Abstract

DESCRIPTION (provided by applicant): The NIH and other federal agencies see provider-based research networks (PBRNs) as a promising model for disseminating and implementing evidence-based clinical services in community-based practice settings. PBRNs are collaborative partnerships between community-based providers and academic institutions to conduct clinical research on an ongoing basis. As an indicator of its commitment to PBRNs, the NIH is investigating the feasibility of training 50,000 community-based health-care practitioners to participate in clinical research and integrate new research findings into routine health care delivery. Yet, reports indicate that PBRNs are challenging to implement and sustain. Further, the extent to which PBRNs actually promote the use of evidence-based clinical services in community-based practice settings remains largely unknown. This project will examine the implementation, impact, sustainability, and business case of the NCI's Community Clinical Oncology Program (CCOP), a federally funded national PBRN that the NIH sees as a model for PBRNs in other disease areas. Specifically, the project will (1) investigate the implementation of the CCOP in community-based practice settings through in-depth case studies of three newly funded CCOP organizations and a survey of all 50 CCOP organizations; (2) examine the impact of the CCOP on clinical practice through longitudinal analysis of adoption rates of evidence-based cancer therapies by CCOP- affiliated and non-CCOP-affiliated providers using SEER-Medicare data; (3) assess the factors affecting sustainability of the CCOP in community-based practice settings through a longitudinal analysis of all CCOP organizations active from 1991 through 2003; and (4) investigate the business case for CCOP participation by providers through analysis of financial and statistical data and in-depth case studies. The project will provide the NIH with much-needed information about what it takes to implement and sustain PBRNs and what it can expect from PBRNs as a model for disseminating and implementing evidence-based clinical services in community-based practice settings.

A. SPECIFIC AIMS

To close the gap between scientific discovery and program delivery, the National Institutes of Health (NIH) has embarked on a fundamental restructuring of the national clinical research enterprise [1]. As part of the Roadmap, the NIH seeks to develop a national system of provider-based research networks (PBRNs) to advance scientific knowledge and promote the use of evidence-based clinical services in community-based practice settings. PBRNs are collaborative partnerships between community-based providers and academic institutions to conduct clinical research on an ongoing basis. Developing a national system of PBRNs will entail integrating and expanding existing networks as well as building new ones [2, 3]. As an indicator of its commitment to this initiative, the NIH is investigating the feasibility of training and certifying 50,000 community-based health-care practitioners (e.g., physicians, dentists, and nurses) to participate in clinical research and integrate new research findings into routine health care delivery [2]. Only a systems change of this magnitude, NIH leaders believe, can ensure the translation of scientific advances into large-scale improvements in health and substantial reductions in health disparities [1].

Reflecting the NIH's confidence in this approach to closing the discovery-delivery gap, several Institutes and other federal agencies are developing and supporting PBRNs, including the:

- National Institute on Drug Abuse (NIDA)
- Substance Abuse and Mental Health Services Administration (SAMHSA)
- National Institute of Dental and Craniofacial Research (NIDCR)
- Agency for Healthcare Research and Quality (AHRQ)
- HIV/AIDS Bureau of the Health Resources and Services Administration (HRSA)
- Office of AIDS Research in the Office of the Director of the National Institutes of Health (OAR/NIH)
- National Institute of Allergy and Infectious Diseases (NIAID)
- National Heart, Lung, and Blood Institute (NHLBI)

Despite substantial federal commitment to developing and supporting PBRNs, reports indicate that PBRNs are challenging to implement and sustain [4-7]. Further, the extent to which PBRNs actually promote the use of evidence-based clinical services in community-based practice settings—including clinical services that have been proven effective in clinical trials and approved by federal regulatory agencies—remains largely unknown.

This project seeks to provide the NIH with much-needed information about what it takes to implement and sustain PBRNs and what it can expect from PBRNs as a model for disseminating and implementing evidence-based clinical services in community-based practice settings. The project addresses four specific aims:

1. Identify the organizational factors associated with the effective implementation of a federally funded national PBRN in community-based practice settings.

2. Examine the impact of a federally funded national PBRN in promoting the use of evidence-based clinical services in community-based practice settings.

3. Assess the organizational, network, and environmental factors associated with the sustainability of a federally funded national PBRN in community-based practice settings.

4. Develop a model and produce practical tools for community-based provider organizations to evaluate the business case for participating in a federally funded national PBRN.

To address these aims, the project will study the National Cancer Institute's (NCI) Community Clinical Oncology Program (CCOP), a federally funded national PBRN with a 22-year history of translating research into practice. The CCOP is a three-way partnership involving the NCI's Division of Cancer Prevention, selected cancer centers and clinical cooperative groups, and 50 local networks of community hospitals and physicians.

