## A. SPECIFIC AIMS

Low rates of minority participation in clinical trials and slow diffusion of clinical trials results to minority populations contribute to persistent disparities in health outcomes. Federally funded provider-based research networks (PBRNs) have shown that they can conduct clinical trials in community practice settings where most people get their care [1-4]; yet, PBRNs vary in their success in engaging minority patients in clinical trials, and the strategies that more successful ones use to achieve higher rates of minority participation in clinical trials are poorly understood. A promising strategy is to establish PBRNs that involve health care organizations that serve large minority populations. Whether such networks are more successful than others in achieving high minority participation rates in clinical trials is unknown. Implementing networks in these settings can be challenging due to resource issues, organizational culture, and community relationships. Finally, research indicates that PBRNs can speed the adoption of evidence-based clinical services in community practice [5-13]. However, it is not clear whether the positive dissemination effect of PBRNs that has been documented in other studies extends to the care that minority patients receive, whether they are part of a clinical trial or not. Without further knowledge, the potential of PBRNs to reduce health disparities cannot be fully realized or enhanced.

Our ***long-term goal*** is to understand how federally funded PBRNs can promote the dissemination and implementation of research findings into everyday clinical practice. Our ***objectives in this competing renewal application***, which represent the next steps in our research program, are to determine how a federally funded PBRN achieves high levels of minority participation in cancer clinical trials, and to examine the impact of a federally funded PBRN on the adoption of evidence-based cancer care for minority patients. Our ***central hypothesis***, building on the work we accomplished and the insights we developed in our original R01 study, is that federally funded PBRNs can reduce disparities in access to and receipt of state-of-the-art, evidence-based care by promoting community-based provider participation in research, which increases geographic access to clinical trials and facilitates research translation into clinical practice. We have formulated our hypothesis based on our research on the National Cancer Institute's (NCI) flagship PBRN, the Community Clinical Oncology Program (CCOP). The ***rationale*** for the proposed research is that, with the knowledge gained from the attainment of our research objectives, the NIH can develop and support PBRNs that not only engage minority populations in clinical trials, but also translate that research into better care for minority patients.

We will test our central hypothesis and, thereby, accomplish our objectives by pursuing three ***specific aims***:

**Aim 1: Identify the organizational factors associated with the effective implementation of a federally funded PBRN designed to increase minority participation in clinical trials.** We *propose,* based on our prior work, that: (1) our conceptual model of innovation implementation identifies the key organizational determinants of effective implementation, and (2) the implementation challenges that PBRN-affiliated health care organizations face, and the means they use to address them, differ as a function of the length of the organization's PBRN participation and the PBRN's focus on engaging minority patients in clinical trials.

**Aim 2: Evaluate the organizational strategies that a federally funded PBRN uses that lead consistently to high rates of minority participation in clinical trials.** We *propose* two working hypotheses: (1) the organizational strategies that lead consistently to high minority participation rates are complex, involving multiple tactics; and (2) there are multiple organizational strategies that lead consistently to high minority participation rates (i.e., there is no one best way, but rather multiple ways to achieve the same outcome).

**Aim 3: Examine the impact of a federally funded PBRN in promoting the adoption of evidence-based clinical services for minority patients.** We *propose*, again on the basis of our prior work, that PBRN-affiliated hospitals and physicians adopt evidence-based clinical services in treating minority patients more rapidly than non-affiliated hospitals and physicians adopt such practices.

In terms of ***expected outcomes***, Aim 1 will produce scientific knowledge of the organizational determinants of effective implementation of PBRNs in health care organizations that serve large minority populations. Aim 2 will identify a set of evidence-based organizational strategies that PBRN-affiliated health care organizations can use to achieve high levels of minority participation in clinical trials. Aim 3 will indicate whether federally funded PBRNs are a promising approach for translating clinical trials results into clinical care provided to minority patients. In addition to advancing implementation science, the proposed project is expected to produce generalizable knowledge that could have a ***positive impact*** on the health outcomes of minority populations.

## B. RESEARCH STRATEGY

**B1. Significance**. Clinical trials are considered the gold standard for evaluating the efficacy of interventions to treat, control, and prevent cancer. Socio-demographic diversity among clinical trials participants is essential to assess potential subgroup differences in intervention effects and ensure that clinical trials benefits and burdens are equitably shared. Yet, overall rates of racial/ethnic minority participation in cancer clinical trials are low and significant disparities in participation exist [14-15]. Barriers to minority participation include limited geographic access, lack of provider awareness, unfavorable provider attitudes, and patient mistrust [16-17]. Although barriers to minority participation have been extensively studied, there are few proven methods for overcoming them [18]. PBRNs and other forms of collaboration between academically based investigators and community based physicians are a promising approach for increasing access to clinical trials and reducing disparities in participation. Since 1983, one such network, the Community Clinical Oncology Program (CCOP) has enrolled one-third of all patients in NCI treatment trials and a majority of participants in NCI cancer prevention and cancer control trials [1]. The community physicians and hospitals that participate in the network (themselves also called CCOPs) have enrolled one-fifth of all minority patients on NCI clinical trials, with those serving large minority populations (i.e., minority-based CCOPs, or MBCCOPs) contributing a disproportionate share of minority enrollment [19]. Yet, CCOPs and MBCCOPs vary in their success in achieving high rates of minority enrollment and the strategies that successful ones use are poorly understood. Moreover, MBCCOPs encounter unique implementation challenges because they involve fiscally challenged safety-net hospitals, rely upon overburdened providers, serve large numbers of uninsured patients, and operate in communities facing significant resource constraints [19-20]. How MBCCOPs overcome these challenges is not known. Finally, significant racial/ethnic disparities exist in the receipt of evidence-based cancer therapies [e.g., 21, 22-28]. Community-based provider participation in NCI clinical trials through CCOP and other mechanisms appears to accelerate the uptake of evidence-based cancer therapies into clinical practice [5-12]. It is not clear, though, whether the positive dissemination effect of PBRNs applies equally to the care provided to minority patients.

Our research contribution is expected to be (1) detailed understanding of the organizational determinants of effective implementation of PBRNs designed to engage minority patients in clinical trials, (2) identification of organizational strategies that PBRN-affiliated health care organizations use that consistently lead to high levels of minority participation in research, and (3) evidence about the effectiveness of PBRNs in disseminating evidence-based cancer treatments to minority patients. *This contribution is <u>significant</u> for its potential to improve public health by reducing disparities in access to and receipt of state-of-the art, evidence-based cancer therapies*. This contribution could be broadly generalizable. A national survey conducted in 2006 found that half of 244 responding clinical research networks were similar to CCOP in terms of funding, design, and operation [29]. Thus, once the organizational strategies that lead to high levels of minority participation in clinical trials are identified, the NCI and other federal institutes and agencies (see Table 1) could disseminate these strategies to the PBRNs they fund and support, including those implemented through Clinical Translation Science Awards (CTSAs)[30]. The research will also provide the NCI and the NIH with timely information about what it takes to implement a federally funded PBRN in health care organizations that serve large minority populations and what to expect from federally funded PBRNs generally in accelerating the speed with which evidence-based clinical services reach minority patients. This information could be used to strengthen the disparities-reducing potential of existing federally funded PBRNs and guide federal investment in new PBRNs in cancer and other diseases.

