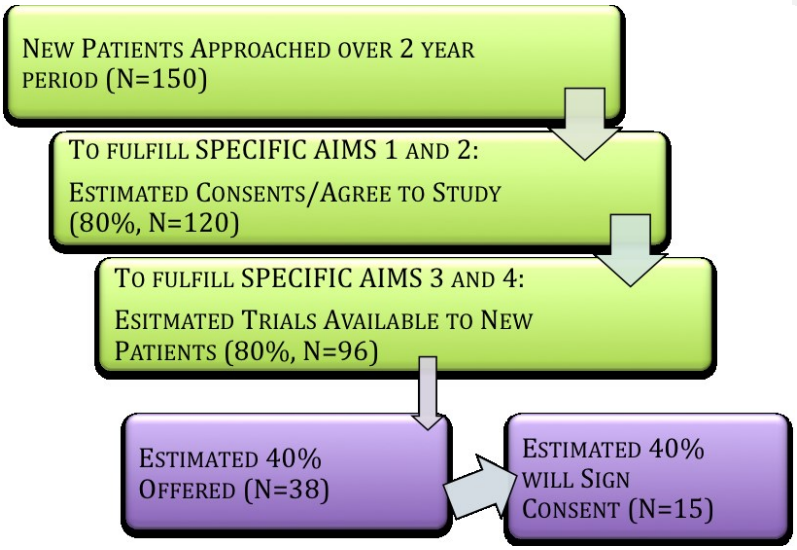
The Gastric Cancer clinic is part of the University of Chicago GI Oncology clinic. It is staffed primarily by Dr. Dan Catenacci. We would like to add this clinic to our study. This expands our tumor types from those seen in the thoracic clinic allowing for more generalizability of our study while at the same time speeding accrual to the trial. We have selected this clinic because like the thoracic oncology program, the gastric cancer program has trials available to patients with all stages of gastric cancer including multiple trials for patients with metastatic disease. His program also overlaps with the Thoracic oncology program

Formatted: Font: 12 pt, Bold
Formatted: Font: 12 pt, Bold
Formatted: Font: Bold
Formatted: Font: (Default) Arial, 12 pt, (Asian) Japanese
Formatted: Indent: First line: 0.49"

	in the treatment of esophageal cancer.
2.3 Study Design	**V. Study Design and Methodology** **Study Type and Sample Size** This will be a pilot study performed at an urban academic center in south-side Chicago to collect preliminary data in hopes of conducting a larger, randomized intervention. Based on the last two years in our Thoracic oncology clinic at the University of Chicago, we estimate that 600 new patients will be seen over the 2-year period of this study, an amount that will easily provide the number of patients necessary to fulfill the requirement of this pilot study. For this study, over 2 years, we will contact 150 new lung cancer patients of which 80% (120) will agree to participate in our study. Based on the current clinical trial portfolio in the Thoracic oncology clinic (***see Appendix 5***), which has grown substantially since our last study, it is estimated that trials are now technically available for about 80% of the new patient population (for our pilot of 120 patients that leaves about 100). Of our 100, we estimate, based on our previous work, that a clinical trial will actually be offered to 40% of these patients (40). **Patient Population/Recruitment** All new cancer patients presenting to the University of Chicago outpatient oncology clinics are currently pre-screened for cancer type and set up for appointments by our new patient intake coordinators. New patients with Non-Small Cell Lung cancer and Small Cell carcinoma will be contacted by our study coordinator who will call them 2-3 days prior to their appointment to ascertain their interest in participating in the research study. Those interested will be asked to arrive at their new visit 60-90 minutes prior to the appointment time. **Study Procedure** Patients will use the Talking Touchscreen (TT) to complete a pre-intervention survey which will ascertain clinical trial knowledge (detailed in SA#1, surveys in ***Appendix 4***) and the following information using the instruments detailed in SA#4: socio-demographics, health literacy, anxiety, depression, and social support. They will then use the TT to view the NCI's educational module on "Taking Part in Cancer Treatment Research Studies". (see ***Appendix 3*** for a sample screen shot). The NCI

Formatted: Font: 12 pt

	booklet will be adapted as an interactive multimedia learning program. This interactive program and the pre/post survey assessments will run on the same tablet PCs. The "Listen and Learn Modules" allow persons with diverse literacy and computer skills to learn and go at their own pace. Once the session is complete, patients will complete a post-intervention survey to measure any change in clinical trial knowledge and a feasibility (evaluation) survey (detailed in SA#2, survey in ***Appendix 4***) to discern patient attitudes toward their using technology as a means of information collection and dissemination during their doctor's visit. The researcher will also complete a simple questionnaire addressing the effect, if any, of introducing technology into the patient visit. **Talking Touchscreen Design and Implementation** The integration and programming of the measurement tools and the NCI's "Taking Part in Cancer Treatment Research Studies" pamphlet (***Appendix 1***) into the TT will be handled by the Informatics team at Northwestern University's Assessment Center (Assessment Center℠; http://www.assessmentcenter.net/) and educational software developers at the CancerHelp Institute(www.cancerhelp.org) under the supervision of Co-PI Elizabeth Hahn, a medical sociologist and biostatistician, and a team including a Senior Developer, an IT Project Manger, and a user support specialist who will be available for logistic troubleshooting relating to hardware and software malfunctions which may occur. As detailed in the preliminary study section above, this group has significant expertise in the scope of work being performed in this study and in particular adapting interactive health messaging to low literacy health populations. Audio recordings for the TT will be done by Wordly Voices (http://www.worldlyvoices.com/) a company whose sole focus is on recording custom voice prompts.
2.4 Study Flowchart	