Using innovation and organization theory, we will conduct a series of *distinct, but conceptually integrated* studies employing both quantitative and qualitative methods. We will investigate implementation through in-depth case studies of three newly funded CCOP organizations and a survey of all 50 CCOP organizations. We will examine the impact of the CCOP through longitudinal analysis of time-specific adoption rates of evidence-

based cancer therapies among CCOP-affiliated and non-CCOP-affiliated provider organizations using SEER-Medicare data. These therapies have been proven effective clinical trials and have received FDA approval. We will assess the factors affecting sustainability through a longitudinal analysis of all CCOP organizations active between 1991 and 2003 using secondary data sources. Finally, we will examine the business case for CCOP participation through analysis of financial and statistical data and case studies of 5 CCOP organizations.

Studying the CCOP offers a unique opportunity to advance scientific knowledge about dissemination and implementation. First, the CCOP permits an examination of the impact of PBRNs as a model for disseminating evidence-based clinical services across a wide range of treatment modalities (e.g., surgery, radiation, and medical therapies). Second, with a 23-year history and with new CCOP organizations joining the program, the CCOP not only enables the investigation of start-up and early implementation, but also allows for the examination of mature implementation and sustainability. Third, extensive secondary data exist that describe the organization, operations, environment, performance, and clinical impact of CCOP organizations. Fourth, as a national network of 50 sites implementing a common set of clinical research protocols, the CCOP offers a large enough number of comparable sites to permit statistical analysis of quantitative data. Finally, on a practical note, the CCOP has already served as a model for other federally supported national PBRNs [8], and the NIH continues to look to the CCOP for guidance and inspiration as it implements the Roadmap.

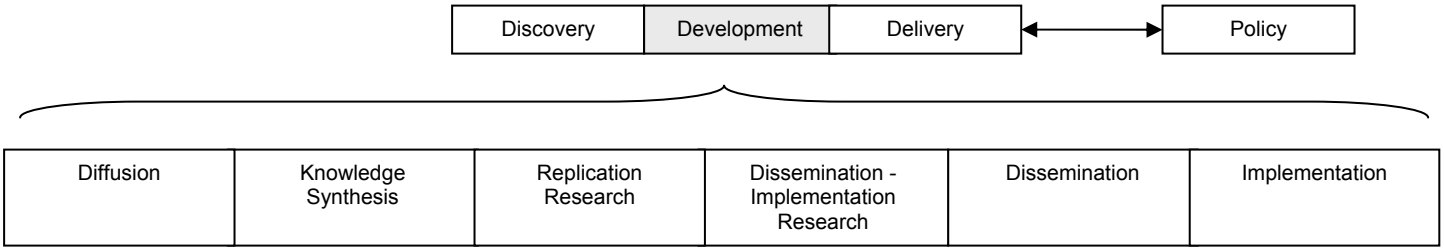
The proposed five-year project responds to the NIH's call for research on models to disseminate and implement evidence-based prevention, treatment, and quality of life improvement services in clinical practice settings. Specifically, the project responds to the NIH's call for (a) studies that focus on the development and testing of theoretical models of implementation processes (Aim 1); (b) studies that measure the extent to which interventions promote the use of evidence-based clinical services by providers (Aim 2); and (c) longitudinal studies on the factors that contribute to the sustainability of evidence-based improvements in clinical practice (Aim 3). The project also examines a critical, but neglected issue: the return on investment to organizations that adopt complex interventions designed to promote the use of evidence-based clinical services (Aim 4).

B. BACKGROUND AND SIGNIFICANCE

B1. Closing the gap between discovery and delivery is essential for improving the public's health.

The NIH increasingly recognizes the need to rapidly and effectively translate biomedical research into clinical practice [1-3, 9, 10]. Within the NCI, for example, consensus is growing that closing the gap between discovery and delivery is key to achieving the goal of eliminating cancer disparities and reducing suffering and death due to cancer by 2010 [11-13]. In recent years, the NCI has launched several dissemination initiatives to accelerate the development phase of the discovery-delivery continuum (See Figure 1). Examples include the Cancer Control PLANET, the cancer prevention and cancer control research network, the community networks program, the posting of evidence reviews on the NCI website, and the provision of supplemental funding for research dissemination [11].

Figure 1. The Discovery-Delivery Continuum



Source: Kerner, J.F. Overview of the State of Dissemination of Evidence-Based Interventions: Art, Science, or Both? Presented at *Emerging Issues In Dissemination Research: Implications for Cancer Prevention and Control.* University of North Carolina at Chapel Hill, June 2, 2005.

Similarly, other Institutes and federal agencies have deployed a variety of dissemination strategies to promote research dissemination. These include the formulation of practice guidelines, the facilitation of consensus conferences, the production of evidence reviews, and the development of information resources [8].

B2. Implementation is the 'final frontier' in closing the gap between discovery and delivery.

While dissemination is essential, implementation is the 'final frontier' in closing the discovery-delivery gap. Implementation refers to the introduction and early use of evidence-based clinical services in practice settings.