**Table 1. Institutes and Agencies Supporting PBRNs**

National Institute on Drug Abuse
National Institute of Mental Health
Substance Abuse and Mental Health Services Administration
National Institute of Dental and Craniofacial Research
Agency for Healthcare Research and Quality
HIV/AIDS Bureau of Health Resources and Services Administration
Office of AIDS Research in the Office of the Director
National Institute of Allergy and Infectious Diseases
National Heart, Lung, and Blood Institute

**B2. Innovation**. While the disparities-reducing *potential* of PBRNs has been recognized for some time [19-20, 31-34], it has not been systematically examined. Research on PBRNs has described their development, structures, and operations [3, 29, 35-40]; discussed their benefits, barriers, and facilitators [2, 41-53]; and identified “lessons learned” from first-hand accounts [4, 54-55]. Our work in the current R01 study [6, 56-62], and that of others [5-13, 63], has examined the implementation, impact, sustainability, and business case of PBRNs, but it has not focused on the implementation of PBRNs in health care organizations that serve large minority populations, the organizational strategies that PBRNs use to achieve high levels of minority participation in clinical trials, or the impact of PBRNs in accelerating the translation of research results into

clinical care for minority patients. *The research proposed in this application is innovative, in our opinion, because it represents a new and substantive departure from the status quo, namely the limited scientific study of the disparities-reducing potential of PBRNs.* By opening a new line of inquiry, our proposed research is expected to advance scientific knowledge of effective strategies and implementation approaches for reducing disparities in clinical trials participation and receipt of evidence-based clinical services. Other innovative features of our proposed research include the use of a novel analytic method (fuzzy-set qualitative comparative analysis) to identify strategies that lead consistently to high levels of minority participation and the development of data sources that extend our inquiry beyond Surveillance Epidemiology and End Results (SEER) regions.

## B3. Approach

**B3.1. Progress Report**. This progress report covers the period August 15, 2007 (date of award) through February 28, 2012 (submission of competing renewal application). In our original R01 study, we pursued four aims. Our research team has been productive. We have published 14 articles [6, 21, 64-75], submitted 2 additional manuscripts [59, 76], and began work on 4 more in our no-cost-extension year.

Aim 1 was to identify the organizational factors associated with the implementation of a federally funded PBRN in community-based practice settings. *Through in-depth longitudinal case studies, we found that our organizational model of innovation implementation was useful for investigating the organizational factors influencing start-up and early implementation of community-based provider participation in research (CBPPR) in 3 newly funded CCOPs* [61]. Consistent with the model's predictions, weak implementation policies and practices contributed to a weak implementation climate which, in turn, led to inconsistent CBPPR over time and across physicians. In one CCOP, strong innovation-values fit compensated for (i.e., moderated the effect of) weak implementation climate [61]. Through our research, we developed a theory of organizational readiness for change [73] and clarified the meaning and measurement of implementation climate [74]. In the proposed project, we turn our attention to the distinctive challenges of implementing CBPPR in health care organizations that serve large minority populations. We expect the conceptual model we developed and tested in our original R01 study will again prove useful, but we also anticipate refining and expanding it based on the knowledge we gain about the organizational factors that influence CBPPR implementation in *young and mature MBCCOPs*.

Aim 2 was to examine the impact of a federally funded PBRN in promoting the use of evidence-based clinical services in community-based practice settings. Through longitudinal analysis of SEER-Medicare data, we found that *CCOP-affiliated hospitals and physicians more rapidly adopted evidence-based cancer therapies than did non-CCOP-affiliated hospitals and physicians.* Specifically, we observed that hospitals affiliated with NCI's clinical cooperative groups, a cohort that includes CCOP-affiliated hospitals, more rapidly adopted sentinel lymph node biopsy than did hospitals with no such affiliation [6]. We also observed that Stage III colon cancer patients seen by CCOP providers were more likely to receive the innovative therapy, oxaliplatin, and guideline-concordant care than were similar patients receiving care from other community providers [63]. We are currently analyzing the CCOP dissemination effect for intensity-modulated radiation therapy versus conventional radiation therapy for localized prostate cancer and bevacizumab for metastatic lung cancer. Our investigations to date indicate that CBPPR through CCOP and other mechanisms accelerates the translation of research results into clinical practice. What remains unclear, however, is whether CBPPR through CCOP and other mechanisms reduces disparities in the receipt of evidence-based cancer therapies. In theory, it should, but our preliminary studies (see *Section B3.8*) suggest the answer is not so simple and that more investigation is needed to determine whether PBRNs like CCOP can play an important role addressing health disparities.

Aim 3 was to assess the organizational, network, and environmental factors associated with the sustainability of a federally funded PBRN in community-based practice settings. With approval from our Project Officer, we eliminated the aim from the grant and pursued it through a contract. We report our progress here because it demonstrates our capability to carry out Aim 2 of the proposed project. *Using fuzzy-set qualitative comparative analysis [77-79], we identified two organizational strategies that consistently led to high treatment trial enrollment among CCOPs in 2010* [80]. Having a large treatment trial menu was necessary to achieve high levels of treatment trial enrollment, but it was not sufficient unless combined with large cancer patient volume or many participating sites. In the proposed project, we plan extend our prior work by identifying organizational strategies that CCOPs and MBCCOPs use to achieve high levels of minority enrollment in clinical trials.

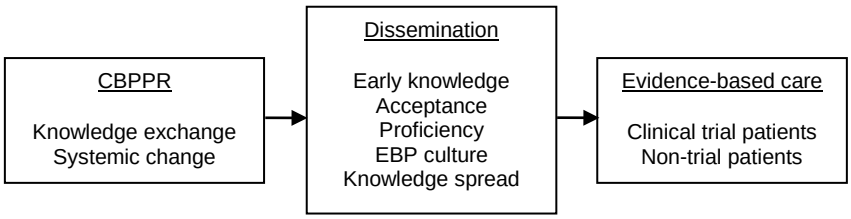
Aim 4 was to develop a model and produce practical tools for community-based provider organizations to evaluate the business case for participating in a federally funded PBRN. With approval from our Project Officer,

we eliminated Aim 4 in order to absorb a 22% budget cut. In Year 2, we conducted a small pilot study and in Year 3 we received an administrative supplement to pursue the work we originally proposed. We identified the motives and benefits, challenges and facilitators, and business case considerations of CCOP participation [58-60]. We also developed a method and tool for evaluating the business case [70].

**B3.2. Logic Model for Dissemination through Provider-Based Research Networks**

PBRNs are a promising model for disseminating evidence-based clinical services because they involve knowledge exchange and systemic change (see Figure 1). Knowledge exchange occurs through CBPPR. Through CBPPR, academic researchers learn about clinical issues facing community providers, obtain provider input on study feasibility, and gain insight from providers' practice-based knowledge [1]. Community providers learn about trial results sooner, accept trial results more readily (since the trials involve their own patients), and gain proficiency with new clinical services being tested [1, 19, 61]. To engage in CBPPR, community providers make systemic changes in organizational structure, staffing, workflows, and policies. These changes create a research infrastructure and promote a culture of evidence-based practice [1, 19]. Knowledge spreads when providers engaged in CBPPR interact with other providers in multidisciplinary clinics, tumor board meetings, and other venues where treatment planning and consultation occur [61]. These mechanisms, together, promote the adoption of evidence-based care for both clinical trial patients and non-trial patients [5-7, 11-12, 63].