2.5 Study Procedures

Specific Aims in Detail
We have listed each specific aim with corresponding procedures and data analysis plan:

Specific Aim 1: *To determine whether TT delivery of educational clinical trial information can improve clinical trial knowledge overall and in within low literacy populations in particular.*

Hypothesis 1a: The interactive multimedia TT educational tool will results in significant gains in patients' pre-post assessments for each of the domains listed below.

Knowledge
Patients will self-administer pre- and post-tests on the TT. The Clinical Trial questionnaire was developed by Jacobsen and colleagues [3] and contains the following items (*see* ***Appendix*** **4**):

Attitudes toward clinical trials- 20 item likert measure of Positive attitudes toward clinical trials (eg, "being in a clinical trial benefits other patients") and negative attitudes (eg, "being in a clinical trial is likely to cause a patient harm. After reverse coding the negative items, responses to all items are combined into an average score (possible range, 1 to 5).
Knowledge about clinical trials-13 items have response options true, false, or don't know. The total score represents the number of items

answered correctly (possible range, 0 to 13).
Perceived ability (self-efficacy)- 9 item likert scale to measure ability to carry out actions involved in making an informed decision about clinical trial participation (eg, "I think I could get the information I need to decide whether to be in a clinical trial"). After reverse coding the negative items, responses to all items are combined into an average score (possible range, 1 to 5).
Willingness to participate in clinical trials will be measured using one likert scaled item: "If a cancer clinical trial were offered to you, would you agree to take part in it?" ("definitely yes" to "definitely no").

Specific Aim 2: *To determine the feasibility and acceptability of TT in a busy urban academic medical center oncology clinic.*

Feasibility
The use of new information technologies has been recommended as a strategy for improving access to health information and for enhancing the quality of communication in healthcare delivery.[99] Our preliminary data show the number one reason that patients did not consent to a trial if offered was that they felt *overwhelmed by the information* (56%).

Hypothesis 2a: By providing the patient important information as to the options they may have in terms of their cancer treatment, directly prior to their talking with their physician and through use of an easy interactive tool, such as the proven TT in low-literacy populations, we will not interrupt or decrease the patient experience but enhance the physician-patient interaction, leading to increased participation in clinical trials. This pilot study will provide to us the opportunity to understand the feasibility of using technology as a way to educate a cancer population about clinical trials within the healthcare environment of a busy, urban hospital setting. We will use this as an opportunity to understand how to integrate technology into clinic flow so that it is not disruptive but rather increases the efficacy of the physician-patient visit by educating patients as to clinical trials before seeing the physician. We estimate that the survey items will take 20-30 minutes to complete and that patients will spend ***15-30 minutes with the TT***. Our experience is that 60 minutes is not an unreasonable burden, given the waiting time and other factors associated with a new visit. We will administer a simple evaluation questionnaire following the completion of the patient encounter with the TT, to measure their experience, including degree of difficulty.

Hypothesis 2b: The use of the TT will not effect clinic flow nor pose an additional burden to patient, physician or staff.
The researcher will also complete a simple questionnaire addressing the effect, if any, of introducing technology into the patient visit.

Data Analysis

We will administer a simple evaluation questionnaire to understand the patient's experience with the TT. We will adapt other questionnaires used in a previous TT study and will calculate descriptive summaries of the responses.

Specific Aim 3: *To evaluate the proportion of patients who sign consent to enroll in a cancer-specific treatment clinical trial when one is offered, compared to historical data.*

At the completion of the physician visit for that day, physicians will fill out a previously validated form asking the following questions:

- Is there a clinical trial here for this cancer and stage, regardless of the patient's other characteristics?
- Did you discuss a clinical trial with this patient?
- Did the patient specifically ask you about a clinical trial before you brought it up?
- Was the patient offered participation in a treatment-related clinical trial?
- If offered, did the patient sign consent?

Actual enrollment in a clinical trial (signed consent) will be confirmed using linkage to our clinical trial database, e-VELOS, which we used successfully in our previous study.

In our previous trial, 40% of patients offered a clinical trial enrolled in a trial. For our low literacy population, 30% enrolled when offered. We expect to be able to improve on these baseline values both by increasing patient understanding of the trial process and by improving their communication with their physician.

