PACCT: Partnering Around Cancer Clinical Trials

Principal Investigator
Susan Eggly, Ph.D.
Associate Professor
Population Studies and Disparities Research Program
Department of Oncology
Wayne State University
Detroit, MI 48201

Co-Investigators
Louis A. Penner, Ph.D., Wayne State University
Terrance L. Albrecht, Ph.D., Wayne State University
Mark Manning, Ph.D., Wayne State University
Seongho Kim, PhD, Wayne State University
Lauren Hamel, Ph.D., Wayne State University
Ellen Barton, Ph.D., Wayne State University
Elisabeth Heath, MD, Wayne State University
Michael Carducci, MD, Johns Hopkins University
Dina Lansey, MSN, Johns Hopkins University

List of Appendices

Overview

This project, funded by the National Cancer Institute (R01CA200718-01 (Eggly, PI), has the overall goal of increasing rates at which African American and White men **make an informed decision to participate** in a cancer clinical trial. The research will be conducted at two sites: Wayne State University/Karmanos Cancer Institute (Detroit) and Johns Hopkins/Sidney Kimmel Comprehensive Cancer Center (Baltimore, MD). The research utilizes two distinct research designs to evaluate two separate behavioral interventions. The first is a between-subject randomized controlled trial to evaluate a **patient-focused intervention**; the second is a within-subject interrupted time series design to evaluate a **physician-focused intervention**. In the patient-focused intervention, patients are randomized to an intervention or usual care group, and comparison of outcomes is made between groups. In the physician-focused intervention, physicians participate during a pre-intervention period (20 months) followed by the intervention (2 months) and then the post-intervention period (20 months); outcomes are compared prior to and following the intervention. Together, these interventions are designed to influence a **primary outcome**—patients' decisions to enroll in a clinical trial; and several **secondary outcomes**--physicians' offers of a trial, the quality of patient-physician communication during clinical interactions, patients' understanding of the trial offered, and patients' actual enrollment in the trial. Participants will include 32 physicians who see patients with prostate cancer at one of the two data collection sites, and 440 of their African American and White patients. Of these, up to 16 physicians and 220 patients will be recruited at KCI/WSU. An additional 16 physicians and 220 patients will be recruited at Hopkins.

Background and Specific Aims

Cancer clinical trials are essential for testing the safety and efficacy of promising treatments and translating new knowledge into tangible benefits for patients; they also represent state-of-the art treatment for individuals with cancer.[1,2] However, only a small percentage of cancer patients ever enroll in a trial.[3,4] Estimates of the proportion of trials that fail to meet scientific objectives because of insufficient accrual range from 22-50%.[5,6] Low accrual jeopardizes researchers' ability to assess the safety and effectiveness of new approaches to cancer care, wastes resources, and precludes follow-up studies.[6,7]

Under-enrollment is an even greater problem among minorities, particularly African Americans,[4,8,9,10] despite NIH requirements to include minorities in clinical research.[11] Minority under-enrollment limits the generalizability of findings,[10,12] and, given the Institute of Medicine's recommendation that every individual with cancer should have access to high quality clinical trials,[2] minority under-enrollment represents a racial/ethnic disparity in cancer care that may lead to disparities in treatment outcomes and survival.[1,13,14]

Under-enrollment of African Americans and other minorities is often attributed to patients' negative attitudes toward trials,[15-17] but research suggests a more complicated picture.[10,18-21] National and system factors, such as a lack of available trials, strict eligibility criteria, and competing demands on under-resourced hospitals also present significant barriers that likely have a disproportionate effect on minority enrollment.[2,8,19,22-24] Several national, regional, and consortia efforts are addressing either patient or system factors.[10,20,25,26] However, even when medical institutions have a trial infrastructure and trials are available, physicians are often unwilling or unprepared to discuss trials with some patients, and some patients are mistrustful of physicians or of trials.

In a National Cancer Institute-commissioned monograph on multilevel interventions, authors challenged researchers to move beyond reductionist interventions that focus on only one level (e.g., patient, provider, or system).[27-29] We plan to conduct a multilevel intervention focused on African American men with prostate cancer, but designed to influence African-American and White *patients' attitudes* about physicians and about trials; *physicians' attitudes* about patients and about trials; *and patient-provider clinical interactions* in which trials may be discussed. **Our overall goal is to increase rates at which African American and White men make an informed decision to participate in a trial; thus the intervention has societal benefits in that it has potential to increase overall enrollment in trials, and may have additional benefits for African American patients, who are consistently underrepresented in clinical trials.**

We bring together a highly experienced, multidisciplinary team from two NCI-designated comprehensive cancer centers that each have a very functional trial infrastructure and a diverse population of patients, but still need to improve trial enrollment, especially among minorities: Wayne State University/Karmanos Cancer Institute (WSU/KCI) and Johns Hopkins University/Sidney Kimmel Comprehensive Cancer (Hopkins). **We will recruit physicians and their African American and White patients with prostate cancer to participate in this research.** The design allows us to determine the relative effects of the intervention on both racial groups.

We propose to test the following ***Specific Aims.*** **(PLEASE NOTE that the data to support tests of hypotheses consistent with these aims will be fully collected *after* we have received IRB permission to implement the physician intervention.)**

1) **Determine the effects of the interventions on outcomes.** The primary outcome is rate of patients' decisions to enroll in a clinical trial; the secondary outcomes are physicians' offers of a trial, the quality of patient-physician communication during clinical interactions, patients' understanding of the trial offered, and patients' actual enrollment in the trial.

   a) Determine the effects of the patient-focused intervention on outcomes. **Hypothesis 1a**: Outcomes will be improved in the patient intervention group, relative to a usual care group.
   b) Determine the effects of physician-focused intervention on outcomes. **Hypothesis 1b:** Outcomes will be significantly improved for patients after the physician intervention, as compared to outcomes before the physician intervention.
   c) Determine the combined effects of the two interventions on outcomes. **Hypothesis 1c:** There will be a multiplicative effect of the two interventions that yield improvements in primary and secondary outcomes over and above the independent effects of each intervention.

2) **Compare the effects of the interventions on outcomes for African American versus White men. Hypothesis 2: The** effects of the intervention will be significantly greater among African American than White men. We will also conduct exploratory analyses of the moderating effects of other variables on outcomes (e.g., decision preferences, health literacy, race-related attitudes, disease severity, trial characteristics).