**Figure 1. PBRN Logic Model**

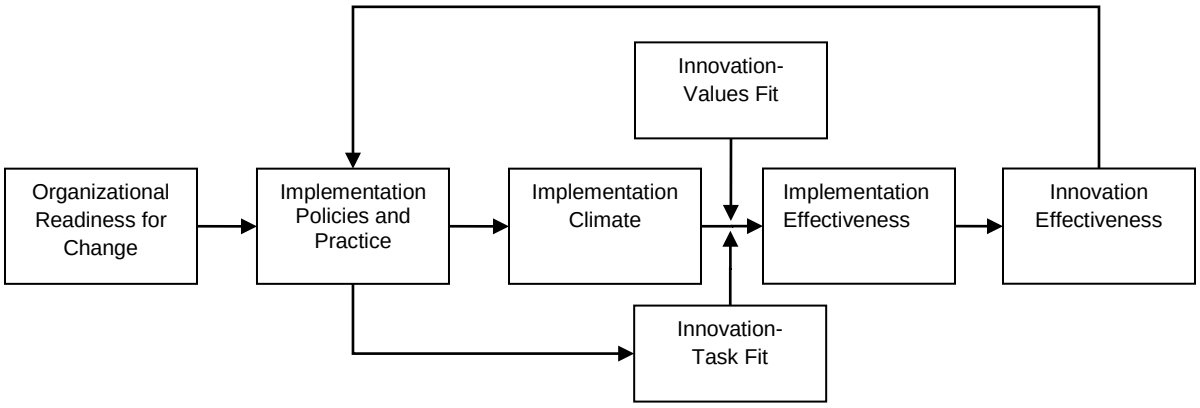



**B3.3. Conceptual Model**. Our proposed study draws on an organizational model of innovation implementation that we have tested and refined in prior work, including the original R01 [73, 81-83]. An *innovation* is a technology or practice that an organization uses for the first time, regardless of whether others have used it [84-86]. *Implementation* refers to the courses of action through which an innovation is put to use [84, 86]. For CCOP, MBCCOP, and other PBRNs, the innovation is CBPPR. CBPPR is a complex innovation for community-based providers because its implementation requires systemic changes in structure, staffing, workflows, and policies. CBPPR is a dynamic innovation because the clinical services tested through CCOP, MBCCOP, and other PBRNs change over time and pose ever-changing implementation challenges [87].

Since our conceptual model is described extensively elsewhere [73, 81-83], we summarize it here (see Figure 2 next page). The effective implementation of an innovation (CBPPR) is a function of the organization's readiness for change, the policies and practices that it puts into place to support implementation, the climate for implementation these policies and practices produce, the extent to which intended innovation users (e.g., physicians) perceive that innovation use fosters the fulfillment of their values, and the extent to which the innovation fits local task requirements (e.g., trial feasibility). The benefits of an innovation (e.g., rapid adoption of evidence-based cancer therapies) depend on effective implementation (i.e., consistent, high-quality CBPPR). In this study, implementation effectiveness is operationally defined as enrollment of new patients into clinical trials (accrual). The NCI uses this outcome-based measure of CBPPR implementation in evaluating CCOP and MBCCOP performance, as do several published studies [87-93], because the NCI funds CCOPs and MBCCOPs to conduct clinical trials research in community-based practice settings.

**B3.4. Study Setting**. The CCOP has served as a model for other federally funded PBRNs, like the NIDA Clinical Trials Network [94] and the NIAID Community Program for Clinical Research on AIDS. Established in 1983, the CCOP is a three-way partnership between the NCI's Division of Cancer Prevention (NCI/DCP), selected cancer centers and clinical cooperative groups ("CCOP research bases") and community-based networks of hospitals and physicians ("CCOPs"). NCI/DCP provides direction and funding; CCOP research bases design clinical trials; and CCOP organizations assist with patient accruals, data collection, and dissemination of study findings. As of December 2010, 47 CCOPs operated in 28 states and included 400 hospitals and 3,250 physicians [1]. The minority-based CCOP ("MBCCOP") was initiated in 1990 to expand the NCI's clinical trials network to minority populations. MBCCOPs must serve a patient population that is at least 30 percent minority [19-20]. As of 2010, 16 MBCCOPs operated in 12 states and Puerto Rico and included 55 hospitals and 325 physicians. Table 2 further describes the 63 CCOPs and MBCCOPs.

**Figure 2. Conceptual Model of Organizational Factors Affecting CCOP Implementation**




CCOPs are led by a physician principal investigator who provides local program leadership. CCOP staff members include an associate physician principal investigator, a program coordinator, research nurses or clinical research associates, and regulatory specialists. These staff members coordinate the review and selection of new clinical trials protocols for CCOP participation, disseminate protocol updates to participating physicians, and collect and submit study data [1, 83, 95-96]. CCOP-affiliated physicians enroll or refer patients to clinical trials and typically include medical, surgical and radiation oncologists; general surgeons; urologists; gastroenterologists; and primary care physicians. Through membership in CCOP research bases, CCOP-affiliated physicians participate in the development of clinical trials by proposing study ideas, providing input on study design, and, sometimes, serving as principal or co-principal investigator for a trial [1, 83, 95-96].

**Table 2. Description of CCOPs (N = 47) and MBCCOPs (N = 16) in 2009-2010**

| CCOPS | Mean | STD | Low | High | MBCCOPs | Mean | STD | Low | High |
|---|---|---|---|---|---|---|---|---|---|
| # hospitals | 9 | 6 | 1 | 28 | # hospitals | 5 | 4 | 1 | 16 |
| # physicians | 46 | 38 | 9 | 209 | # physicians | 21 | 14 | 4 | 64 |
| # treatment trials | 35 | 17 | 3 | 79 | # treatment trials | 18 | 10 | 5 | 39 |
| # treatment accruals | 103 | 74 | 6 | 451 | # treatment accruals | 51 | 39 | 11 | 170 |
| # CP/C trials | 19 | 9 | 2 | 53 | # CP/C trials | 8 | 4 | 2 | 20 |
| # CP/C accruals | 104 | 103 | 6 | 553 | # CP/C accruals | 33 | 25 | 5 | 80 |

Source: 2009-2010 CCOP/MBCCOP grant progress reports and NCI's CCOP, MBCCOP, and Research Base Management System
Notes: # treatment trials = treatment trials open with at least one patient enrolled; # CP/C trials = cancer prevention and control trials open with at least one patient enrolled; accruals = patients enrolled in NCI clinical trial.

### B3.5. Aim 1: Identify the organizational factors associated with the effective implementation of a federally funded PBRN designed to increase minority participation in clinical trials.

***Introduction.*** We will test the *working hypothesis* that our conceptual model identifies key organizational determinants of effective implementation of a federally funded PBRN designed to increase minority participation in clinical trials. We will also test the *working hypothesis* that the implementation challenges that PBRN-affiliated health care organizations face, and the means they use to address them, differ as a function of the PBRN's focus on engaging minority patients in clinical trials (MBCCOP vs. CCOP) and the length of organizational participation in PBRNs (MBCCOP age). These hypotheses are informed by our original R01 [61] and by other studies [19, 95, 97]. Although we expect our conceptual model will identify the key organizational determinants of effective CBBPR implementation in MBCCOP, we anticipate refining and expanding the model based on study findings. For example, we expect that innovation-task fit and innovation-values fit will moderate the relationship of implementation climate on implementation effectiveness in MBCCOPs, as they did in CCOPs. However, we might find that, for MBCCOPs, external factors such as state budgets and politics play a more important role in determining implementation effectiveness than either innovation-task fit or innovation-values fit because MBCCOPs often involve safety-net hospitals dependent on public funding. With respect to MBCCOP age, our original R01 findings suggest that young MBCCOPs will focus on implementing policies and practices that promote shared decision-making (e.g., frequent meetings), relationship building (e.g., outreach), and capacity building (e.g., hiring and training). Organizational life-cycle theories [98-102] suggest that mature MBCCOPs will focus instead on implementing policies and practices that promote operational efficiency (e.g., standard operating procedures) and accountability (e.g., performance monitoring and feedback). Our *approach* to testing these hypotheses involves conducting in-depth, longitudinal case studies of 3 young and 3 mature

MBCCOPs and using the data we collected from 3 young CCOPs in the original R01 for comparison. The *rationale* for this aim is that successful completion of the proposed work will inform the NCI and the NIH about what it takes to implement PBRNs in hospitals and physician practices that serve large minority populations. In terms of *outcomes,* we expect to produce scientific knowledge that could guide efforts to expand opportunities for minority patients to participate in clinical trials in health care organization where they get their care.