Specific Aim 4: To evaluate the associations between socio-demographics, health literacy, patient-reported outcomes (anxiety, depression, social support) and clinical trial enrollment, using the Behavioral Model for Vulnerable Populations.[25]

Instruments

Tables 3 and 4 contain the instruments we will use:

TABLE 3: PROMIS INSTRUMENTS (www.nihpromis.org)

Construct	Social Support Measure Tools	Scoring for all PROMIS Psychometrics	Background Information/Psychometrics
PROMIS Companionship Scale	PROMIS V 2.0 short form-4 items. .	**Reliability**: The degree to which a measure is free of error. It can be estimated by the	PROMIS developed several instruments to measure the quality of social support, which refers to functional aspects of supportive relationships, i.e., interpersonal

			internal consistency of the responses to the measure, or by correlating total scores on the measure from two time points when there has been no true change in what is being measured (for z-scores, reliability = 1 - SE2). **Standard Error (SE):** The possible range of the actual final score based upon the scaled T-score. With a T-score of 52 and a SE of 2, the 95% confidence interval around the actual final score ranges from 48.1 to 55.9 (T-score + (1.96*SE) = 52+ 3.9 = 48.1 to 55.9).**Alpha=0.96** **Minimum** number of items (4) must be answered in order to receive a score for emotional support CAT. **As additional items** are administered, the potential for error is reduced and confidence in the respondent's score increases. CAT will continue until either the standard error drops below a specified level, or the participant has answered the maximum number of questions (12), whichever occurs first.	relationships that serve particular functions. This includes the interactive process by which emotional, instrumental or informational support is obtained from one's social network. It also includes companionship, feeling cared for and valued as a person, communication with others, and feelings of belonging and trust. Measures of social support generally seek information about a person's perception of the availability or adequacy of resources provided by others. The social support measures do not use a time frame (e.g. over the past seven days). ---------- Assesses perceived availability of someone with whom to share enjoyable social activities such as visiting, talking, celebrations, etc.
	PROMIS Emotional Support Scale	PROMIS v2.0 short form-8 items	**Alpha=0.98**	Assesses perceived feelings of being cared for and valued as a person; having confidant relationships.
	PROMIS	PROMIS v2.0-	**Alpha=0.95**	Assesses perceived availability of

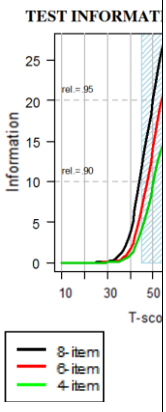
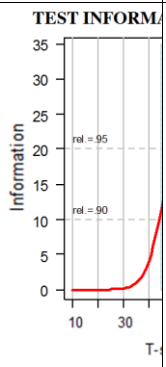
Informational Scale	8 item short form		helpful information or advice.
PROMIS Instrumental Support Scale	PROMIS v2.0-8 item short form	**Alpha=0.96**	Assesses perceived availability of assistance with material, cognitive or task performance.
PROMIS Anxiety Scale	8-item PROMIS Short Form V 1.0-Anxiety 8A		Measures self-reported fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness). Anxiety is best differentiated by symptoms that reflect autonomic arousal and experience of threat. Only one behavioral avoidance item is included in the item bank; therefore, behavioral fear avoidance is not fully evaluated. The anxiety short form is generic rather than disease-specific. It assesses anxiety over the past seven days.
PROMIS **Depression** Scale	8-item PROMIS short form		Assesses self-reported negative mood (sadness, guilt), views of self (self-criticism, worthlessness), and social cognition (loneliness, interpersonal alienation), as well as decreased positive affect and engagement (loss of interest, meaning, and purpose). Somatic symptoms (changes in appetite, sleeping patterns) are not included, which eliminates consideration of these items' confounding effects when assessing patients with comorbid physical conditions. The depression short form is generic rather than disease-specific. It assesses depression over the past seven days.

TABLE 4: ADDITIONAL INSTRUMENTS

Construct	Measure	Reference	Background Information/Psychometric
Demographics	Standard questionnaires used in our clinic.		Collecting employment, income, education, country of origin (including parents'), race, height, weight, marital status (i.e. married or cohabitating), length of marriage/relationship, specific cancer diagnosis and length of disease.
Medical Forms	1. Health Literacy single-item screener 2. Health	Wallace 2006[100] Hahn et al.,	1. a single item previously validated by Wallace and colleagues in an urban university primary care clinic. • When compared to the Rapid Estimate of Adult Literacy in Medicine