Two issues confront those who wish to cross this frontier. First, providers often remain unconvinced that sufficient evidence exists to support the implementation of research-tested clinical services in "real-world" practice settings. As a recent Institute of Medicine report [8, p.39] notes, "The treatment community perceives there is a surfeit of 'efficacy' research (studies conducted under controlled experimental conditions) and a shortage of 'effectiveness' research (where treatment modalities are studied under real-world conditions)." Others too note that most research on clinical services takes place in academic medical centers, yet most care gets delivered in community settings [14-16]. For many community-based providers, evidence-based practice awaits more practice-based evidence. These observations suggest that the acceptance and implementation of evidence-based clinical services in community-based practice settings depends less on dissemination, which connotes a one-way flow of knowledge from researchers to providers, than on knowledge exchange, which involves bidirectional communication between researchers and providers (i.e., a partnership) [8, 17].

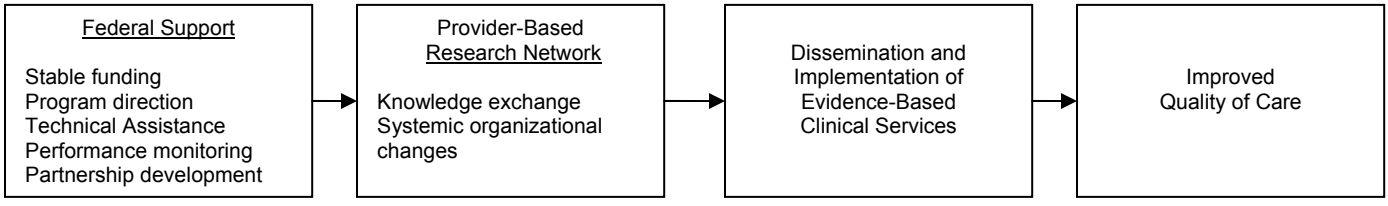
Second, implementation remains a daunting challenge no matter how strong or credible the evidence. For all but the simplest clinical services, successful implementation depends on administrative support, adequate financial and human resources, and organizational culture that values scientifically based practice [18]. Indeed, systematic reviews indicate that multifaceted interventions that target organizational staffing, office workflow, and information systems are more effective in changing provider behavior than interventions that increase provider awareness and knowledge, such as continuing education and academic detailing [19-21]. These findings suggest that the implementation of evidence-based clinical services requires systemic organizational changes that create a supportive infrastructure and culture in community-based practice settings.

B3. Provider-based research networks are a promising model for dissemination and implementation.

The NIH and other federal agencies have recognized that closing the gap between discovery and delivery requires a partnership between researchers and providers. To foster such partnerships, several Institutes and federal agencies are developing provider-based research networks, or PBRNs [4, 22-27]. PBRNs are partnerships between community-based physicians and academically-based investigators that share an ongoing commitment to clinical research and possess an organizational infrastructure that transcends a single study [4, 28]. PBRNs generally pursue the twin goals of advancing the evidence-base by conducting research in clinical settings where most people get their care, and translating research results into better care [29]. In PBRNs, community-based providers assume primary responsibility for collecting research data, but also participate in other aspects of the research process [4].

PBRNs are a promising model for disseminating and implementing evidence-based clinical services—and, ultimately, improving quality of care—because they involve both knowledge exchange and systemic organizational changes (see Figure 2). Knowledge exchange occurs through community-based provider participation in research (CBPPR). By engaging providers in the research process, researchers gain insight into the clinical issues (needs) of community-based practice settings, obtain provider input on study design and implementation considerations (feasibility), and discover the tacit practice-based knowledge that exists in community-based practice settings (acceptability). CBPPR promotes a sense of trust and ownership that enhances providers' acceptance of clinical research results and strengthens their commitment to acting on research findings. However, CBPPR does not occur spontaneously or effortlessly. To participate in PBRNs, provider organizations often must implement systemic changes in organizational staffing, office workflow, information systems, and reward structures. These systemic changes also facilitate the spread of knowledge and use of evidence-based clinical services by creating an organizational infrastructure that supports clinical research and an organizational culture that values scientifically-based practice. Some, but not all, PBRNs receive federal support in the form of stable funding, program direction, technical assistance, performance monitoring, and partnership development.

Figure 2. Logic Model of Federally Funded National Provider-Based Research Networks



Substantial federal commitment exists to develop and support PBRNs as a means for disseminating and implementing evidence-based clinical services in community-based practice settings. Yet, reports indicate that PBRNs themselves are challenging to implement and sustain. Difficulties include developing a research agenda, creating a clinical research infrastructure, coping with regulatory compliance issues, obtaining funding, and sustaining member interest [4-7]. Further, although many PBRNs have shown that they can complete studies and advance scientific knowledge [6], the extent to which PBRNs actually promote the use of evidence-based clinical services in community-based practice settings remains largely unknown. Many PBRNS are too new, too small, or lack reliable outcome data to measure their impact as a model for dissemination.

B4. The CCOP is a prototype for other federally funded national provider-based research networks.