***Justification & Feasibility***. Since it issued the Roadmap in 2003 [52], the NIH has promoted CBPPR through PBRNs, CTSAs, and other mechanisms. The Roadmap has spurred discussion of the potential benefits of CBPPR [44, 103-104], infrastructure and workforce training needs for CBPPR [105-106], common barriers to increasing CBPPR [44-45, 107], and strategies for overcoming those barriers [44-45]. Missing, however, is an empirical investigation of the organizational factors that facilitate or hinder the implementation of CBPPR in health care organizations that serve large minority populations. An early evaluation of the MBCCOP network (1990-1991) showed that MBCCOPs were effective at engaging minority patients in clinical trials [20]. However, the evaluation reported that MBCCOPs face significant implementation challenges arising from poor institutional resources, misaligned organizational culture, and troubled community relationships. A 2005 focus group of MBCCOP PIs reported that MBCCOPs had overcome some of these challenges (e.g., forming productive IRB relationships) while others had persisted (e.g., safety-net hospitals' fiscal health) [19]. While informative, neither the evaluation nor the focus group identified the organizational factors associated with the effective implementation of CBPPR through MBCCOPs. Such knowledge is critically important for developing and supporting PBRNs to reduce disparities in clinical trials participation. Our approach to producing such knowledge entails conducting longitudinal case studies of MBCCOPs at various stages of CBPPR implementation. Our research team has the expertise (see *Biographical Sketches* and *Budget Justification*), experience (see Section *B3.1. Progress Report*), and access (see *Letters of Support*) to carry out this study.

***Research Design***. We will use a multiple, holistic case study design with the MBCCOP as the unit of analysis [108]. Case study methods are well-suited for studying implementation, which tends to be fluid, non-linear, and context-sensitive [109-110]. In addition to permitting in-depth analysis of individual cases, case study methods offer analytic strategies for comparing patterns across cases [111-112]. Our prior work will inform the study design, data collection, and analysis procedures [83, 96, 113-114]. The explanatory power of cases derives from in-depth examination of causal mechanisms (how things happen), causal complexity (how multiple factors/variables *combine* to produce outcomes), and temporality (what proceeds what)[112].

The sample will consist of 3 MBCCOPs that received initial program funding between 2009 and 2011; 3 mature MBCCOPs matched to the young MBCCOPs on geographic location, organizational size (e.g., number of affiliated physicians), and hospital characteristics (e.g., public, safety net hospitals); and 3 young CCOPS that we studied in the original R01. See attached letters of support. Table 3 describes the sample.

**Table 3. Description of MBCCOPs (and CCOPs) Selected for Study, 2009- 2010**

| MBCCOP | Central Office Location | First Year Funded | Number of Enrolling Sites | Number of Enrolling Physicians | Number of Patients Enrolled | Percent Enrolled Minority |
|---|---|---|---|---|---|---|
| **Young MBCCOPs** | | | | | | |
| Boston Medical Center MBCCOP | MA | 2010 | 1 | 31 | 27 | 41% |
| Queens Cancer Center MBCCOP | NY | 2010 | 2 | 7 | 21 | 90% |
| UMD New Jersey MBCCOP | NJ | 2009 | 1 | 9 | 23 | 87% |
| **Mature MBCCOPs** | | | | | | |
| LSU Health Sciences Center | LA | 1994 | 10 | 37 | 93 | 38% |
| SUNY Downstate Medical Center MBCCOP | NY | 2007 | 4 | 10 | 49 | 94% |
| Stroger-Cook County Hospital MBCCOP | IL | 2002 | 1 | 14 | 135 | 81% |
| **Young CCOPs (data collected 2008-2011)** | | | | | | |
| Heartland Research Consortium CCOP | MO | 2005 | 5 | 10 | 146 | 7% |
| Beaumont CCOP | MI | 2002 | 3 | 64 | 185 | 11% |
| St Vincent Hospital Regional Cancer Center | WI | 2002 | 8 | 24 | 204 | 5% |

Source: 2009-2010 CCOP/MBCCOP grant progress reports and NCI's CCOP, MBCCOP, and Research Base Management System. Number of patients enrolled includes patients enrolled in NCI cancer treatment trials or NCI cancer prevention and control trials in 2009-2010. Matches cases: Boston and LSU; Queens and SUNY Downstate; and UMDNJ and Stroger-Cook County. Young CCOP data collected in original R01 study.

***Data Collection Strategy.*** In Year 1, a two-person research team will site visit each MBCCOP. In Years 2-4, site visits will occur "virtually" through telephone interviewing, a method we used successfully in the original R01. During site visits, the team will conduct 8-10 one-hour individual interviews with the MBCCOP Principal

Investigator, Associate Principal Investigator, Administrator, research nurses and clinical research associates (CRAs), MBCCOP physicians, and MBCCOP hospital leaders (N= 48-60 total per year). We will use a semi-structured interview guide to gather data on the constructs appearing in our conceptual model. We will model the interview guides on those we used in the original R01 to ensure comparability with the data we collected from the 3 young CCOPs in the earlier study. Interviews will be audio-taped and transcribed verbatim.

The research team will also obtain data from MBCCOP grant applications and annual progress reports. These documents describe MBCCOP governance structure, research staffing, communication procedures, education and training activities, research base relationships, and financial and in-kind contributions from participating providers. We will request these documents from the sites directly, as we did the original R01. We will obtain accrual data for all 9 cases from their first year of NCI funding onwards from the NCI's CCOP, MBCCOP, and Research Base Management System. The System supplies accrual data for each CCOP and MBCCOP, sorted by clinical trial, CCOP research base, physician, and patient race/ethnicity.

***Data Analysis***. We will employ a pattern-matching logic to guide data analysis [108]. In pattern-matching, an observed pattern is compared to a predicted one (e.g., the pattern in the conceptual model). If the patterns match, the conceptual model is said to receive support. If they do not match, the investigator reformulates the conceptual model by developing and investigating alternative hypotheses.

Analysis will proceed in three phases. First, we will use qualitative data analysis software to code the study data. The coding manual that we developed in the original R01 will provide a starting list of codes, which we will supplement with emergent codes as analysis proceeds. After training and calibration, two research team members will independently code each transcript, compare their coding, and reconcile coding discrepancies.