	Literacy Assessment Using Talking Touchscreen Technology (Health LiTT).	2011[101]	(REALM) instrument, the question, "How confident are you filling out medical forms by yourself?" had an Area Under the Receiver-Operator Curve (AUROC) of 0.82 (95% CI:0.77-0.86) for limited health literacy and 0.79 (95% CI:0.74-0.83) for limited or marginal health literacy. • Health LiTT is a novel, self-administered multimedia test that meets psychometric standards (reliability of 0.90 or higher) for measurement of individual respondents, especially in the low to middle range of health literacy. Health literacy has been previously shown to correlate with disparities in health outcome.
Comorbidities	Self-Administered Comorbidity Questionnaire (SCQ)	Katz et al., 2003	• Contains 12 medical conditions developed based on their frequency in general practice and their inclusion in published and commonly used comorbidity instruments. • Patients are asked if they have the condition, if they receive treatment for it and if the condition limits their activity. The highest possible score is 36, but in our survey will be 33 since we will eliminate the cancer comorbidity in that all patients have this in our cohort. • This survey has been shown to have excellent test-retest reliability (ICC of 0.81) and moderate to high concordance with the Charlson Index (kappa>= 0.46 for all conditions except lung disease). • In terms of predictive validity the instrument also has modest associations with health status one year after assessment of comorbidities as measured by correlations with the Physical Component Summary of the SF-36 (R2 0.22 of which 69% was explained by SCQ comorbidity score) and was superior to the Charlson Index in that regard.
Clinical Trial Knowledge Survey	Pre/Post Test Survey measuring change in knowledge, attitudes and beliefs and effect on behavior	Jacobsen et al., 2012[3]	Instrument measuring at baseline and follow-up: Attitudes towards clinical trials, knowledge about clinical trials, self-efficacy for clinical trial decision, receptivity to clinical trial information, willingness to participate in clinical trials.

Health Literacy- As in SA#2 above.

	Psychosocial Measures-Participants will use the TT to complete short forms for anxiety, depression, and social support developed in the Patient-Reported Outcomes Measurement Information System (PROMIS) initiative (www.nihpromis.org). All PROMIS measures are based on T-scores, with a mean of 50 and a standard deviation of 10 in the reference population. Raw scores for this study will be calculated and then transformed to T-scores using PROMIS look-up tables (see http://www.assessmentcenter.net/Manuals.aspx). In addition, the following tumor specific factors will be obtained-cancer type (NSCLC, SCLC), stage, and line of therapy for current stage as ascertained by physician survey but broken down as follows: • Never treated with chemo • Received first line treatment only • Received second-line treatment • Received three or greater lines of treatment. **Data Analysis** Categorical variables will be summarized as frequency counts and percentages and continuous variables will be summarized as medians and ranges. A logistic regression model will be set up with health literacy (as defined above) as the primary independent variable and enrollment in a clinical trial if one is offered as the primary dependent variable. The second model will control for race, income, cancer stage, line of treatment and co morbidity score.
2.6 Study Duration	Study duration will be 2 years.
2.7 Statistical Analysis and Sample Size Justification	The principal investigator is supported by a Biostatistics Core Facility offered through the University Chicago's Comprehensive Cancer Center, which provides collaborative statistical support to investigators for the design, conduct, and analysis of clinical trials, observational and population-based studies, and basic science research projects. Variables/Time Points of Interest These are described in detail under each specific aim listed in the Study Procedures section, above. Statistical Methods These are described in detail under each specific aim listed in the Study Procedures section, above. Sample Size: (Power described above under each Specific Aim.) **For Specific Aims 1 and 2:** **Data Analysis**

	Three subscales on the pre- and post-questionnaire will assess attitudes towards clinical trials, knowledge about clinical trials and perceived ability. Change scores will be calculated and evaluated using a paired *t*-test. A sample size of 120 will have 80% power to detect an effect size as small as 0.258 using a paired *t*-test with a 0.050 two-sided significance level. Based on our previous study, we estimate that 60% of these patients will have high health literacy (72) and the remaining 40% (48) will have low health literacy. We will evaluate differences in pre- and post-test changes by health literacy group. We will also estimate the correlation between change scores and the continuous measure of health literacy. **For Specific Aims 3 and 4:** Based on the current clinical trial portfolio in the Thoracic oncology clinic (see Appendix 4), it is estimated that trials are available for 80% of the new patient population (including patient eligibility) (100 patients over 2 years) and of these, 40% will be offered participation (40). Our previous data suggested that when offered, 40% of these patients will sign consent. We hypothesize that our TT intervention will increase both the percentage of patients offered a trial (because of active participation from the patient in inquiring about trials) and in the percentage of patients who sign when offered. These impacts will be most profound in the low literacy group. An effect size of 0.20 (H0: 0.4, HA:0.6) is a reasonable estimate for this pilot to be able to produce a clinically significant improvement in cancer clinical trial enrollment. A sample size of 40 (those offered enrollment) should give us 80% power to detect a 20% difference in trial enrollment from our baseline hypothesized value of 40% at a one-sided alpha level of 0.05.
2.8 Specific Drug Supply Requirements	NA
2.9 Adverse Experience Reporting	NA
2.10 Itemized Study Budget	A preliminary study budget must be provided with the initial proposal submitted to give guidance to the MISP Review Committee as to the expected study costs. A refined itemized budget detailing the costs associated with the study should be provided with the final protocol or included in the study agreement as Exhibit B.