The CCOP has served as a model for other federally funded national PBRNs, like the NIDA Clinical Trials Network and the NIAID Community Program for Clinical Research on AIDS [8], because it is a large network with a history of completing studies and advancing scientific knowledge. Further, some evidence suggests that the CCOP works as a model for promoting the use of evidence-based clinical services in community-based practice settings, including services proven effective in clinical trials and approved by the FDA [30-32].

What is the CCOP? 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 ("CCOP organizations"). NCI/DCP provides overall 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 2005, 50 CCOP organizations located in 35 states, the District of Columbia, and Puerto Rico participated in NCI-sponsored clinical trials. The CCOP includes 403 hospitals and more than 4000 community physicians [33]. In FY 2005, the CCOP budget totaled $92.7 million. The median CCOP organization award was $649,513.

CCOP organizations are led by a physician principal investigator who provides local program leadership. CCOP staff members include an associate principal investigator, a program coordinator, research nurses or clinical research associates, data managers, and regulatory specialists. These staff members coordinate the review and selection of new clinical trial protocols for CCOP participation, disseminate protocol updates to the participating physicians, and collect and submit study data [34]. CCOP-affiliated physicians accrue or refer participants to clinical trials, and typically include medical, surgical and radiation oncologists, general surgeons, urologists, gastroenterologists, and primary care physicians (e.g., OB/GYNs). Through their membership in CCOP research bases, CCOP-affiliated physicians also participate in the development of clinical trials by proposing study ideas, providing input on study design, and, occasionally, serving in the role of principal investigator or co-principal investigator for a clinical trial [34, 35].

How has the CCOP evolved? Although the CCOP initially focused on the evaluation of cancer therapies, NCI/DCP expanded its scope in 1987 by requiring CCOP research bases to design and conduct cancer prevention and control (CP/C) clinical trials and requiring CCOP organizations to meet annual cancer control accrual targets [36, 37]. NCI/DCP defines ***cancer prevention research*** as studies that evaluate new methods of detecting cancer risk and preventing primary and secondary cancers, and ***cancer control research*** as studies that evaluate symptom management, rehabilitation, and continuing care interventions designed to minimize the burden of cancer and improve quality of life. Despite some initial implementation challenges [34, 38], the CCOP has demonstrated its ability to design and conduct dozens of CP/C trials simultaneously, including large chemoprevention trials involving tens of thousands of study participants [33, 39].

What have we learned from the CCOP? The CCOP has a demonstrated track record of completing studies in community-based settings and advancing scientific knowledge about cancer care. An early evaluation of the program (1983-1985) showed that, even within the first five years of operation, the CCOP was effective in disseminating state-of-the-art cancer treatment protocols to community-based practice settings [40]. Moreover, several of the CP/C trials implemented through the CCOP have garnered national attention and changed the standard of care for at-risk populations and cancer patients (see Appendix A for examples) [39]. A later evaluation (1988-1990) provided some evidence that CCOP participation affected physician practice patterns. Specifically, the evaluation showed that CCOP physicians more rapidly adopted new breast cancer treatments shown to be effective in clinical trials than did other physicians who treated the same cancers in the same hospitals or nationally [30, 32]. The CCOP also appeared to have affected the practice patterns of non-CCOP physicians. The evaluation showed that non-CCOP attending physicians increasingly referred to CCOP physicians their node negative, estrogen receptor positive pre-menopausal breast cancer patients as well as

their older (fifty and above) node negative patients in 1988 and 1989, following the 1988 NCI Clinical Alert strongly encouraging node negative breast cancer patients to consider adjuvant chemotherapy [31, 32]. More generally, other studies show that physician participation in cancer research networks like the CCOP promotes compliance with treatment guidelines for early-stage breast cancer [41]. The second evaluation also identified several factors associated with successful implementation of the CCOP in community-based practices [42, 43].

While much has been learned about the CCOP, significant changes have occurred since 1990 that raise questions about the continued relevance of the earlier CCOP evaluations for the NIH as it implements the Roadmap. The past 15 years have witnessed an explosion of new cancer treatment options, a shift from inpatient to outpatient cancer care delivery, a move toward and away from restrictive forms of managed care, a wave of consolidation among provider organizations, a widespread dissemination of evidence reports and systematic reviews, and a significant reduction in Medicare reimbursement for chemotherapy. In light of these changes, the NIH needs updated, enhanced information about the CCOP as it seeks to develop and support national PBRNs modeled on this program in other disease areas.

B5. Dissemination and implementation research must address several knowledge gaps in order to guide federal efforts to close the discovery-delivery gap through PBRNs.

In addition to providing the NIH with updated information about the CCOP, research on dissemination and implementation must address several persistent knowledge gaps and practical needs.