Second, we will conduct a within-case analysis. For each case, we will generate reports of all text segments for each construct's code. We will assess each construct's "salience" by counting the text segments assigned to the construct's code. We will assess each construct's "valence" by counting the positively and negatively valenced text segments for the construct's code. Team members will discuss discrepancies in the assignment of valence to text segments until they reach agreement. They will discuss giving greater weight to text segments that seem particularly revealing about a construct's "salience" and "valence" in a given case. Decisions to differentially weight text segments must be justified to the PI. With input from NCI/DCP program officials, we will rate each case as high, medium, or low in implementation effectiveness based on 5-year accrual level or accrual trend. We will assess support for conceptual-model hypothesis as follows [112, 115]. We will begin by examining the pattern of covariance among constructs using combinatorial logic. Cases that exhibit positive implementation climate and positive innovation-values fit and positive innovation-task fit should exhibit high implementation effectiveness. Cases that exhibit positive values for two of these factors should exhibit medium implementation effectiveness. Cases that exhibit positive values for one or none of these factors should exhibit low implementation effectiveness. We will use a similar combinatorial logic to assess the relationship between implementation policies and practices and implementation climate. Next, we will examine the interview and documentary data for indicators of temporal ordering and causal attribution (e.g., participants' accounts and progress reports attribute a strong implementation climate to the use of specific implementation policies and practices). Discrepancies between the expected pattern (conceptual model) and the observed pattern (cases) will be explored in the data and the literature, resulting perhaps in a revised conceptual model.

Third, we will conduct a between-case analysis using Yin's replication logic [111]. The 9 cases will be arrayed into a 2 x 2 table with age (young/mature) crossed by type (MBCCOP/CCOP), with the mature-CCOP cell empty. Literal replication occurs when occupants of the same cell exhibit similar patterns from the within-case analysis for theoretically predictable reasons (i.e., they are similar in age and type). Theoretical replication occurs when occupants of different cells exhibit different patterns from the within-case analysis for theoretically predictable reasons (e.g., they differ by age or type). We will create case-ordered effects matrices to support the application of replication logic [112]. Case-ordered effects matrices are useful for ascertaining whether a cause is associated with an expected pattern of diverse effects across cases. To illustrate, we will create a matrix to examine whether young MBCCOPs exhibit a different *pattern* of implementation policies and practices than mature MBCCOPs, as predicted by organizational lifecycle theories (see *Aim 1 Introduction*).

***Expected Outcomes***. Aim 1 will generate scientific knowledge of the organizational determinants of effective implementation of CBPPR in health care organizations that serve large minority populations. The NCI and NIH could use this knowledge to expand opportunities for minority patients to participate in clinical trials by

developing and supporting cancer- and other disease-focused PBRNs in health care organizations where many minority patients get their care (see Table 1 for list of federal institutes and agencies developing and supporting PBRNs). Aim 1 will also contribute to implementation science by refining and expanding the organizational model of innovation implementation that we tested in our original R01.

***Potential Problems & Alternative Strategies***. We do not anticipate any difficulty recruiting MBCCOPs to participate in this study (see *Letters of Support*). In the unlikely event that we do, we would select a suitable replacement. NCI/DCP continues to receive applications for the MBCCOP program. We could replace a young MBCCOP with a newly funded MBCCOP at any time during the study and use the partial data collected from both MBCCOPs to achieve Aim 1 objectives. Similarly, we could replace a mature MBCCOP at any point and use the partial data collected from both MBCCOPs to achieve the Aim 1 objectives. While the match might not be as close with replacement MBCCOPs, we would alter our data collection tools and processes to explore and account for unmatched differences in geographic location, organizational size, and hospital characteristics. Case study research methods offer a level of flexibility in research design that quantitative research methods do not [112]. We would take advantage of this flexibility if we were to encounter difficulties in study retention.

**B3.6. Aim 2: Evaluate the organizational strategies that a federally funded PBRN uses that lead consistently to high rates of minority participation in clinical trials.**

***Introduction.*** We will test the *working hypothesis* that the organizational strategies that lead consistently to high minority participation rates are complex, involving multiple tactics. We will also test the *working hypothesis* that there are multiple organizational strategies that lead consistently to high minority participation. Our *approach* for testing these hypotheses involves a novel analytic method—fuzzy-set qualitative comparative analysis—coupled with conventional regression procedures. The *rationale* for this aim, based on our original R01 and discussions with NCI/DCP program officials, is CCOP and MBCCOP leaders want to increase minority participation, and expend considerable effort trying to do so, but they do not know which methods work. Knowledge of what strategies work is essential for reducing disparities in clinical trials participation. In terms of *outcomes,* we expect to produce a set of evidence-based organizational strategies that PBRN-affiliated health care organizations can use to achieve high levels of minority participation in clinical trials.

***Justification & Feasibility***. After two decades of research, we know a great deal about the barriers to minority participation in clinical trials [16-17]. We know far less about the effectiveness of strategies to overcome these barriers. In their systematic review, Lai and his colleagues [18] found only one randomized controlled trial that tested the efficacy of recruitment strategies to increase minority enrollment in a cancer treatment trial. The results were disappointing [116]. Patient navigation and clinical trial shared resources appear to be promising approaches [117-118], but require more rigorous evaluation. Observational study of the strategies that CCOPs and MBCCOPs use that lead consistently to high levels of minority enrollment in clinical trials could provide practical guidance to federal efforts to increase minority participation rates and stimulate further scientific inquiry. Our team has the necessary expertise and experience using fuzzy-set qualitative comparative analysis to carry out this investigation (see *B3.1 Progress Report* and *Budget Justification*).

***Research Design***. We will use a cross-sectional study design with the CCOP and MBCCOP as the unit of analysis. We will survey all CCOPs and MBCCOPs (N = 63). Table 2 above describes the sample (see *Section B3.3. Study Setting*). Table 4 describes the range in CCOP and MBCCOP minority enrollment in 2010.

**Table 4. Minority Enrollment in NCI Clinical Trials for CCOPs (N = 47) and MBCCOPs (N = 16) in 2009-2010**

| CCOPS | Mean | STD | Low | High | MBCCOPs | Mean | STD | Low | High |
|---|---|---|---|---|---|---|---|---|---|
| White | 176 | 143 | 12 | 719 | White | 31 | 26 | 0 | 101 |
| Black | 16 | 22 | 0 | 143 | Black | 21 | 20 | 0 | 77 |
| Hispanic | 6 | 9 | 0 | 49 | Hispanic | 19 | 32 | 0 | 131 |
| Other* | 9 | 15 | 0 | 83 | Other* | 13 | 41 | 0 | 192 |

Source: 2009-2010 CCOP/MBCCOP grant progress reports and NCI's CCOP, MBCCOP, and Research Base Management System. Number of patients enrolled includes patients enrolled in NCI cancer treatment trials or NCI cancer prevention and control trials in 2009-2010.
* In this table, "Other" includes American Indian or Alaskan Native, Asian, Native Hawaiian or Pacific Islander, more than one race, unknown or other

***Data Collection Strategy.*** The research team will obtain data from the NCI's CCOP, MBCCOP, and CCOP Research Base System on minority enrollment in NCI clinical trials and number of NCI clinical trials open for patient enrollment. The team will obtain data from the NCI's State Cancer Profiles website on the number of incident minority cancer cases in the service areas of each CCOP and MBCCOP (i.e., service areas will be defined as counties in which a CCOP or MBCCOP has a clinic, hospital, or other site in which patients could

enroll in NCI clinical trials; adjacent counties may be included in some analyses). Consistent with the approach used to generate national estimates of clinical trials participation rates [14-15], we will calculate the minority enrollment rate for each CCOP or MBCOCP as the number of minority trial enrollees divided by the number of incident minority cancer cases in the CCOP's or MBCCOP's service area. Although there is a three-year lag in the county level cancer prevalence provided by State Cancer Profile, we can obtain more timely estimates, by applying a multilevel regression model [119-120] using Behavioral Risk Factor Surveillance Survey to project current-year cancer prevalence at the county level.