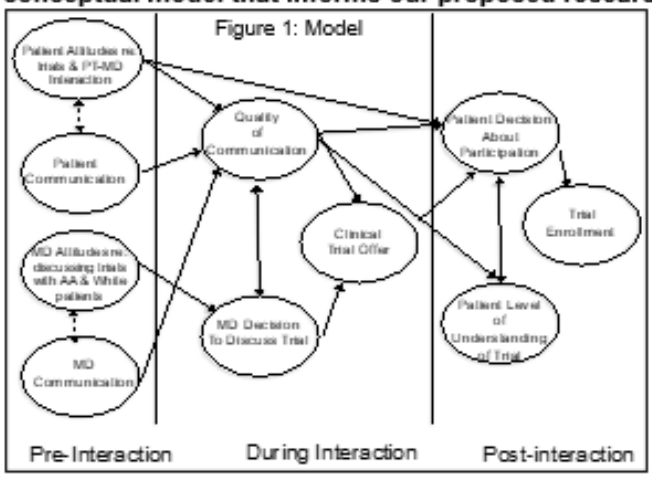
3) **Examine the extent to which patient-physician communication mediates the relationship between the intervention and outcomes.**
   Hypothesis 3: The quality of communication will mediate the effects of the patient and physician intervention on trial offers, and, in turn, on patient understanding of trials offered and decisions to participate. Because the specific meditational variables to be tested will emerge from the analyses related to the first two hypotheses, this is an exploratory hypothesis.

This research is **highly significant. First,** it has clear potential to increase clinical trial participation rates of African American and White men with prostate cancer, thus improving the generalizability of findings from these trials to a more diverse patient population. **Second**, the research will provide data to support the proposed social psychological and communication science derived mechanisms by which the interventions affect outcomes. **Third**, the longitudinal design will provide descriptive information which is currently unavailable on the proportion of patients with prostate cancer that are eligible for a trial, are offered a trial, agree to participate, and/or enroll. **Fourth,** findings can inform the development of future interventions to improve trial enrollment of other underrepresented populations (e.g., Hispanic patients, older patients) and in other contexts. **Fifth,** multilevel interventions have the potential to achieve substantial and sustained change, and to produce effects that are at least additive and possibly multiplicative. **Finally,** this research directly addresses racial disparities in cancer care by improving access to high quality clinical care for African American men suffering the disproportionate burden of disparities in prostate and other cancers.

Conceptual Model

Our proposed intervention is driven by an **innovative conceptual model** (Figure 1) derived from our 15 years of novel, transdisciplinary clinical research on patient and physician communication, cancer clinical trials, and racial/ethnic health disparities. Our intervention translates well-validated theories from social psychology and communication science that have never been applied to address the critical need for increasing trial enrollment. Also, whereas prior interventions to improve rates of trial enrollment have generally focused on a single level, the proposed intervention addresses this complex problem by influencing multiple levels--*patients*' trial-related attitudes and communication, *physicians'* trial-related attitudes and communication, *patient-physician clinical interactions* during which trials may be discussed, and ultimately, rates of trial participation by African American (and White) patients. The research is also **methodologically innovative**. Our research design combines a randomized trial with an interrupted time series quasi-experiment.[30] Also, we will collect multiple data sources that will allow us to examine processes through which the intervention influences outcomes: patient and

physician self-reports, patient medical records, and video recordings of clinical interactions using our state-of-the-art video recording[31] and observational coding systems.[32-34] **In the next paragraph, we explain the conceptual model that informs our proposed research.**



Conceptual Model (Fig. 1). Our model proposes that patient and physician individual attitudes and beliefs prior to a clinic visit and their interpersonal communication during the clinic visit interact to directly and indirectly influence outcomes related to patients' decisions about trial participation. We focus on patients who are eligible for clinical trials because, despite their eligibility, only a small percentage enroll in a trial.[21,35] We focus on physicians because, although other providers such as research nurses are critical to enrolling patients in trials, physicians make the final decision about whether to offer a trial to specific patients[36] and patients generally learn about trials, at least initially, from their physicians. Also, patients consider physicians to be their primary and preferred source of information.[37] As shown in Figure 1, the quality of patient-physician communication during clinic visits is considered the most central and proximal influence on patients' decisions about participating in trials. We focus on communication for two reasons: 1) it is through these interpersonal processes among health care organizations, providers, patients, and families that health care is transacted;[38-40] and 2) our and others' research has shown that the quality of communication in racially discordant clinical interactions (e.g., African American patient, non-African American physician) is lower than in racially concordant interactions.[34,41-47] This is particularly important because very few oncologists are African American, and thus oncology interactions for African American patients are almost always racially discordant.[48] The model builds on the goals of patient-centered care in the 2001 IOM report, Crossing the Quality Chasm,[49] and the conceptual model in the NCI monograph on patient-centered communication.[39] Several variables that affect physician offers and patient decisions, such as trial availability and characteristics, eligibility criteria, and disease severity, are not displayed in the model, but will be included in our analyses.

APPROACH

All procedures, including the separate implementation of patient-focused and physician-focused interventions, will begin at each data collection site (WSU and Hopkins) only after IRB approval has been provided at that site. We will conduct both interventions over the course of the study (5 years); This application specifically describes details of the patient-focused procedures. The physician-focused intervention is briefly described, and will be developed later and will begin only after additional IRB approval has been received and physicians are re-consented.

Overview. We propose to conduct two related interventions focused on patients and physicians and to evaluate the effects on the **primary outcome, patient decisions to enroll in a trial**, and the following secondary outcomes: (a) physician offers of a clinical trial, (b) quality of patient-physician communication during clinical interactions, (c) patient understanding of trials offered, and (d) patient enrollment in the trial. The first intervention is a patient-focused intervention targeting patients' attitudes and beliefs about their physician and their role in patient-physician interactions and their communication during clinic visits. The second intervention is a physician-focused intervention targeting physicians' attitudes and beliefs about their patients and discussing trials with them and their communication during clinic visits when trials may be discussed. (We stress that we will seek separate secondary IRB approval for this physician intervention, and this intervention will not be implemented without this separate approval and physician reconsent.) Aim 1 is to determine the independent and the combined effects of the interventions on outcomes. Aim 2 is to examine whether the magnitude of the effects of the intervention are different for African American versus White men. Aim 3 is to examine the extent to which the quality of patient-physician communication mediates the relationship between the intervention and outcomes. In the following sections, we provide details about research design and procedures.

Research Settings and Participants

Data Collection Sites. The proposed research will be conducted at two NCI-designated comprehensive cancer centers. Both sites provide prostate cancer care in catchment areas with large populations of African Americans and actively recruit patients to clinical trials through national and regional consortia. Both sites are active members of the Prostate Cancer Clinical Trials Consortium (PCCTC). In its four years of participation in the PCCTC, KCI/WSU has been involved in 32 therapeutic and biomarker prostate trials, 21 (66%) of which address advanced stage disease. From 2008-2013, JHKCC has participated in 46 therapeutic (and 4 other intervention) trials for advanced stage disease and 27 therapeutic (and 19 other intervention) trials for early stage disease.