2.11 References	**References** 1. Comis RL, Miller JD, Aldige CR, et al: Public attitudes toward participation in cancer clinical trials. J Clin Oncol 21:830-5, 2003 2. Evans KR, Lewis MJ, Hudson SV: The role of health literacy on african american and hispanic/latino perspectives on cancer clinical trials. J Cancer Educ 27:299-305, 2012 3. Jacobsen PB, Wells KJ, Meade CD, et al: Effects of a Brief Multimedia Psychoeducational Intervention on the Attitudes and Interest of Patients With Cancer Regarding Clinical Trial Participation: A Multicenter Randomized Controlled Trial. Journal of Clinical Oncology, 2012 4. Giuliano AR, Mokuau N, Hughes C, et al: Participation of minorities in cancer research: the influence of structural, cultural, and linguistic factors. Ann Epidemiol 10:S22-34, 2000 5. Swanson GM, Ward AJ: Recruiting minorities into clinical trials: toward a participant-friendly system. J Natl Cancer Inst 87:1747-59, 1995 6. Sateren WB, Trimble EL, Abrams J, et al: How sociodemographics, presence of oncology specialists, and hospital cancer programs affect accrual to cancer treatment trials. J Clin Oncol 20:2109-17, 2002 7. Murthy VH, Krumholz HM, Gross CP: Participation in cancer clinical trials: race-, sex-, and age-based disparities. Jama 291:2720-6, 2004 8. Magai C CN, Adjei BA, Hershman D, Neugut A.: Psychosocial influences on suboptimal adjuvant breast cancer treatment adherence among African American women: implications for education and intervention. Health Educ Behav Dec;35:835-54, 2008 9. Cameron L LE, Leventhal H: Seeking medical care in response to symptoms and life stress. Psychosom Med. 57:37-47, 1995 Jan-Feb 10. Consedine NSM, Carol; Bonanno, George A. : Moderators of the emotion inhibition-health relationship: A review and research agenda. Review of General Psychology 6:204-228, Jun 2002 11. Consedine NS MC, Krivoshekova YS, Ryzewicz L, Neugut AI.: Fear, anxiety, worry, and breast cancer screening behavior: a critical review. Cancer Epidemiol Biomarkers Prev. 13:501-10, 2004 Apr 12. Gelberg L, Andersen, R.M., Leake, B.D.: The Behavioral Model for Vulnerable Populations: application to medical care use and outcomes for homeless people. Health Serv Research 34:1273-1302, 2000 13. Ford JG, Howerton MW, Lai GY, et al: Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. Cancer 112:228-42, 2008 14. Masi CM, Blackman DJ, Peek ME: Interventions to enhance breast cancer screening, diagnosis, and treatment among racial and ethnic minority women. Med Care Res Rev 64:195S-242S, 2007 15. Peek ME, Han JH: Disparities in screening mammography. Current status, interventions and implications. J Gen Intern Med 19:184-94, 2004 16. Ford JG, Howerton M. W., Bolen S., et al: Knowledge and

Access to Information on Recruitment of Underrepresented Populations to Cancer Clinical Trials. Rockville (MD): Agency for Healthcare Research and Quality (US); 2005 Jun. (Evidence Reports/Technology Assessments, No. 122.) Preface. Available from: http://www.ncbi.nlm.nih.gov/books/NBK37796/.

17. Baker TB, Hawkins R, Pingree S, et al: Optimizing eHealth breast cancer interventions: which types of eHealth services are effective? Transl Behav Med 1:134-145, 2011

18. Gustafson DH, Hawkins R, McTavish F, et al: Internet-Based Interactive Support for Cancer Patients: Are Integrated Systems Better? J Commun 58:238-257, 2008

19. Abernethy AP, Ahmad A, Zafar SY, et al: Electronic patient-reported data capture as a foundation of rapid learning cancer care. Med Care 48:S32-8, 2010

20. Makoul G, Cameron KA, Baker DW, et al: A multimedia patient education program on colorectal cancer screening increases knowledge and willingness to consider screening among Hispanic/Latino patients. Patient Educ Couns 76:220-6, 2009

21. Davis TC, Williams MV, Marin E, et al: Health literacy and cancer communication. CA Cancer J Clin 52:134-49, 2002

22. Doak CC, Doak LG, Friedell GH, et al: Improving comprehension for cancer patients with low literacy skills: strategies for clinicians. CA Cancer J Clin 48:151-62, 1998

23. Hahn EA, Cella D, Dobrez DG, et al: The impact of literacy on health-related quality of life measurement and outcomes in cancer outpatients. Qual Life Res 16:495-507, 2007

24. Hahn EA, Du H, Garcia SF, et al: Literacy-fair measurement of health-related quality of life will facilitate comparative effectiveness research in Spanish-speaking cancer outpatients. Med Care 48:S75-82, 2010

25. Gelberg L, Andersen RM, Leake BD: The Behavioral Model for Vulnerable Populations: application to medical care use and outcomes for homeless people. Health Serv Res 34:1273-302, 2000

26. Jemal A, Siegel R, Xu J, et al: Cancer statistics, 2010. CA Cancer J Clin 60:277-300, 2010

27. DiMasi JA, Hansen RW, Grabowski HG: The price of innovation: new estimates of drug development costs. J Health Econ 22:151-85, 2003