The research team will obtain data on the organizational tactics that CCOPs and MBCCOPs use to recruit and enroll minority patients into clinical trials by surveying CCOP and MBCCOP Administrators at the annual CCOP Research Meeting. The team will mail surveys to non-attending Administrators and follow up with attending, but non-responding Administrators. We used this approach in the original R01 study and attained a 100% Administrator response rate (see *Section B.3.1. Progress Report*). Data on organizational tactics will include number of affiliated physicians, number of sites where clinical trial enrollment occurs, number of research staff, community outreach and education activities, use of patient navigation, translation of research materials, physician outreach and education activities, monitoring and reporting of physician enrollment of minority patients, and other tactics identified from review of the literature, consultation with NCI/DCP program officials, and informal focus groups with CCOP and MBCCOP PIs and Administrators.

***Data Analysis***. We will use fuzzy-set qualitative comparative analysis (fsQCA) to identify organizational strategies that CCOPs and MBCCOPs use that lead consistently to high minority enrollment in NCI clinical trials. Developed 12 years ago [78], fsQCA originated in sociology [121-135], spread to organization and management science [136-142], and only recently reached health services and health promotion research [143-147]. FsQCA uses a set-theoretic approach to examine how causes and conditions combine in different ways to produce outcomes of interest [78-79]. FsQCA is well-suited for examining causal complexity and causal heterogeneity (equifinality) in small- to medium-size studies [136, 138].

Analysis will proceed in six steps. First, we will transform study measures into fuzzy-set membership scores. Use of expert judgment (substantive knowledge) is the preferred method of transforming un-calibrated measures into calibrated scores that indicate fuzzy-set membership [78-79]. Hence, we will ask NCI/DCP program officials to use their substantive knowledge to specify 3 values for each measure: full membership in the set of interest (e.g., "definitely high minority enrollment"), full non-membership in the set of interest ("definitely not high minority enrollment"), and a cross-over point that reflects maximum ambiguity about set membership ("neither high minority enrollment nor not-high minority enrollment"). To illustrate, in our earlier work [80], NCI/DCP program officials specified the following values for "high levels of treatment trial enrollment": 100 patients for full membership in the high-enrollment set, 70 patients for cross-over point, and 50 patients for full non-membership in the high-enrollment set. FsQCA transforms measures into fuzzy-set membership scores by using the cross-over point as an anchor from which deviation scores are calculated, taking the values of full membership and full non-membership as the upper and lower bounds. Fuzzy-set membership scores range from 1.0 (full membership) to 0.0 (full non-membership). We will conduct sensitivity tests to account for potential uncertainty in NCI/DCP program officials' substantive knowledge [148].

Second, we will construct a data matrix (known as a truth table) with $2^k$ rows, where $k$ is the number of organizational tactics included in the analysis. Each row indicates a specific combination of organizational tactics (hereafter a combination is called an "organizational strategy"), with the full table listing all logically possible organizational strategies. We will then sort CCOPs and MBCCOPs (hereafter referred to as "cases") into the rows of the truth table based on their fuzzy-set membership scores. Specifically, we will assign cases to the row for which they have a fuzzy-set membership score greater than .5 [79]. Such a score signals that the case is more in than out of the set using that organizational strategy. Mathematically, a case can have only one membership score greater than .5 in all of the logically possible combinations in the truth table [79].

Third, we will reduce the number of rows in the truth table based on two criteria: (1) the minimum number of cases that use an organizational strategy, and (2) the minimum consistency of an organizational strategy [79]. We will set the minimum number of cases that use a strategy equal to 1 so that our analysis is maximally inclusive. Logically possible strategies with no assigned cases will be subjected to counterfactual analysis (see below). In fsQCA, *consistency* refers to the degree to which cases exhibiting a specific combination of causal conditions also exhibit the outcome of interest [78]. Consistency is measured as $(X_i \leq Y_i) = \sum[\min(X_i, Y_i]/ \sum(X_i)$,

where *X* is the fuzzy-set membership score in a set for an organizational strategy and *Y* is the fuzzy-set membership score in the set for high minority enrollment. Consistency indicates how closely a perfect subset relation is approximated. By establishing a benchmark for consistency, probabilistic tests can be used to assess whether consistency is greater than could be expected by chance. We will set the benchmark for consistency at => 0.80, which is higher than the minimum recommended benchmark of 0.75 [79].

Fourth, we will use an algorithm based in Boolean algebra (the Quine-McCluskey algorithm) to eliminate logically redundant organizational strategies. To illustrate, suppose that cases that exhibit high minority enrollment have many open clinical trials, see many minority cancer patients, and have many enrolling sites. Suppose that other cases that exhibit high minority enrollment have many open clinical trials, see many minority cancer patients, and do *not* have many enrolling sites. These two organizational strategies can be logically reduced to one—having many open clinical trials and seeing many minority cancer patients—because the evidence indicates that cases exhibit the same outcome whether they have many enrolling sites or not.

Fifth, we will examine the empirical relevance of the organizational strategies that consistently lead to high minority enrollment by inspecting their coverage of the outcome. *Coverage* refers to the degree of overlap among two or more sets [78-79]. Coverage is measured as $(X_i \leq Y_i) = \sum[\min(X_i, Y_i)]/ \sum(Y_i)$, where X is the fuzzy-set membership score in a set representing an organizational strategy and Y is the fuzzy-set membership score in the set representing high minority enrollment. As with the partitioning of explained variance in regression, coverage can be partitioned into shared coverage and unique coverage in fsQCA.

Finally, we will regress the fuzzy-set membership scores in the outcome (high minority enrollment) on the fuzzy-set membership scores in the organizational strategies identified by fsQCA and theoretically relevant control variables (e.g., CCOP/MBCCOP maturity). FsQCA is more versatile than regression in modeling causal complexity, but has limited capabilities to control for potentially spurious relationships [140]. Supplementing fsQCA with regression will allow us to assess the robustness of our results against potential confounders.

***Expected Outcomes***. Aim 2 is expected to produce a set of evidence-based organizational strategies that PBRN-affiliated health care organizations can use to achieve high levels of minority enrollment in clinical trials. Our work will contribute to the limited scientific knowledge that exists about effective strategies for increasing minority clinical trials participation. The strategies that we identify should be generic enough to be 'translatable" other PBRNs (e.g., the combination of several sites where clinical trial enrollment occurs, extensive community outreach and educational activities, and use of patient navigators). The NCI and the NIH could use our results to enhance PBRNs' capabilities to reduce racial disparities in clinical trials participation, thereby accelerating the testing of the effectiveness of clinical services in minority populations.

***Potential Problems & Alternative Strategies***. Based on our prior work using fsQCA, we do not anticipate any difficulty identifying organizational strategies that *consistently* lead to high minority enrollment in clinical trials. If we were to obtain a null result, we would hold follow-up focus groups with the PIs and Administrators of CCOPs and MBCCOPs that exhibited high minority enrollment. We would use the focus group sessions to identify organizational strategies (or effect-modifying contextual conditions) that we might have missed in our preparatory work for this aim. We would then collect additional data the following year and re-run our analysis.

**B3.7. Aim 3: Examine the impact of a federally funded PBRN in promoting the adoption of evidence-based clinical services for minority patients.**

***Introduction.*** We will test the *working hypothesis* that PBRN-affiliated hospitals and physicians adopt evidence-based clinical services in treating minority patients more rapidly than non-affiliated hospitals and physicians do. The logical basis for this hypothesis is described above (see *B3.2 Conceptual Model*). The *rationale* for this aim is that completion of the proposed work will provide NCI and the NIH with missing, fundamental knowledge about the effectiveness of federally funded PBRNs to reduce disparities in the receipt of evidence-based state-of-the-art cancer therapies.