First, the existing knowledge base offers little guidance on how to effectively implement a federally funded national PBRN in community-based practice settings. From a provider perspective, PBRN participation is a complex innovation because it requires systemic organizational changes in structure, staffing, workflows, and policies. Most studies of complex innovations in health care focus on demonstrating efficacy or effectiveness [19, 21, 44]. Few examine the implementation process itself. Although medical informatics offers a growing list of organizational factors that act as facilitators or barriers for implementing electronic medical records and other complex innovations [45-49], this literature has not yet produced a coherent theoretical model that describes how various factors interrelate or which ones matter more than others in different contexts. Diffusion of Innovation Theory [50] may seem like a promising candidate for such a model, but this classic theory is not well-suited for understanding innovations where: (1) individuals cannot adopt the innovation until the primary adoption decision has occurred at a higher level of authority; (2) innovation use requires the adopting organization to provide specialized training, resource allocation, and user support; (3) innovation effectiveness depends on active, coordinated innovation use by multiple organizational members [51-53]. Organization science offers theoretical models of implementation [51, 54]; however, these models reflect their origins in the manufacturing context. What is missing is a theoretically informed, empirically grounded organizational model of implementation that is suitable for complex innovations like PBRNs and is adapted to the clinical context.

Second, the knowledge base concerning the impact of models to promote the use of evidence-based clinical services does not offer a clear indication of what works and when. Systematic reviews find that most strategies for changing physician behavior show a mixed pattern of effectiveness [19-21, 44]. Drawing firm conclusions from the primary research literature is difficult due to substantial cross-study variability in research methods (e.g., study designs and measures), strategy design (e.g., different forms of audit and feedback), types of providers targeted (e.g., generalists versus specialists), and types of care provided (e.g., surgical versus medical care). To advance the knowledge base about the conditions under which particular models or strategies work, research is needed that holds methodological factors and strategy design factors constant while varying systematically such factors as the type of care provided or the type of provider targeted.

Third, the knowledge base offers little detail about the factors affecting the sustainability of complex innovations like PBRNs. Given the substantial time and resources required to develop and implement PBRNs, a thorough understanding of these factors is critical for both the efficient and effective allocation of scarce resources and for the maintenance of the beneficial outcomes that PBRNs produce. Despite the importance of sustainability, adoption and implementation have garnered far more research attention. With few exceptions [55-57], studies examining sustainability of complex innovations—including community health coalitions and other novel forms of inter-organizational collaboration—have taken a single- or multiple-case study approach [58-64]. These studies have identified several factors affecting sustainability, albeit on an exploratory and atheoretical basis. While informative, these small-sample studies do not provide a strong foundation for generalization or for the development of managerial or policy recommendations.

Finally, the knowledge base is virtually silent on whether, and under what conditions, a business case exists for provider participation in a PBRN. As defined by Leatherman and her colleagues [65, p. 18]:

> A business case exists…if the entity that invests in the intervention realizes a financial return on its investment in a reasonable time frame, using a reasonable rate of discounting. This may be realized in 'bankable dollars' (profit), a reduction in losses for a given program or population, or avoided costs. In addition, a business case may exist if the investing entity believes that a positive indirect effect on organizational function and sustainability will accrue within a reasonable timeframe.

A recent review of the broader quality literature reveals a lack of attention to the cost of implementing quality-enhancing innovations [65]. A similar neglect exists with respect to provider participation in PBRNs. Studies of the costs of clinical trials have focused almost exclusively on the incremental costs of patient care associated with trial enrollment; however, currently much of these costs are covered by insurance. Few studies have evaluated the administrative and other incidental costs associated with clinical research that are borne partially or fully by participating provider organizations. Those studies that have evaluated these non-clinical costs have found wide variation across provider organizations [66-68]. Finally, we are aware of no studies that document the financial benefits that might accrue to provider organizations as a result of PBRN participation. While philanthropic or other motives may drive participation, there is growing recognition that without an adequate financial return, it is difficult for organizations to sustain quality-enhancing innovations [65]. Thus, a critical need exists to evaluate the financial implications of provider participation in PBRNs. The lack of a business case—or even the lack of data to evaluate the business case—may thwart the adoption, implementation, and sustainability of PBRNs. This, in turn, limits the potential impact of PBRNs as a model for promoting the use of evidence-based clinical services in community-based practice settings.

B6. Significance of the Research Project

The magnitude of the gap between discovery and delivery cannot be understated. Neither can the gap between what we know and what we need to know about how to promote the use of evidence-based clinical services in community-based practice settings. The proposed project will significantly advance scientific knowledge about models for disseminating and implementing evidence-based clinical services by:

- Developing a theoretically informed, empirically grounded organizational model of implementation processes that is adapted to the context of clinical practice. The model will not only identify the key organizational factors associated with implementation effectiveness, but also describe the interplay of these factors both in start-up and early implementation as well as in later, mature implementation.

- Providing an updated and more comprehensive picture of the impact of a federally funded national PBRN in promoting the use of evidence-based clinical services in community-based practice settings, including services proven effective in clinical trials and approved by federal regulatory agencies. Do the positive effects of CCOP participation on clinical practice found in earlier evaluations persist in today's much different healthcare environment? If so, do these positive effects occur across multiple medical conditions or only across a few? Do they occur for all treatment modalities or only a few?