The main coordinating site, KCI/WSU, is an NCI-designated comprehensive cancer center located in Detroit, Michigan. From 2009-2011 an average of **289** new prostate cancer patients were seen each year. Of these, on average, ~60% (n=174) were African American and ~40% (n=115) were White. The second site, JHKCC, is also an NCI-designated comprehensive cancer center providing care in Baltimore, Maryland. From 2009-2011, an average of approximately **1300** new patients with prostate cancer were seen each year. Of these, on average, 15% (~200) were African American, ~82% (n=1000) were White, and ~3% were "other".

Participants and Recruitment. Research participants will include physicians and their patients with prostate cancer.

We will recruit up to **32 physicians (medical oncologists, urologists, and radiation oncologists)** who regularly treat patients with prostate cancer at one of the two research sites (WSU/KCI or Hopkins) and who can recruit patients to available trials. Dr. Eggly and/or research staff will attend a clinical staff meeting to explain the study to physicians, and then meet with interested physicians individually to answer questions and obtain consent. Physicians who consent will agree to complete baseline measures, to inform their eligible patients about this study during a regularly scheduled clinic visit (or ask another member of their clinical team to do so), to allow video recording of selected patient visits, and to complete very brief questionnaires after patient visits. They will also be told they may be asked to participate in a training intervention at a later date. Based on past studies (see reference list), we expect no physician attrition.

We will recruit adult **patients** of these physicians (ages ≥18) if they self-identify as Black, African American, or White and non-Hispanic. Members of other ethnic minorities will not be included because (a) the focus of this study is on only these two racial groups; and (b) the numbers of other minority patients seen at these cancer centers are presently too small to be included as unique groups in the analyses. **Other inclusion criteria are:** a) confirmed diagnosis of prostate cancer, b) seeing a participating physician for less than a year and expecting to see this physician at least once in the following year, and c) able to read and write English well enough to understand and sign consent documents (with the assistance of research staff) and respond to questionnaires. We received a waiver of HIPAA documentation to confirm these inclusion criteria, but written HIPAA documentation will be obtained at consent. Patients will be excluded if physicians/staff determine they will not be eligible for a trial during the study period (e.g., entering hospice; moving away). Once a patient is deemed eligible, physicians (or their staff) will explain the study and ascertain interest. Interested patients will be formally consented by research staff. Patients' family/companions are not the focus of the study and will not be recruited; however, if they are present during a video recorded visit, the study will be explained to them and consent will be obtained at that time using an information sheet (See Appendix C: Companion Information Sheet). Companion communication behaviors may be included in ancillary analyses. Further recruitment details are below.

We plan to recruit a total of **440 patients**, including 220 African Americans and 220 White patients. We will recruit patients in the order they are identified as eligible and interested, but we will attempt to recruit no more than 60 total patients per physician, half who self-identify as Black/African American and half who self-identify as White. Further, we will recruit family members and other health care providers that may appear in our video recordings. We anticipate recruiting a total of **200 family members** and **100 other health care providers**. Considering the fact that many patients may never become eligible for an available trial or may leave the study for medical or social reasons, we estimate that approximately 216 of these participants will be eligible for a clinical trial. Thus, **our estimated sample for the primary analyses is 216 patients who will be video recorded discussing a trial with a participating physician**. We will recruit half of the patient sample (i.e., 220 AA and White men) as quickly as possible following their physician's consent at the beginning of data collection (the first 20 months/pre-physician intervention). These patients will actively participate until they either receive a trial offer or until the physician intervention is implemented. We will recruit the second half of the patient sample

(also 220 AA and White men) immediately following the physician intervention; these patients will participate actively until they receive a trial offer or until data collection ends.

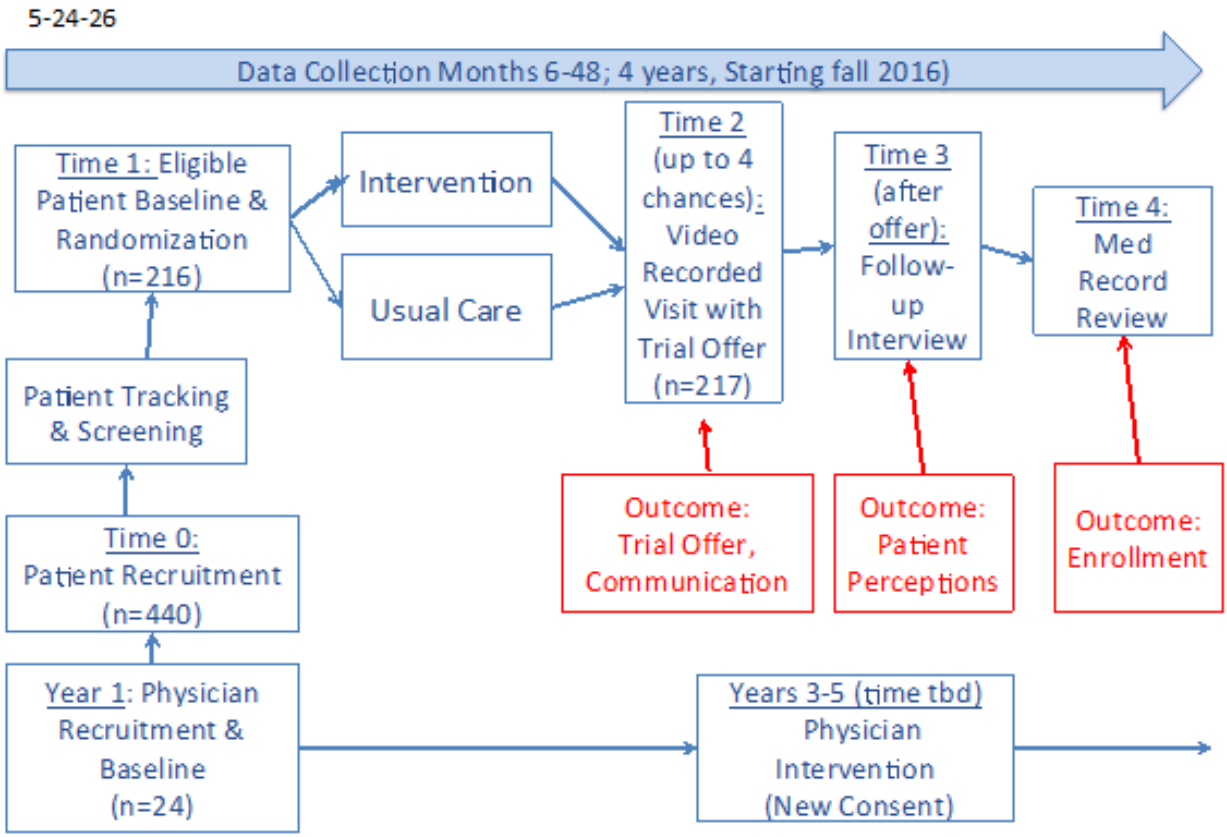
Study Design, Interventions, and Measures

Study Design Overview (See Figure 2). This 5-year study involves two related interventions and research designs conducted over a 42-month data collection period. These interventions begin after IRB approval is received and physicians are consented.