28. Adams CP, Brantner VV: Estimating the cost of new drug development: is it really 802 million dollars? Health Aff (Millwood) 25:420-8, 2006

29. Cheng SK, Dietrich MS, Dilts DM: Predicting accrual achievement: monitoring accrual milestones of NCI-CTEP-sponsored clinical trials. Clin Cancer Res 17:1947-55, 2011

30. Lara PN, Jr., Paterniti DA, Chiechi C, et al: Evaluation of factors affecting awareness of and willingness to participate in cancer clinical trials. J Clin Oncol 23:9282-9, 2005

31. Bleyer WA: The U.S. pediatric cancer clinical trials programmes: international implications and the way forward. Eur J Cancer 33:1439-47, 1997

32. Du W, Gadgeel SM, Simon MS: Predictors of enrollment in lung cancer clinical trials. Cancer 106:420-5, 2006
33. Simon MS, Du W, Flaherty L, et al: Factors associated with breast cancer clinical trials participation and enrollment at a large academic medical center. J Clin Oncol 22:2046-52, 2004
34. Adams-Campbell LL, Ahaghotu C, Gaskins M, et al: Enrollment of African Americans onto clinical treatment trials: study design barriers. J Clin Oncol 22:730-4, 2004
35. Albain KS, Unger JM, Crowley JJ, et al: Racial Disparities in Cancer Survival Among Randomized Clinical Trials Patients of the Southwest Oncology Group. Journal of the National Cancer Institute 101:984-992, 2009
36. Dignam JJ: Efficacy of systemic adjuvant therapy for breast cancer in African-American and Caucasian women. J Natl Cancer Inst Monogr:36-43, 2001
37. Dignam JJ, Colangelo L, Tian W, et al: Outcomes among African-Americans and Caucasians in colon cancer adjuvant therapy trials: findings from the National Surgical Adjuvant Breast and Bowel Project. J Natl Cancer Inst 91:1933-40, 1999
38. Dignam JJ, Ye Y, Colangelo L, et al: Prognosis after rectal cancer in blacks and whites participating in adjuvant therapy randomized trials. J Clin Oncol 21:413-20, 2003
39. Yothers G, Sargent DJ, Wolmark N, et al: Outcomes Among Black Patients With Stage II and III Colon Cancer Receiving Chemotherapy: An Analysis of ACCENT Adjuvant Trials. Journal of the National Cancer Institute 103:1498-1506, 2011
40. Lynch GF, Gorelick PB, Raman R, et al: A pilot survey of African-American physician perceptions about clinical trials. J Natl Med Assoc 93:8S-13S, 2001
41. Mills EJ, Seely D, Rachlis B, et al: Barriers to participation in clinical trials of cancer: a meta-analysis and systematic review of patient-reported factors. Lancet Oncol 7:141-8, 2006
42. Klabunde CN SB, Butler B, Atkins J Factors influencing enrollment in clinical trials for cancer treatment. Southern Medical Journal 92:1189-1193, 1999
43. Ray M, Smith DM, Olopade OI, et al: A prospective paired survey of oncologist and patient attitudes towards therapeutic cancer clinical trial (CT) enrollment in a diverse academic health center patient population. . Journal of Clinical Oncology, 2010 ASCO Annual Meeting Proceedings 28 (suppl; abstr 6120) 2010
44. Mc Daid C , Hodges Z , Fayter D, et al: Increasing participation of cancer patients in randomised controlled
trials: a systematic review. Trials 7:16, 2006
45. Paskett ED, Cooper MR, Stark N, et al: Clinical trial enrollment of rural patients with cancer. Cancer Pract 10:28-35, 2002
46. Hutchison C, Cowan C, McMahon T, et al: A randomised controlled study of an audiovisual patient information intervention on informed consent and recruitment to cancer clinical trials. Br J Cancer 97:705-11, 2007