***Justification & Feasibility***. Our research [6, 63], and that of others [5-13, 63], shows that federally funded PBRNs accelerate the speed with which evidence-based clinical services reach patients treated in community practice settings (see *Section B3.1 Progress Report*). While the positive dissemination effect of PBRNs should, in theory, apply equally to the care that minority patients receive, there is little evidence to support or refute this proposition. Further, our preliminary studies indicate a conundrum. On the one hand, we observed that racial

disparities in the receipt of sentinel lymph node biopsy persisted even among patients seen in hospitals affiliated with NCI's cooperative groups, a cohort that includes CCOP-affiliated hospitals [21]. On the other hand, in a study of Stage III colon cancer treatment, we found the innovative therapy, oxaliplatin, was adopted 28% faster among Black patients seen at CCOPs compared to those seen at non-CCOP providers, whereas it was only adopted 12% faster among White patients seen at CCOPs compared to those seen at non-CCOP providers [149]. This finding suggests the positive dissemination effect of PBRNs could disproportionately benefit African American patients, regardless of whether they participate in a clinical trial or not. We need larger sample sizes, however, to substantiate this possibility. Our *approach* involves studying a wider range of evidence-based cancer therapies and developing new data resources to extend scientific inquiry beyond SEER states and regions. Our team is experienced using SEER-Medicare data and linking state cancer registry and administrative claims data (See *Biographical Sketches,* and *Facilities & Other Resources*).

***Research Design***. We will use a two-group, longitudinal design to control for clustering of patients within providers. Depending on the specific analysis, either hospitals or physicians will be the primary clustering unit. In either case, there will be two provider cohorts: those affiliated with CCOP/MBCCOPs, and those not affiliated. The sample will consist of all providers in 13 states with SEER-funded cancer registries, and 5 states with National Program of Cancer Registries (NPCR)-funded registries. For the observation period (2000-2009), this permits an analysis of 37 CCOPs/MBCCOPs in 18 states encompassing 45% of the US population, and 50% of the US minority population. It includes 134 CCOP-affiliated hospitals and 570 physicians. Patient cohorts will be defined according to year of diagnosis, allowing race- and provider group-specific *longitudinal* analysis of populations' differential innovation adoption rates. We will use propensity score methods to control for potential selection bias and improve balance among provider and patient comparison groups.

***Data Sources.*** SEER-Medicare, the primary data source, is a population-based dataset linking SEER tumor registries to Medicare beneficiaries' health insurance claims. SEER includes information for each incident cancer case in the SEER region including, but not limited to, diagnosis (e.g., stage, grade, and select biomarkers), date of diagnosis, demographics, and type of initial cancer treatment. These data are linked to Medicare claims, which include procedure-level diagnostic and treatment information for inpatient hospital stays, outpatient care, physician services, and durable medical equipment for 95% of beneficiaries [150]. SEER-Medicare includes data on hospital characteristics. We will augment SEER-Medicare data by linking Medicare claims to cancer registry case data in from five non-SEER states: North Carolina, South Carolina, Ohio, Missouri, and Illinois. This will double the number of CCOPs/MBCCOPs and CCOP/MBCCOP-affiliated hospitals, double the number of minority cancer patients, and mitigate sample distribution challenges arising from the clustering of 25% of minorities into 3 tight geographic areas in SEER. SEER and NPCR registries use the same data capture and coding guidelines; merging these data will be relatively seamless. Our team has extensive experience linking registry and claims data to support studies of racial disparities, care patterns, and outcomes [6, 21, 63, 151-153]. We will work with NCI/DCP officials to identify unique physician identification numbers (UPINs) and hospital identification numbers of CCOP/MBCCOP-affiliated hospitals [63]. We will use data from the American Medical Association (AMA) Physician Masterfile and the Medicare Online Survey Certification and Reporting (OSCAR) database to further characterize hospitals and physicians in our models.

***Data Collection Strategy.*** We will obtain SEER-Medicare data from NCI SEER-Medicare Program, as we did in the original R01. We will obtain linked NPCR registry and Medicare data for the five non-SEER states by working with the CMS Research Data Assistance Center (ResDAC), as we did in other studies [154-156]. Briefly, the process entails NPCR registries identifying eligible cancer cases and sending "finder files" to the CMS Research Data Distribution Center (RDDC). The RDDC links the finder files to Medicare claims and sends the claims and a dataset crosswalk file to the research team. For the linked files, the NPCR registries send to the research team the remainder of the cancer registry data. See letters of support from the NCI SEER-Medicare Program and the NPCR registries included in the study.

***Measures.*** The main outcome is defined within the context of the first course of treatment following cancer diagnosis, and measured as whether the patient received the innovative, evidence-based cancer treatment of interest or not. The primary independent variables are CCOP/MBCCOP affiliation of providers on health care claims. (CCOP and MBCCOP affiliation will be measured separately, but for brevity we refer to them hereafter as "CCOP.") CCOP-affiliation will be measured in several ways to find optimal statistical fit, including a binary variable (any/no CCOP-affiliated claims), a continuous count of claims, and a proportion of claims. We used this approach in the original R01 study [157]. The dependent variable is the observed patient-level adoption of

evidence-based cancer care, defined as receipt of the treatment of interest within the appropriate treatment window. Patient race will be measured as Caucasian, African American, or all other races, as defined by Medicare and validated by SEER. Covariates will include patient-level factors (e.g., tumor characteristics, age, comorbidities, gender, education, income, and year of treatment initiation), organization-level factors (e.g., total hospital beds, total discharges, medical school affiliation, and presence of therapeutic radiology), physician-level factors (e.g., age, gender, specialty, board certification, and training cohort), and environment-level factors (e.g., urban/rural [MSA], population size, per capita income, provider density, and geographic region).

To enhance the generalizability of our study findings, we will examine the adoption of evidence-based cancer treatments in breast, prostate, colon, lung, and pancreatic cancer—five cancers which comprise over half of US cancer incidence and mortality for Caucasians and African Americans [158-159]. Each cancer is distinct in terms of patient demographics, survival, and prevention/detection technologies. For these cancers, we have identified several evidence-based treatments as candidates for study based on the strength of clinical evidence, the period of observation (2000-2009), and the availability of necessary data. We will examine different treatment modalities (e.g., medical, surgical, or radiation therapies) because their diffusion is likely to differ according to different factors. For example, surgical and radiation therapy innovations may be more likely to depend on local availability of harder-to-acquire skill sets or capital intensive technologies compared to novel chemotherapeutic agents [160]. The innovations listed in Table 5 are new in the last 20 years, have proven effective in clinical trials, received FDA approval, were reimbursed by Medicare, and thus are specifically identifiable in the data.