- Examining how 'real world' factors like managed care penetration, provider competition, market consolidation, leadership stability, staff turnover, and resource predictability affect the sustainability of a federally funded national PBRN in community-based practice settings over a 13-year time horizon.

- Assessing the level and distribution of costs of maintaining clinical research capacity in community-based practice settings, develop a model, and produce practical tools that will allow provider organizations considering initial or continued investment in the CCOP or other types of PBRNs to evaluate the business case for participation.

In the context of the NIH Roadmap, the proposed project is expected to have significant reach across the national clinical research enterprise. The CCOP has already served as a model for other NIH-supported

PBRNs [8], and NCI/DCP officials continue to provide advice to Roadmap steering committees. We expect that the NIH will continue to look to the CCOP program for guidance and inspiration as it implements the Roadmap initiatives. Given the magnitude of the "systems change" that the NIH envisions, the project may also have a significant impact on the public's health by helping the NIH to accelerate the translation of scientific advances into large-scale improvements in health and substantial reductions in health disparities.

C. PRELIMINARY STUDIES AND EXPERIENCE

An interdisciplinary team of investigators has been assembled to work on this project, bringing together the perspectives and skills of organization science, finance, economics, oncology, and statistics. *The investigators have built a dense network of collaborative relationships with each other in prior work. As a result, they know each other well and know how to work together. Sections C5-C8 describe the prior work most relevant to the proposed project. Appendix A provides a full list of all prior collaborative activities among team members.*

C1. Health Services Research Investigative Team

Bryan Weiner, Ph.D. (Principal Investigator) is an Associate Professor in the Department of Health Policy and Administration, School of Public Health, University of North Carolina at Chapel Hill (UNC); and Director of the Program on Health Care Organization at the Cecil G. Sheps Center for Health Services Research. He has published extensively on the subjects of organizational change, implementation of innovations, and inter-organizational relationships. Dr. Weiner serves as the Co-Director of the newly established Dissemination Core of the Lineberger Comprehensive Cancer Center at UNC, and also as the Director of the Dissemination/Health Policy Core of the Carolina Community Network to Reduce Cancer Disparities.

William R. Carpenter, Ph.D., MHA (Co-Investigator) is an Adjunct Instructor in the Department of Health Policy and Administration, UNC School of Public Health; and a Post-Doctoral Fellow in the Cancer Control Education Program at the UNC Lineberger Comprehensive Cancer Center. His research focuses on the performance determinants of organizations engaged in community-based clinical research, the diffusion of innovations in cancer care, and the spillover effect of clinical trials participation on quality of care.

Shoou-Yih Daniel Lee, Ph.D. (Co-Investigator) is an *Associate* Professor in the Department of Health Policy and Administration, UNC School of Public Health; and Research Fellow at the Cecil G. Sheps Center for Health Services Research. He has published extensively on the subjects of health care organization performance, strategic change, and organizational networks in health care.

Kristin L. Reiter, Ph.D. (Co-Investigator) is an Assistant Professor in the Department of Health Policy and Administration, UNC School of Public Health; and Research Fellow at the Cecil G. Sheps Center for Health Services Research. Her research focuses on investment decision making in health care organizations, the effect of pay-for-performance on hospital quality, and the measurement of the business case for quality.

George Pink, Ph.D. (Co-Investigator) is an Associate Professor in the Department of Health Policy and Administration, UNC School of Public Health; and Senior Research Fellow at the Cecil G. Sheps Center for Health Services Research. His research focuses on hospital financial performance and measuring the business case for quality.

C2. Clinical Investigative Team

Paul A. Godley, MD, Ph.D. (Co-Principal Investigator) is an Associate Professor in the Hematology/ Oncology Division of the Department of Medicine, UNC School of Medicine; and Director of the Program on Health Disparities at the Cecil G. Sheps Center for Health Services Research. His clinical and research interests are prostate cancer treatment and screening, and health care disparities.

Richard M. Goldberg, MD (Investigator) is a Professor and Chief of the UNC Division of Hematology/ Oncology. His research focuses primarily on colorectal cancer clinical and translational studies, gastrointestinal cancers, the development of new cancer drugs and drug combinations, and clinical trials methodology. He is the Chair of the Gastrointestinal Cancer Committee for the NCI cooperative group Cancer and Leukemia Group B (CALGB). Dr. Goldberg is a recipient of the Mayo Clinic Individual Achievement Award.

Lisa Carey, MD (Investigator) is an Associate Professor in Hematology/Oncology, and is the Medical Director of the UNC Breast Center. Her research interests focus on breast cancer, including examination of different subtypes of breast cancer, evaluation of new chemotherapy agents in early breast cancer, and examination of tumor characteristics that predict response to therapy. She is a recipient of the Doris Duke Clinical Scientist Award and a National Cancer Institute career development award.