47. Lai GY, Gary TL, Tilburt J, et al: Effectiveness of strategies to recruit underrepresented populations into cancer clinical trials. Clin Trials 3:133-41, 2006
48. Education Network to Advance Cancer Clinical Trials (ENACCT) and
Community-Campus Partnerships for Health (CCPH). (2008). Communities as Partners in Cancer Clinical Trials: Changing Research, Practice and Policy. Silver Spring, MD.
49. Health Literacy: A Prescription to End Confusion. in Committee on Health Literacy, Board on Neuroscience and Behavioral Health (The National Academics Press, Washington, D.C., 2004).
50. U.S. Department of Health and Human Services. Healthy People 2010: Understanding and Improving Health. Washington, D.C.: U.S. Government Printing Office;2000. 2nd ed.
51. Committee on Health Literacy, Board on Neuroscience and Behavioral Health. Health Literacy: A Prescription to End Confusion. Washington,D.C.: The National Academics Press; 2004.
52. Kirsch IS, Jungeblut A, Jenkins L, et al: Adult Literacy in America: A First Look at the Results of the National Adult Literacy Survey., in Education UDo (ed). Washington, D.C., National Center for Education Statistics, 1993, pp 178
53. Pagan JA, Brown CJ, Asch DA, et al: Health Literacy and Breast Cancer Screening among Mexican American Women in South Texas. J Cancer Educ, 2011
54. Shelton RC, Jandorf L, Ellison J, et al: The influence of sociocultural factors on colonoscopy and FOBT screening adherence among low-income Hispanics. J Health Care Poor Underserved 22:925-44, 2011
55. Garbers S, Schmitt K, Rappa AM, et al: Functional health literacy in Spanish-speaking Latinas seeking breast cancer screening through the National Breast and Cervical Cancer Screening Program. Int J Womens Health 1:21-9, 2010
56. Bennett CL, Ferreira MR, Davis TC, et al: Relation between literacy, race, and stage of presentation among low-income patients with prostate cancer. J Clin Oncol 16:3101-4, 1998
57. Kim SP, Knight SJ, Tomori C, et al: Health literacy and shared decision making for prostate cancer patients with low socioeconomic status. Cancer Invest 19:684-91, 2001
58. Hahn EA, Cella D: Health outcomes assessment in vulnerable populations: measurement challenges and recommendations. Arch Phys Med Rehabil 84:S35-42, 2003
59. Health literacy: report of the Council on Scientific Affairs. Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs, American Medical Association. JAMA 281:552-7, 1999
60. Schillinger D, Piette J, Grumbach K, et al: Closing the loop: physician communication with diabetic patients who have low health literacy. Arch Intern Med 163:83-90, 2003
61. Health Literacy: A Prescription to End Confusion, Committee on

Health Literacy, Board on Neuroscience and Behavioral Health. Washington, D.C., The National Academics Press, 2004
62. Krieger JL, Parrott RL, Nussbaum JF: Metaphor use and health literacy: a pilot study of strategies to explain randomization in cancer clinical trials. J Health Commun 16:3-16, 2011
63. Cassileth BR, Zupkis RV, Sutton-Smith K, et al: Informed consent -- why are its goals imperfectly realized? N Engl J Med 302:896-900, 1980
64. Penman DT, Holland JC, Bahna GF, et al: Informed consent for investigational chemotherapy: patients' and physicians' perceptions. J Clin Oncol 2:849-55, 1984
65. Sutherland HJ, Lockwood GA, Till JE: Are we getting informed consent from patients with cancer? J R Soc Med 83:439-43, 1990
66. Williams CJ, Zwitter M: Informed consent in European multicentre randomised clinical trials--are patients really informed? Eur J Cancer 30A:907-10, 1994
67. Fallowfield L, Lipkin M, Hall A: Teaching senior oncologists communication skills: results from phase I of a comprehensive longitudinal program in the United Kingdom. J Clin Oncol 16:1961-8, 1998
68. Tannock IF: The recruitment of patients into clinical trials. Br J Cancer 71:1134-5, 1995
69. Lindau ST, Tomori C, Lyons T, et al: The association of health literacy with cervical cancer prevention knowledge and health behaviors in a multiethnic cohort of women. American Journal of Obstetrics and Gynecology 186:938-943, 2002
70. Barlund DC: The mystification of meaning: doctor-patient encounters. J Med Educ. 51:716-25, 1976
71. Murphy PW CA, Walker L, Arnold CL, Chesson LM Comparing the effectiveness of video and written material for improving knowledge among sleep disorders clinic patients with limited literacy skills. Southern Medical Journal 93:297-304, 2000
72. Manfredi C, Czaja R, Price J, et al: Cancer patients' search for information. J Natl Cancer Inst Monogr:93-104, 1993
73. Manfredi C, Czaja R, Buis M, et al: Patient use of treatment-related information received from the Cancer Information Service. Cancer 71:1326-37, 1993
74. Whelan TJ, Mohide EA, Willan AR, et al: The supportive care needs of newly diagnosed cancer patients attending a regional cancer center. Cancer 80:1518-24, 1997
75. Chapman K, Rush K: [Patient and family satisfaction with cancer information: pamphlet evaluation]. Can Oncol Nurs J 13:164-75, 2003
76. Coulter A: Patient information and shared decision-making in cancer care. Br J Cancer 89 Suppl 1:S15-6, 2003
77. Monnier J, Laken M, Carter CL: Patient and caregiver interest in internet-based cancer services. Cancer Pract 10:305-10, 2002
78. Eysenbach G: The impact of the Internet on cancer outcomes. CA Cancer J Clin 53:356-71, 2003