***Data Analysis***. We will measure the main outcome by defining $Y_{ij}$ to be 1 if the treatment was adopted for the *j*th patient in the *i*th provider (CCOP or non-CCOP affiliated), and 0 otherwise. Associated with $Y_{ij}$ will be a vector $x_{ij}$ of covariates for the patient ($x_{ij,patient}$), the provider ($x_{ij,provider}$), time trends ($x_{ij,time}$), and the environment ($x_{ij,environment}$). With two actors associated with treatment decisions (providers and patients), we will take two approaches with propensity score methods to ascertain the optimal model: (1) balancing patients by factors associated with both their seeking care from a CCOP (exposure) and their treatment selection (outcome); and (2) balancing providers by factors associated with both their practicing in a CCOP (exposure) and their treatment selection (outcome). After applying propensity score methods, we will model the probability of a treatment adoption, $pr(Y_{ij} = 1) = E[Y_{ij}] = \pi_{ij}$, as a function of the covariates $x_{ij}$ using logistic regression as follows:

$$\text{logit}(\pi_{ij}) = x_{ij,}{}^{T}{}_{provider}\alpha + x_{ij,}{}^{T}{}_{\text{patient}}\beta + x_{ij,}{}^{T}{}_{time}\gamma + x_{ij,}{}^{T}{}_{environment}\delta$$

| **Table 5. Evidence-Based Cancer Treatments** |
|---|
| Breast Cancer |
| Utilization of HER-2 Testing [161-162] |
| Trastuzumab (Herceptin) [161-162] |
| Colon/Rectal Cancer |
| Adjuvant chemo w/in 4 months |
| Oxaliplatin adjuvant therapy for Stage III colon cancer [163-164] |
| Irinotecan in multi-agent therapy for Stage IV colon cancer [163, 165] |
| RT w/in 6 mo. for Stage III rectal cancer [166-167] |
| Prostate Cancer |
| Hormone therapy vs. orchiectomy for Stage IV [27, 168-169] |
| RT + hormone therapy vs. RT alone for intermediate or high-risk local disease [168, 170] |
| Lung Cancer |
| RT + chemo for limited-stage small cell [171-172] |
| RT + chemo for Stage III non-small cell [173-175] |
| Pancreatic Cancer |
| Gencitibine [176] |

We will include race-by-CCOP-affiliation interaction terms to examine racial differences in adoption of evidence-based services between CCOP providers and their non-CCOP counterparts. Time covariates will be examined as six-month or one-year intervals, as well as linear, quadratic or higher-order polynomials as statistically appropriate. These functions of time represent the diffusion curves. To investigate whether time trends differ between CCOP-affiliated and non-affiliated providers, we will include interaction terms for CCOP participation and time. For the small group of patients who did not receive any hospital-based care, we will perform a separate analysis with only physician, patient, and time covariates. Patients within a hospital are correlated with each other. Generalized estimating equations (GEE) [177] will take the correlation into account for the logistic regression model. An exchangeable working correlation will be used with the sandwich variance estimator to provide protection from misspecification of the correlation structure. General software is available in SAS PROC GENMOD, but it tends to be slow for large clusters. The exchangeable working correlation can be fitted efficiently to large clusters using SAS/IML code developed by Investigator Bahjat Qaqish. Special-purpose software will be developed if generally available software proves impractical for this type of modeling.

***Power Analysis***. To assess the power we consider a regression model with race, CCOP participation, and the interaction effect between race and CCOP participation. The response is binary; hence, variance does not exceed 1/4. Using the data from our previous research on SEER-Medicare [62, 178], we found the standard

error of the interaction effect is at most 0.048. This gives 80% power with alpha=0.05 for detecting an interaction effect of 0.133 or more in the probability of evidence-based service adoption between race (i.e., white and African American) and the CCOP participation. This analysis is very conservative by assuming very small within-provider correlation (correlation =0.01). With higher within-provider correlation and the addition of NPCR states, statistical power will increase. With the addition of approximately 100 CCOPs providers from the additional states, and assuming each contributes 50 white and 5 African American patients, we will be able to detect an interaction effect of 0.093 or more with the standard error of 0.033 at 80% power.

***Expected Outcomes***. Aim 3 is expected to produce evidence about the effectiveness of federally funded PBRNs in disseminating evidence-based cancer treatments to minority patients. It is possible that factors motivating providers to affiliate with PBRNs would also motivate them to adopt evidence-based cancer care. However, preliminary studies suggest the relationship between PBRN affiliation and adoption of evidence-base cancer care for minorities is variable, and consequently not simply a function of differential predispositions (see *Aim 3, Justification & Feasibility*). Further, they suggest associations between PBRN affiliation and adoption of evidenced-based care should be empirically examined and not assumed to be fact. Propensity-score methods will help control for non-random assignment to PBRNs, strengthening this novel empirical examination of observed associations and their constituent elements (e.g., personal characteristics vs. CCOP influence).

***Potential Problems & Alternative Strategies***. We do not foresee difficulties acquiring the data for Aim 3 (see *Letters of Support*). It is possible that we might experience unanticipated delays in data acquisition. In the unlikely event that we do, we have scheduled all of Year 1 for data acquisition. We can begin Aim 3 data management and analysis in Year 2 and complete the proposed work on time (see *Project Management and Timetable*). We also do not anticipate any problems linking the data for Aim 3. SEER-Medicare and CMS (ResDAC/RDDC) use data linkage algorithms with strong sensitivity and specificity. Further, our algorithm for linking CCOP provider, SEER-Medicare, AMA Masterfile, and OSCAR proved robust in the original R01 study. If data linkage issues were to arise, we would work with SEER-Medicare and CMS to resolve these issues.

**B3.8. Project Management and Timetable**. Dr. Weiner (PI) will provide overall scientific leadership and manage the project with assistance from a full-time, experienced project manager (see *Budget Justification*). Planned work flow is described below (see Table 6). As in the original R01, the PI will chair monthly meetings in which all investigators (including MDs) attend in person or by phone to discuss administrative issues, receive updates, discuss methodological issues, review interim results, and plan scientific manuscripts. The close physical proximity of investigators' offices will facilitate interim communication and informal meetings.

**Table 6. Timetable**

| | Year 1 | | | | Year 2 | | | | Year 3 | | | | Year 4 | | | | Year 5 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |
| Aim 1 | | | | | | | | | | | | | | | | | | | | |
| Study development | ■ | | | | ■ | | | | ■ | | | | ■ | | | | | | | |
| Data collection | | ■ | | | | ■ | | | | ■ | | | | ■ | | | | | | |
| Data analysis | | | ■ | ■ | | | ■ | ■ | | | ■ | ■ | | | ■ | ■ | | | | |
| Dissemination activity | | | | | | | | | ■ | ■ | ■ | ■ | | | | | ■ | ■ | ■ | ■ |
| Aim 2 | | | | | | | | | | | | | | | | | | | | |
| Study development | | | | | ■ | ■ | | | | | | | | | | | | | | |
| Data collection | | | | | | | ■ | ■ | | | | | | | | | | | | |
| Data analysis | | | | | | | | | ■ | ■ | | | | | | | | | | |
| Dissemination activity | | | | | | | | | | | ■ | ■ | ■ | | | | | | | |
| Aim 3 | | | | | | | | | | | | | | | | | | | | |
| Study development | ■ | ■ | ■ | | | | | | | | | | | | | | | | | |
| Data collection | ■ | ■ | ■ | ■ | ■ | | | | | | | | | | | | | | | |
| Data analysis | | | | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | |
| Dissemination activity | | | | | | | | ■ | ■ | | | ■ | ■ | | | ■ | ■ | | | ■ |

**B3.9. Future Directions**. Upon completion of the proposed project, we anticipate transitioning the focus of our research program from *understanding* how federally funded PBRNs accelerate translation and reduce disparities to *enhancing* their capabilities to do so. Based on our work in the original R01 and the proposed project, we will be ready to develop and test strategies to (a) promote effective implementation of CBPPR, (b) speed adoption of evidence-based clinical services, and (c) increase minority participation in clinical trials.

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