Mark A. Socinski, MD (Investigator) is an Associate Professor in Hematology/Oncology, and the Director of UNC's Multidisciplinary Thoracic Oncology Program. His research involves clinical trials in non-small cell (NSCLC) and small cell lung cancer (SCLC), examining the optimal chemotherapeutic approach to advanced, metastatic NSCLC, and innovative approaches to the integration of high-dose conformal radiation therapy. He is an advisor with the American College of Chest Physicians Lung Cancer Guidelines Committee.

C3. Statistical Methods Team

Bahjat Qaqish, Ph.D. (Investigator) is an Associate Professor in the Department of Biostatistics, UNC School of Public Health; and a member of the UNC Lineberger Comprehensive Cancer Center. His research interests include generalized linear models, correlated discrete data and statistical computing. He has worked on cancer prevention and control studies including the Prescribe for Health study.

Marisa E. Domino, Ph.D. (Investigator) is an Associate Professor in the Department of Health Policy and Administration, UNC School of Public Health; and Research Fellow at the Cecil G. Sheps Center for Health Services Research. Her research focuses on the economics of mental health and the diffusion of technologies.

C4. Scientific Advisory Board

A Scientific Advisory Board will be constituted to provide oversight and offer counsel on study design, interpretation of findings, and dissemination of study results. Board members will include scientific experts in organization theory, survey methods, statistics, as well as experts knowledgeable about federally supported national PBRNs in cancer, mental health, and substance abuse treatment.

- Arnold D. Kaluzny, Ph.D., Professor, University of North Carolina at Chapel Hill
- Richard B. Warneke, Ph.D., Professor, University of Illinois at Chicago
- Mary Fennell, Ph.D., Professor, Brown University
- Gary Cutter, Ph.D., Professor, University of Alabama at Birmingham
- Betty Tai, Ph.D., Director, Clinical Trials Network, National Institute on Drug Abuse (NIDA)
- CCOP Principal Investigator (to be determined)
- William Harlan, MD, Division of Services and Intervention Research, National Institute of Mental Health

C5. Integrating Cancer Prevention and Control Research into Community Clinical Oncology Programs

Weiner, Carpenter, and colleagues have examined the organizational adaptations that occur at the local level to facilitate community clinicians' participation in emerging areas of cancer clinical research (NCI contract #263-MQ-217378). Specifically, they conducted interviews with current or former CCOP principal investigators, nurses, and clinical research associates from 24 CCOP organizations with varied track records in enrolling participants in CP/C clinical trials. Many CCOP organizations have established "parallel structures" of research staff to work solely or primarily on cancer prevention trials. Because these trials target cancer-free populations to which oncologists have limited access, CCOP organizations have sought to develop physician referral networks. However, direct-to-consumer marketing through media, mass mailings, and partnerships with cancer screening clinics has yielded greater numbers of study participants. A forthcoming article reporting these study findings will appear in *Cancer Control: The Journal of the Moffitt Cancer Center* [69] (See Appendix A). In a follow-up study, Weiner and his colleagues examined the organizational models and task environments of CCOP organizations with high accruals to cancer prevention trials (NCI contract #263-MQ-404175). A forthcoming article in *Oncology Nursing Forum* reports the study findings [70] (See Appendix A). The findings from this work will inform our project's study design, instrument development, and data analysis strategies.

In a similar vein, Weiner, Carpenter, and colleagues examined the structural and strategic adaptations that CCOP research bases have made to integrate CP/C research into their scientific agendas and organizational structures (NCI contract #263-MQ-217378). An article in *Cancer* describes the study findings [35] (See Appendix A). In a secondary analysis, Weiner and his colleagues examined the determinants of CP/C research program implementation in CCOP research bases using a model of organizational implementation like the one guiding this project. The article describing these findings is under review [34](See Appendix A).

C6. Effects of Managed Care and Competition on Community-Based Clinical Research

Carpenter, Weiner, Lee, Domino, and colleagues have examined the effects of managed care penetration and provider competition on the performance of the CCOP organizations. Using longitudinal data from several

sources, they studied the effects of these factors on a panel of 49 CCOP organizations. Managed care penetration was positively associated with accrual in areas of low to moderate penetration and negative in the areas of high penetration. Greater hospital competition was associated with a decline in trial enrollment. The differential effects of these factors on treatment and CP/C research performance suggest that the sustainability of these two "research programs" depends on different strategies and administrative methods. A forthcoming article in *Medical Care* reports the study findings [71] (see Appendix A). The proposed project will build on this work by examining the effects of a broader range of potential determinants of performance and sustainability.