79. Peterson KA, Radosevich DM, O'Connor PJ, et al: Improving Diabetes Care in Practice: findings from the TRANSLATE trial. Diabetes Care 31:2238-43, 2008
80. Basch EM, Thaler HT, Shi W, et al: Use of information resources by patients with cancer and their companions. Cancer 100:2476-83, 2004
81. Roter DL, Hall JA, Katz NR: Relations between physicians' behaviors and analogue patients' satisfaction, recall, and impressions. Med Care 25:437-51, 1987
82. Bertakis KD, Roter D, Putnam SM: The relationship of physician medical interview style to patient satisfaction. J Fam Pract 32:175-81, 1991
83. Liang W, Burnett CB, Rowland JH, et al: Communication between physicians and older women with localized breast cancer: implications for treatment and patient satisfaction. J Clin Oncol 20:1008-16, 2002
84. Ong LM, Visser MR, Lammes FB, et al: Doctor-patient communication and cancer patients' quality of life and satisfaction. Patient Educ Couns 41:145-56, 2000
85. Ashton CM, Haidet P, Paterniti DA, et al: Racial and ethnic disparities in the use of health services: bias, preferences, or poor communication? J Gen Intern Med 18:146-52, 2003
86. Kaplan SH, Greenfield S, Ware JE, Jr.: Assessing the effects of physician-patient interactions on the outcomes of chronic disease. Med Care 27:S110-27, 1989
87. Kerr J, Engel J, Schlesinger-Raab A, et al: Communication, quality of life and age: results of a 5-year prospective study in breast cancer patients. Ann Oncol 14:421-7, 2003
88. Velikova G, Booth L, Smith AB, et al: Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. J Clin Oncol 22:714-24, 2004
89. Sepucha KR, Belkora JK, Mutchnick S, et al: Consultation planning to help breast cancer patients prepare for medical consultations: effect on communication and satisfaction for patients and physicians. J Clin Oncol 20:2695-700, 2002
90. Brown RF, Butow PN, Dunn SM, et al: Promoting patient participation and shortening cancer consultations: a randomised trial. Br J Cancer 85:1273-9, 2001
91. Connecting Americans to their Healthcare, Working Group on Policies for Electronic Information Sharing Between Doctors and Patients, Markle Foundation, 2004
92. Cegala DJ, Broz, S.L. : Provider and patient communication skills training, in Thompson TL, Dorsey, A., Miller, K. (ed): Handbook of Health Communication. Mahwah, NJ, Lawrence Erlbaum Associates, Inc., 2003, pp 95-119
93. Wired for Health and Well-Being: The Emergence of Interactive Health Communication, in Services DoHaH (ed). Science Panel on Interactive Communication and Health. Washington, D.C., 1999
94. Greimel ER, Gappmayer-Locker E, Girardi FL, et al: Increasing women's knowledge and satisfaction with cervical cancer screening. J

	Psychosom Obstet Gynaecol 18:273-9, 1997 95. Denizard-Thompson NR, Singh S, Stevens SR, et al: iPod technology for teaching patients about anticoagulation: a pilot study of mobile computer-assisted patient education. Prim Health Care Res Dev 13:42-7, 2012 96. Krishna S, Balas EA, Spencer DC, et al: Clinical trials of interactive computerized patient education: implications for family practice. J Fam Pract 45:25-33, 1997 97. Wilson EA, Makoul G, Bojarski EA, et al: Comparative analysis of print and multimedia health materials: A review of the literature. Patient Educ Couns 89:7-14, 2012 98. Wofford JL, Smith ED, Miller DP: The multimedia computer for office-based patient education: a systematic review. Patient Educ Couns 59:148-57, 2005 99. Kreps GL, Arora NK, Nelson DE: Consumer/provider communication research: directions for development. Patient Educ Couns 50:3-4, 2003 100. Wallace LS, Rogers ES, Roskos SE, et al: Brief report: screening items to identify patients with limited health literacy skills. J Gen Intern Med 21:874-7, 2006 101. Hahn EA, Choi SW, Griffith JW, et al: Health literacy assessment using talking touchscreen technology (Health LiTT): a new item response theory-based measure of health literacy. J Health Commun 16 Suppl 3:150-62, 2011 102. Yost KJ, Webster K, Baker DW, et al: Acceptability of the talking touchscreen for health literacy assessment. J Health Commun 15 Suppl 2:80-92, 2010 103. Hahn EA, Cella D, Dobrez D, et al: The talking touchscreen: a new approach to outcomes assessment in low literacy. Psychooncology 13:86-95, 2004 104. Hahn EA, Garcia SF, Cella D: Patient attitudes and preferences regarding literacy screening in ambulatory cancer care clinics. Patient Related Outcome Measures 1:19-27, 2010
2.12 Publication Plan	Generally, a publication plan is discussed between the investigator and Merck /MSD during time when the protocol is under development. Details of the publication and the obligations to Merck/MSD are outlined in the study agreement. The following should be considered for the publication plan: • What are your publication plans? How many manuscripts do you anticipate? • Include projected target date for manuscript submission and name of the journal • Do you anticipate abstracts? How many? • What scientific meetings would you consider presenting the study results?
2.13 Curriculum Vitae	Investigator should provide curriculum vitae in English and a listing of references to Merck/MSD.

2.13 Protocol Submission for Investigator-Initiated Studies	U.S. protocols should be submitted by US investigators directly or through the Global Research Specialist at www.merckiisp.com Non U.S. protocols should be submitted to the MSD office by the investigators.