The first intervention is a randomized controlled trial focused on patients. This intervention is broken into two separate but identical parts, in which half of the patient sample participates before the physician intervention, and the other half participates after the physician intervention. In the first part, patients of participating physicians will be recruited and tracked until they become eligible for a trial, at which time they will be randomized into an intervention or usual care group. They will continue their participation until: they receive a trial offer, or they have four interactions with their physician without receiving an offer. Regardless of the number of interactions, this group of patients will discontinue their active participation when the physician intervention begins. Thus, these patients will participate for a maximum of 20 months. In the second part, which occurs after the physician intervention has been conducted, the remaining half of the patient sample will be recruited and tracked, and eligible patients will be randomly assigned to the two groups. Again, their participation will continue until they receive a trial offer, they have four interactions with their physician without an offer, or data collection ends, These patients will, thus, also participate for a maximum of 20 months. We will utilize a block-randomized design in which physicians are treated as blocks and patients are randomized to a group.

The second intervention is a within-subjects interrupted time series quasi-experiment focused on physicians.[30] Physicians will recruited at the beginning of data collection, prior to any patient recruitment (i.e., once IRB approval has been received—approximately nine months after the formal start date of this grant award). In this within-subjects design, physicians provide pre-intervention data for 20 months, then receive the intervention and continue their participation for another 20 months (i.e., until the end of data collection). The same physicians will remain in the study throughout data collection; thus they will provide both pre intervention and post intervention data that will be used to examine the effectiveness of the physician-focused intervention.

Figure 2: Study Design and Procedures Overview



Patient Procedures, Measures, and Intervention
Patient Procedures.

Time 0: Patient Recruitment: Participating physicians (or their designee with a clinical relationship) will examine their daily clinic schedule to identify eligible patients who will visit the clinic for a scheduled appointment. We received a waiver of HIPAA documentation to confirm participant inclusion eligibility, and written HIPAA documentation will be obtained at consent. Physicians (or designee) will inform these patients about the study and provide them with a study flyer during or immediately after the visit. (See Appendix E: Flyer). If patients are interested, clinic/research staff will meet with them as soon as possible to explain the study and obtain consent (See Appendix A: Patient Consent Form). At this point, patients will be assigned an ID number and will be asked to complete questionnaires on a tablet device (i.e., iPad) via Qualtrics. Qualtrics is widely used for data collection in both medical and nonmedical settings, and follows very high-level security procedures to protect participant data. The Qualtrics system encrypts data before transmission and is HIPAA compliant. Patients will be asked to complete questionnaires (See Appendix F: Patient Time 0 Questionnaires) including: demographic information, date of prostate cancer diagnosis, preferences for future contact (during study participation), health status, perceived economic burden, health literacy, trust in the medical profession, group-based medical mistrust, and receptivity to discussing a clinical trial. We anticipate these questionnaires will take approximately 20 minutes. Patients will receive a $20 gift card at this time. Then, clinic/research staff will track patients' scheduled visits until they become potentially eligible for an available clinical trial.

Time 1: 1-2 Weeks Prior to First Clinic Visit After Enrollment: Prior to a patient's scheduled appointment with a participating physician, clinic/research staff will determine whether the patient is potentially eligible for an available clinical trial. If there is no trial available, the patient will not be contacted, and tracking will continue until

the next scheduled visit. If/when the patient is found to be potentially eligible for an available trial, clinic/research staff will contact him according to the communication/contact preferences he provided at Time 0. They will remind him about the study and ask him if he is willing to meet with research staff at a convenient place and time to complete the Time 1 (baseline) questionnaire (Appendix G: Time 1 Questionnaires), again administered to the participant through Qualtrics on a tablet device (e.g., iPad) or over the phone. The research staff will NOT directly inform patients about their eligibility. If asked, they will tell patients this is up to the physician and clinical staff. Once the questionnaire is completed, an automated computer program provided by Qualtrics will randomly assign the patient to either the usual care or intervention group. Intervention group patients will receive the intervention at this time, or prior to their upcoming appointment, in the form of a booklet (See Appendix M: Patient Intervention Booklet; see below for details). All patients will receive a $20.00 gift card and be told that their next clinic visit may be video recorded. This visit should take < one hour.

Time 2: Pre- and Post-Clinic Visit: On the **day of a clinic visit** (for those patients who have been prescreened and found to be potentially eligible for an available clinical trial), clinic/research staff will meet with patients to remind them that the visit will be video recorded and to provide a copy of the patient intervention booklet, if needed. Just prior to and following the visit, patients will complete brief questionnaires (See Appendices H and I: Time 2 pre- and post questionnaires). If family members or companions are present, they will be told about the study and asked for consent (See Appendix C: Companion Information Sheet). Similarly, clinical staff who will be in the room during video recording will be provided an information sheet (See Appendix D: Health Care Provider Information Sheet.) Patients will receive a $10.00 gift card following this visit. Also, patients will be asked whether they were offered a clinical trial; if they were not, they will be told that they are still in the study and may be contacted again in the future. They will continue to be tracked for up to a total of 4 visits or until the end of their participation. If they still receive no offer after a fourth visit, they will no longer be tracked. If they are offered a trial, they will proceed to Time 3.

Time 3: Follow-Up Interview: A week after the visit, research staff will contact patients (on the phone or in person as convenient to patients) who were offered a trial to conduct a brief interview (Appendix J: Time 3 Follow-Up Interview). This interview should take approximately 20 minutes. Patients will receive a third $10.00 gift card at the end of this interview.

Time 4: Medical Record Review: Research staff will examine patient medical records to determine participating patients' disease status, co-morbidities, whether and when they were eligible for an available trial, whether they completed procedures for trial enrollment and/or enrolled in a trial, and trial characteristics (e.g., difficulty, complexity) that may affect physicians' decisions to offer a trial and/or patients' decisions to participate.

Patient Intervention (See Appendix G: Patient Intervention). The patient intervention includes both attitude and communication components and is in the form of a booklet (See Appendix M for Patient Intervention Booklet). The first section, the **attitude component**, is based on the well-researched Common Ingroup Identity Model.[50,51] Extensive research shows that establishing a sense of common identity or purpose between interaction participants increases cooperation and trust among members of different social groups. Briefly, patients will be informed that they and their physicians have equally important roles and need to work together as a team to provide the best care for the patient's cancer. Research assistants will briefly review this section with patients and ask them to place their initials at the bottom of the page to confirm their role as member of the patient-doctor team. The second section, the **communication component**, is a Question Prompt List (QPL), which includes instructions and a list of questions related to clinical trials. A QPL is a list of questions related to the physical and psychosocial aspects of illness and treatment that patients may want to ask their physicians during a visit. This communication tool has been used in several settings to encourage and assist patients to participate actively during medical visits (e.g., ask questions, state concerns) and has been shown to improve clinical communication.[52] Patients prepared with a QPL are more likely to ask questions and state their concerns about trials and/or treatments, enabling a shared decision making process. The QPL was adapted from one we used as an intervention in our recently-completed study of patients facing a discussion with an oncologist about chemotherapy. The QPL for use in this study was developed specifically for this study. (See Appendix G: Patient Intervention Booklet.) After the patients have finished reading the "team" component of the booklet, the RA will tell patients that the list was developed by doctors and patients, and that patients might find it helpful during the clinic visit, especially if they discuss a clinical trial with their doctor. The research assistants will be trained NOT to answer questions nor discuss trials, but rather to encourage patients to ask questions during clinic visits. The intervention meetings will be audio-recorded to assess fidelity to the protocol.

Physician Procedures and Measures

Physician Procedures. Physician participation will involve referring their patients to the study, completing baseline measures, and completing measures immediately after clinic visits with participating patients (See Appendix B, Physician Consent). Physicians will be informed that they will be approached at a later date about the physician-focused intervention, and will be asked for re-consent at that time. As noted above, the physician intervention does not occur until 20 months after they enroll in the study, and separate IRB approval will be sought before it is implemented.

Physician Measures (See Appendix K: Physician Baseline Measures.)

***Physician Baseline Measures*:** Within a week of recruitment, physicians will provide demographic information such as age, gender, and years in practice. They will complete measures assessing their attitudes toward trials,[23,53] decisional control preferences,[54] attitudes toward patient-physician relationships,[55] and explicit and implicit racial attitudes (using the Implicit Association Test) toward African Americans and White people.[56] The baseline measures should take <45 minutes to complete (See Appendix N, Physician Baseline Instructions).

Clinic Visits. Following each patient visit, physicians will report whether they discussed and/or offered a trial and their perceptions of the patient's personal attributes and behavior during the visit.[47,57] If a trial was offered, we will also ask physicians about their perceptions of how well the patient understood the trial, his ability to tolerate the trial, and his likely adherence to the trial protocol. This questionnaire should take less than 5 minutes to complete. (See Appendix L, Physician Post Interaction Questionnaire)

Physician Intervention. The physician intervention is implemented via an interrupted time series, within-subject design. Physicians receive the intervention in Phase 2, following IRB approval and re-consent.

The physician-focused intervention includes two components: a communication and an attitude/awareness component. The **communication component** consists of a web-based communication skills training module. The objective of the training module is to improve physicians' communication skills in general (e.g., patient-centeredness, shared decision making) and specific to discussing trials with patients. Once physicians have signed the re-consent forms, they will be provided a link to a website that will allow them to participate in the training. The training includes a didactic video that provides information about the importance of recruiting a diverse population of patients to cancer clinical trials, and encourages them to reflect on communication skills that facilitate effective patient-centered communication and shared decision-making about trials. Training methods will include brief explanations and discussions and video illustrations. The web-based materials also include questions (via a Qualtrics survey) that assess physicians' attitudes and knowledge about clinical trials, prior to and following the training. The training module takes about 1.5 hours. Physicians receive Continuing Medical Education (CME) credit and $100.00 gift card once they complete the training. The script to the didactic video and the Qualtrics survey are attached.

The training is based on communication theory that suggest that in clinical communication, participants exchange both informational and relational messages,[35] and the web-based training will include training in how to provide both. Skill-building in ***informational communication*** involves guidelines for discussing information patients need to make an informed decision about participating in a trial based on the International Ethical Guidelines for Biomedical Research Involving Human Subjects prepared by the Council for International Organizations of Medical Sciences (CIOMS) and the World Health Organization (WHO) (http://www.cioms.ch/frame_guidelines).[58] Skill-building in ***relational communication*** involves explanations and illustrations of communication strategies such as using organizing statements, eliciting questions and concerns (e.g., "Ask-Tell-Ask"), using lay language, assessing understanding by using the "teach-back" method, acknowledging and responding directly and empathically to questions and concerns, and using shared-decision making principles.[58-63] To increase the likelihood the training has long-term effects on physician communication, physician participants will have the opportunity (optional) to follow up the training by individual consulting with Dr. Eggly.

The **attitude/awareness component** will take place after physicians complete the communication component, and is designed to increase the likelihood that physicians will discuss and offer trials to their patients. This component is also intended as a booster to the communication training module. This component consists of a reminder card to be provided to physicians each time one of their participating patients is found to be potentially eligible for a clinical trial, based on screening by the research staff. The reminder card includes the

patient's name, the trials for which he is potentially eligible, a yes/no question eliciting the physician's decision about discussing and offering the patient the trial(s), and information about effective communication about clinical trials. The reminder card will be provided by secure email and/or in person within a few days of the patient's clinic visit. Research staff who give the reminder card in person to the physician will be very careful to ensure privacy and confidentiality because it contains sensitive information, including the patient's name. The reminder card is attached.

Observational Measures. Trained raters will observe and rate video recorded visits. These individuals will have completed all requirements of the IRB (e.g., CITI training, added as key personnel if required). We will follow procedures used in our prior studies to train raters and ensure acceptable inter-rater reliability. Raters will determine whether a trial was discussed and/or offered and assess the quality of trial-related communication, following procedures in our prior research;[64] physician patient-centeredness,[47] and patient active participation in the interaction. [47]

Process Evaluations. Treatment fidelity and participant satisfaction will be assessed using audio and video recordings of the intervention procedures to monitor and assess these processes.

STATISTICAL ANALYSES

Qualitative Analyses of Follow-up Interviews. Audio-recordings/transcripts of follow-up interviews will be analyzed using directed content analysis methods. Directed content analysis is useful when researchers have specific categories in mind based on a priori or existing theory.[65] Using an iterative process, a team of coders, trained and supervised by Dr. Eggly, will listen to the recordings and then develop, refine, and apply a coding system for analyzing patients' perspectives on factors that affected their participation decisions. This aspect of the research is exploratory; findings from this analysis will not be directly integrated into the quantitative analyses and are not directly related to the aims.

Quantitative Data Preparation. Prior to any hypothesis testing we will examine multi-item measures to ensure that total scores and any factors derived from these items have acceptable internal consistency (e.g., Cronbach's α), produce meaningful total scores, and yield distributions appropriate for planned analyses. If there are departures from normal distributions or unequal variances across treatment conditions, we will conduct appropriate data transformations. Where appropriate, we will use confirmatory factor analysis to construct and evaluate measurement models of key constructs prior to conducting hypothesis tests involving these measures.

Models for Hypothesis Testing. Because patients are nested with physicians, multi-level models (MLM) will be used to test hypotheses for Aims 1 and 2. We will use multi-level structural equation models (MSEM) to examine hypotheses for Aim 3.

Power and Sample Size Estimates. A within-subject design is used to evaluate the physician intervention and a randomized control trial is used to evaluate the patient intervention. However, the outcomes of both interventions will be modeled at the patient level in a single model. We used the person-level multi-site/block trial design within Optimal Design to conduct power analyses because the unit of analysis is the patient-physician visit and data from these visits will likely be more similar within physicians than between physicians. The first power analysis is based 216 patients not lost to attrition, who should be eligible for clinical trials and thus randomized into the patient-level intervention. (See Participants and Recruitment—p. 7) We define the *primary outcome* of our study as patients' decisions to enroll in clinical trials, where a "success" is defined as a patient deciding to enroll. Our primary objective (Aim 1) is to examine the extent to which patient- and physician-level interventions affect physician and patient trial-related decisions, and thus we seek a sample size that gives us sufficient power to detect both the main effect of intervention and important interaction effects. We chose GEE power analysis for nested binomial outcomes with within-cluster treatments [66] as the best available model to estimate power for our primary objective; such estimates are lacking for HLM models. With 24 physicians and 9 patients per physician (i.e., 216 patients), a Type I error rate (α) of .05, and ICC of .05, and probability of success under the null hypotheses (pH_0) of .25, we are well powered to detect pH_1 of .35 (b = 0.48, odds-ratio = 1.61) with power > .99. Our secondary objective, (i.e., Aim 2) is to examine whether patient race influences the effectiveness of either patient- or physician-level interventions on our primary outcome, and we remain well

powered to detect 2-way and 3-way interactions. We will also examine effects of the interventions, and between-race differences in effects of the interventions on other binary or continuous outcomes (e.g., trial offers, patients' perceptions of patient-centeredness, perceived involvement in care, trust in physician, etc.). The power analysis described above holds for the binary outcomes. For the continuous outcomes, we used block person-randomized trial module in Optimal Design[67] to estimate power. Considering each of the 24 physicians as "blocks" and assuming about 9 patients per physician, a Type I error rate (α) of .05, between-physicians variability in effect size (σ_δ^2) of .05, 5% of variance in outcomes due to physicians and a medium effect size (d) of .50, power to find effects exceeds .90. Our final objective, (Aim 3) is to explore the extent to which patient-physician communication mediates the effects of the interventions on the outcomes. We will use Multi-level Structural Equation Modeling (MSEM) that control for patient-physician nesting to fit path analyses. The specific structure (i.e. direct and indirect paths of the models) will be guided by results from analyses conducted for our first and second aims. We therefore consider the MSEM exploratory in that we are the first researchers to examine these effects in this context. Thus, at this point we lack the specification of the model parameters needed to provide accurate estimates of power for this exploratory aim.

We will use Multi-Level Models (MLMs) that include separate variables identifying both interventions, as well as a variable indicating the interaction between the two phases. This model allows us to examine the main effect of each intervention, and multiplicative effects of having been exposed to both interventions. For purposes of clarity, we discuss hypotheses for each intervention separately, but as already noted, they will be tested in the same MLMs. We will model most outcomes (specifically, patients' perceptions of patient-centeredness, perceived involvement in care, trust in physician, and team perceptions; patient active participation, and physician patient centeredness, patient understanding of informed consent) as continuous variables. We will use binomial logistic models for binary outcomes (e.g., trial offer) and multinomial logistic regression for categorical outcomes (e.g., patients' self-reported participation decision - "yes", "no", "undecided"). We will also explore whether a single model best captures the meditational processes for both Black and White patients or separate models are needed.

Models for Aim 1: As we have described the objectives and outcomes above, here we generally describe the models that will be used to test support for our hypotheses. All outcomes, and coefficients for each of the intervention effects and interactions between them, will be modeled at the patient level of the model (level-1); that is, they will be nested within physicians (level-2). We will use one MLM for each outcome to test the three Aim 1 hypotheses. We use this particular approach to examine the interventions' effects because it is believed that the two interventions will not only work independently, but also interactively. Thus, we use a model that simultaneously controls for the main and interactive effects of both interventions as we examine their unique contributions.

Control variables: At the patient level of the model, we will control for factors such as decisional control preferences, relevant attitudes, health literacy, number of boosters received, disease severity, co-morbidities, whether there is an available clinical trial for the patient, and if so, characteristics of the trial (e.g., difficulty, complexity). At the physician level, we will control for relevant racial and professional attitudes, and decisional control preferences. Because the physician-focused phase involves a quasi-experimental design, we will also control factors that might threaten the internal validity of the intervention, such as time since study has begun, and number of previous interactions between patients and physicians.

Hypothesis 1a. Outcomes will be significantly improved in the patient intervention group, relative to the usual care group. To test hypothesis 1a, we will fit separate MLMs to examine continuous and binary outcomes assessed during or after each visit in which a trial was discussed. The focal independent variable will be the dummy-coded variable indicating whether the patient was in the usual care or intervention group. Support for hypothesis 1a will be indicated by a significant coefficient for this independent variable (i.e. intervention/usual care).

Hypothesis 1b. Outcomes will be significantly improved for patients after the physician intervention, as compared to outcomes before the physician intervention. The focal independent variable is the dummy-coded variable indicating whether or not the patient's physician has received the physician intervention at the time of the clinic visit. Note that this variable is a within-subject variable among the physicians; however, because we theorize that the patient-physician communication quality is central to offers and acceptance of clinical trials, this variable is introduced in the model at level-1 (patients). Support for hypothesis 1b will be indicated by a significant physician-intervention coefficient (i.e., pre/post physician intervention).

Hypothesis 1c. The combined effects of the two interventions will be multiplicative, rather than simply additive. The focal independent variable is the dummy coded variable for the product interaction term in the model. We expect the physician intervention to be more effective among patients who received the patient intervention; we expect a statistically significant positive coefficient for the interaction term.

Models for Aim 2: Hypothesis 2 (African American – White Differences) - Effects of the intervention will be significantly greater among African American than White men. We will test the hypothesis by introducing 2-way interactions between race and patient- and physician-focused interventions, and a 3-way race by patient-focused by physician-focused intervention variable, to the models. A significant coefficient for the 2-way interaction between race and the patient-focused intervention, will indicate whether the magnitude of the intervention is influenced by patients' race. The coefficient for the 3-way interaction will be used to assess whether the magnitude of the interactive effect of the patient- and physician-focused interventions depends on patients' race. We will probe the specific nature of these interactions with methods outlined by Preacher, et al.[169] We will also explore the moderating effects of other patient level variables (e.g., socio-demographics, race-related attitudes, etc.) in separate analyses.

Models for Aim 3: Hypothesis 3 (Mediating effects of patient-physician communication): **The quality of patient-physician communication will mediate the effect of the interventions on trial offers, and, in turn, on patient understanding of trials offered and decisions to participate.** We will use Multilevel Structural Equation Modeling (MSEM) to assess mediational/indirect effects. We will examine the specific relationships (paths) specified within the models as well as how well the overall model fits the data; we will use standard indices of the quality of fit (e.g. RMSEA, CFI). We will utilize observational measures of communication quality and relevant patient's perceptions of the interaction (see measures above) as measures of the mediating variables of the interest in the model. Separate models will be used for each outcome. Separate models will be conducted for separate outcomes.

References

1. Newman LA, Roff NK, Weinberg AD: Cancer clinical trials accrual: missed opportunities to address disparities and missed opportunities to improve outcomes for all. Annals of surgical oncology 15:1818-9, 2008
2. Nass SJ, Moses HL, Mendelsohn J: A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program Institute of Medicine, Committee on Cancer Clinical Trials and the NCI Cooperative Group Program, 2010
3. Murthy VH, Krumholz HM, Gross CP: Participation in cancer clinical trials: race-, sex-, and age-based disparities. JAMA : the journal of the American Medical Association 291:2720-6, 2004
4. Stewart JH, Bertoni AG, Staten JL, et al: Participation in surgical oncology clinical trials: gender-, race/ethnicity-, and age-based disparities. Annals of surgical oncology 14:3328-34, 2007
5. Cheng SK, Dietrich MS, Dilts DM: A sense of urgency: Evaluating the link between clinical trial development time and the accrual performance of cancer therapy evaluation program (NCI-CTEP) sponsored studies. Clinical cancer research : an official journal of the American Association for Cancer Research 16:5557-63, 2010
6. Korn EL, Freidlin B, Mooney M, et al: Accrual experience of National Cancer Institute Cooperative Group phase III trials activated from 2000 to 2007. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 28:5197-201, 2010
7. Penner LA, Manning M, Eggly S, et al: Prosocial Behavior in Cancer Research: Patient Participation in Cancer Clinical Trials, in Graziano B, Schroeder D (eds): Handbook of Prosocial Behavior. Oxford, UK, Oxford University Press, 2014, pp 653-669
8. 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
9. Fouad MN: Enrollment of minorities in clinical trials: did we overcome the barriers? Contemp Clin Trials 30:103-4, 2009
10. Banda DR, St. Germain D, McCaskill-Stevens W, et al: A critical review of the enrollment of black patients in cancer clinical trials. asco.org:153-157, 2012
11. Freedman LS, Simon R, Foulkes MA, et al: Inclusion of women and minorities in clinical trials and the NIH Revitalization Act of 1993--the perspective of NIH clinical trialists. Controlled clinical trials 16:277-85; discussion 286-9, 293-309, 1995
12. Carpenter WR, Tyree S, Wu Y, et al: A surveillance system for monitoring, public reporting, and improving minority access to cancer clinical trials. Clinical trials 9:426-35, 2012
13. Bolen S, Tilburt J, Baffi C, et al: Defining "success" in recruitment of underrepresented populations to cancer clinical trials: moving toward a more consistent approach. Cancer 106:1197-204, 2006
14. Siegel R, Ward E, Brawley O, et al: Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. CA: a cancer journal for clinicians 61:212-36, 2011
15. Rivers D, August EM, Sehovic I, et al: A systematic review of the factors influencing African Americans' participation in cancer clinical trials. Contemp Clin Trials, 2013
16. Svensson K, Ramirez OF, Peres F, et al: Socioeconomic determinants associated with willingness to participate in medical research among a diverse population. Contemp Clin Trials 33:1197-205, 2012
17. 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

18. Paskett ED, Reeves KW, McLaughlin JM, et al: Recruitment of minority and underserved populations in the United States: the Centers for Population Health and Health Disparities experience. Contemp Clin Trials 29:847-61, 2008
19. McCaskill-Stevens W, Pinto H, Marcus AC, et al: Recruiting minority cancer patients into cancer clinical trials: a pilot project involving the Eastern Cooperative Oncology Group and the National Medical Association. J Clin Oncol 17:1029-39, 1999
20. Diehl KM, Green EM, Weinberg A, et al: Features associated with successful recruitment of diverse patients onto cancer clinical trials: report from the American College of Surgeons Oncology Group. Ann Surg Oncol 18:3544-50, 2011
21. Du W, Gadgeel SM, Simon MS: Predictors of enrollment in lung cancer clinical trials. Cancer 106:420-5, 2006
22. Weiner BJ, Jacobs SR, Minasian LM, et al: Organizational designs for achieving high treatment trial enrollment: a fuzzy set analysis of the Community Clinical Oncology Program. Journal of Oncology Practice 8:287-291, 2012
23. Somkin CP, Altschuler A, Ackerson L, et al: Organizational barriers to physician participation in cancer clinical trials. Am J Manag Care 11:413-21, 2005
24. Langford AT, Resnicow K, Dimond EP, et al: Racial/ethnic differences in clinical trial enrollment, refusal rates, ineligibility, and reasons for decline among patients at sites in the National Cancer Institute's Community Cancer Centers Program. Cancer, 2013
25. Wujcik D, Wolff SN: Recruitment of African Americans to National Oncology Clinical Trials through a clinical trial shared resource. J Health Care Poor Underserved 21:38-50, 2010
26. Minasian LM, Carpenter WR, Weiner BJ, et al: Translating research into evidence-based practice: the National Cancer Institute Community Clinical Oncology Program. Cancer 116:4440-9, 2010
27. Clauser SB, Taplin SH, Foster MK, et al: Multilevel intervention research: lessons learned and pathways forward. J Natl Cancer Inst Monogr 2012:127-33, 2012
28. Taplin SH, Anhang Price R, Edwards HM, et al: Introduction: Understanding and influencing multilevel factors across the cancer care continuum. J Natl Cancer Inst Monogr 2012:2-10, 2012
29. Stange KC, Breslau ES, Dietrich AJ, et al: State-of-the-art and future directions in multilevel interventions across the cancer control continuum. J Natl Cancer Inst Monogr 2012:20-31, 2012
30. West SG, Duan N, Pequegnat W, et al: Alternatives to the randomized controlled trial. Am J Public Health 98:1359-66, 2008
31. Albrecht TL, Ruckdeschel JC, Ray FL, et al: A portable, unobtrusive device for video recording clinical interactions. Behav Res Methods Instrum Comp 37:165-169, 2005
32. Eggly S, Penner L, Albrecht TL, et al: Discussing bad news in the outpatient oncology clinic: Rethinking current communication guidelines. J Clin Oncol 24:716-9, 2006
33. Eggly S, Albrecht TL, Harper FW, et al: Oncologists' recommendations of clinical trial participation to patients. Patient Educ Couns 70:143-8, 2008
34. Eggly S, Harper FW, Penner LA, et al: Variation in question asking during cancer clinical interactions: A potential source of disparities in access to information. Patient Educ Couns 82:63-8, 2011
35. Albrecht TL, Eggly SS, Gleason ME, et al: Influence of clinical communication on patients' decision making on participation in clinical trials. J Clin Oncol 26:2666-73, 2008
36. Kanarek NF, Kanarek MS, Olatoye D, et al: Removing barriers to participation in clinical trials, a conceptual framework and retrospective chart review study. Trials 13:237, 2012
37. Hesse BW, Nelson DE, Kreps GL, et al: Trust and sources of health information: the impact of the Internet and its implications for health care providers: Findings from the first Health Information National Trends Survey. Arch Intern Med 165:2618-24, 2005

38. Albrecht TL, Penner LA, Cline RJ, et al: Studying the process of clinical communication: issues of context, concepts, and research directions. J Health Commun 14 Suppl 1:47-56, 2009
39. Epstein RM, Street R.L J: Patient-centered communication in cancer care: Promoting healing and reducing suffering. Bethesda, MD, National Cancer Institute, 2007
40. McCormack LA, Treiman K, Rupert D, et al: Measuring patient-centered communication in cancer care: a literature review and the development of a systematic approach. Social science & medicine 72:1085-95, 2011
41. Cooper LA, Roter DL, Johnson RL, et al: Patient-centered communication, ratings of care, and concordance of patient and physician race. Ann Intern Med 139:907-15, 2003
42. Johnson RL, Roter D, Powe NR, et al: Patient race/ethnicity and quality of patient-physician communication during medical visits. Am J Public Health 94:2084-90, 2004
43. Gordon HS, Street RL, Jr., Sharf BF, et al: Racial differences in trust and lung cancer patients' perceptions of physician communication. J Clin Oncol 24:904-9, 2006
44. Song L, Hamilton JB, Moore AD: Patient-healthcare provider communication: Perspectives of African American cancer patients. Health psychology : official journal of the Division of Health Psychology, American Psychological Association, 2011
45. Jean-Pierre P, Fiscella K, Griggs J, et al: Race/ethnicity-based concerns over understanding cancer diagnosis and treatment plan. Journal of the National Medical Association 102:184-9, 2010
46. Gordon HS, Street RL, Jr., Sharf BF, et al: Racial differences in doctors' information-giving and patients' participation. Cancer 107:1313-20, 2006
47. Street RL, Jr., Gordon H, Haidet P: Physicians' communication and perceptions of patients: is it how they look, how they talk, or is it just the doctor? Soc Sci Med 65:586-98, 2007
48. Hamel LM, Chapman R, Malloy M, et al: Critical Shortage of African American Medical Oncologists in the United States. J Clin Oncol 33:3697-3700, 2015
49. Crossing the Quality Chasm: A New Health System for the 21st Century. Washington, DC, Institute of Medicine Committee on Quality Health Care in America, 2001
50. Gaertner S, Dovidio JF: A common ingroup identity: A categorization-based approach for reducing intergroup bias, in Nelson T (ed): Handbook of Prejudice. Thousand Oaks, Sage, 2009, pp 489-505
51. Gaertner S, Dovidio JF, Houlette MA: Social categorization, in Dovidio JF, Hewstone M, Esses VM (eds): Handbook of Prejudice, Stereotyping, and Discrimination. Thousand Oaks, CA, Sage, 2010, pp 526-543
52. Eggly S, Tkatch R, Penner LA, et al: Development of a Question Prompt List as a Communication Intervention to Reduce Racial Disparities in Cancer Treatment. J Cancer Educ 28:282-289, 2013
53. Somkin CP, Altschuler A, Ackerson L, et al: Cardiology clinical trial participation in community-based healthcare systems: obstacles and opportunities. Contemp Clin Trials 29:646-53, 2008
54. Janz NK, Wren PA, Copeland LA, et al: Patient-physician concordance: preferences, perceptions, and factors influencing the breast cancer surgical decision. J Clin Oncol 22:3091-8, 2004
55. Krupat E, Rosenkranz SL, Yeager CM, et al: The practice orientations of physicians and patients: the effect of doctor-patient congruence on satisfaction. Patient Educ Couns 39:49-59, 2000
56. Sabin JA, Rivara FP, Greenwald AG: Physician implicit attitudes and stereotypes about race and quality of medical care. Med Care 46:678-85, 2008
57. van Ryn M, Burgess D, Malat J, et al: Physicians' perceptions of patients' social and behavioral characteristics and race disparities in treatment recommendations for men with coronary artery disease. Am J Public Health 96:351-7, 2006
58. Wendler D, Grady C: What should research participants understand to understand they are participants in research? Bioethics 22:203-8, 2008

59. Charles C, Gafni A, Whelan T: Shared decision-making in the medical encounter: what does it mean? (or it takes at least two to tango). Soc Sci Med 44:681-92, 1997

60. Kemp EC, Floyd MR, McCord-Duncan E, et al: Patients prefer the method of "tell back-collaborative inquiry" to assess understanding of medical information. J Am Board Fam Med 21:24-30, 2008

61. Kornburger C, Gibson C, Sadowski S, et al: Using "teach-back" to promote a safe transition from hospital to home: an evidence-based approach to improving the discharge process. J Pediatr Nurs 28:282-91, 2013

62. Bylund CL, Brown R, Gueguen JA, et al: The implementation and assessment of a comprehensive communication skills training curriculum for oncologists. Psychooncology 19:583-93, 2010

63. Back AL, Arnold RM, Baile WF, et al: Approaching difficult communication tasks in oncology. CA Cancer J Clin 55:164-77, 2005

64. Eggly S, Barton E, Winckles A, et al: A disparity of words: racial differences in oncologist-patient communication about clinical trials. Health Expect 18:1316-26, 2015

65. Hsieh HF, Shannon SE: Three approaches to qualitative content analysis. Qualitative Health Research 15:1277-1288, 2005

66. Pan W: Sample size and power calculations with correlated binary data. Controlled Clinical Trials 22:211-227, 2001

67. Raudenbush SW, Spybrook J, Congdon R, et al: Optimal Design Plus Empirical Evidence, (ed 3.01), HLM Software, 2011