C7. Experience with SEER-MEDICARE data

The NCI's Surveillance, Epidemiology, and End Results [72] Program is an authoritative source of information on cancer incidence and survival in the United States. The SEER Program currently collects cancer incidence and survival data from 14 population-based cancer registries and three supplemental registries covering approximately 26 percent of the US population (see http://seer.cancer.gov/about/). The SEER-Medicare dataset is a population-based dataset that joins the NCI's SEER program tumor registry data with Medicare beneficiaries' health insurance claims data. This very large, complex dataset has been the basis of several projects at UNC led by this research project's lead investigators. Carpenter has received specialized training in the use of Medicare claims and SEER-Medicare data for research purposes, provided by the Research Data Assistance Center (ResDAC)—a Centers for Medicare and Medicaid (CMS) contractor that provides free assistance to academic, government and non-profit researchers interested in using Medicare data for research. Godley and Carpenter have used these data to conduct several studies, the results of which are published [73, 74], under review [75], or ongoing (see Appendix A). All projects have received constructive comment and consequent approval by the SEER-Medicare Program.

C8. Business Case Analysis

Pink and his colleagues have examined the business case for two quality-enhancing innovations implemented in two separate health care organizations. Specifically, they conducted interviews with clinical, financial and quality personnel to understand the investment costs and effects on ongoing operations associated with Fetal Fibronectin testing for pregnant women in pre-term labor, and with a pharmacy pain management program. Using these interview data, along with financial and utilization data from the provider organizations' information systems, they developed a spreadsheet-based data collection and analysis tool that can be used to measure the net cash flows accruing to provider organizations implementing quality-enhancing innovations (see Appendix A). We will produce a similar tool for provider organizations participating in the CCOP as one outcome of our study. In addition, Reiter is currently consulting on a project to evaluate the business case for implementing quality-enhancing innovations in Medicaid managed care organizations.

D. DESIGN AND METHODS

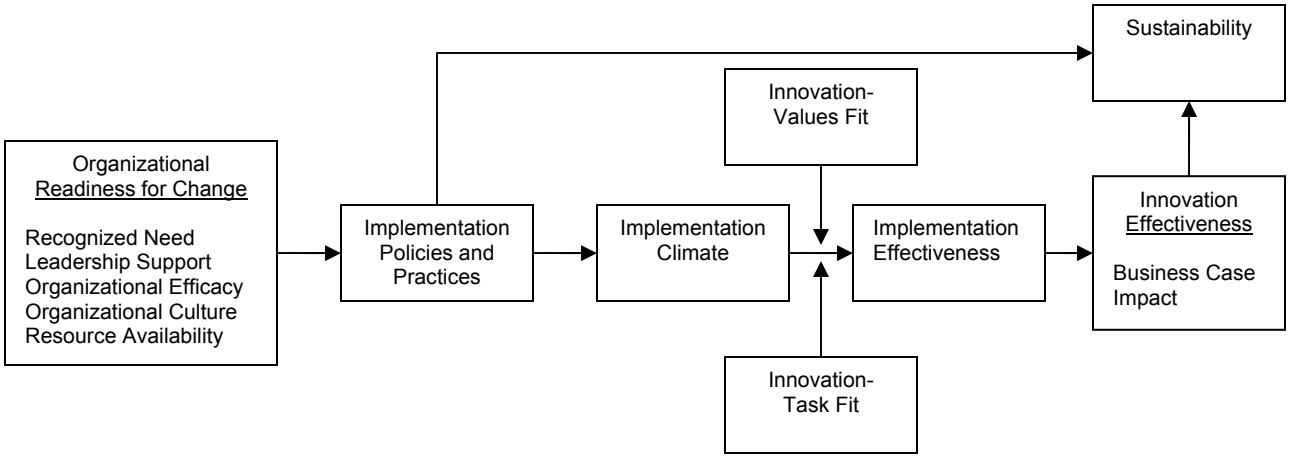
D1. Conceptual Framework

We view CCOP participation as an innovation for local networks of hospitals and physicians (i.e., "CCOP organizations") and use both innovation and organization theory to inform our investigation. An ***innovation*** is a technology or practice that an organization uses for the first time, regardless of whether other organizations have previously used the technology or practice [50, 51, 76, 77]. In the case of the CCOP, and PBRNs more generally, the innovation is community-based provider participation in research, or CBPPR (see Section B3 for discussion). CBPPR is a complex innovation whose implementation requires systemic organizational changes in structure, staffing, workflows, and policies. ***Implementation*** refers to the transition period, following a decision to adopt a new technology or practice, during which intended users actually put the new technology or practice into use [50, 51]. Like other promising innovations in health care, such as electronic medical records and the chronic care model, CBPPR is a dynamic innovation whose meaning and use evolves over time [78]. CBPPR is dynamic because the clinical services tested and diffused through the CCOP change over time and pose an ever-changing set of implementation challenges [34]. With dynamic innovations, implementation is a never-ending process (consider clinical information systems implementation, another dynamic innovation).

To guide the project, we have adapted an organizational model of innovation implementation that we have developed and refined in prior work (see Figure 3). Briefly, the model posits that the effective implementation of the innovation (CBPPR) is a function of the CCOP organization's readiness for change, the quality of the implementation policies and practices that it puts into place, the climate for implementation that results from

these policies and practices, the extent to which intended users of the innovation (e.g., physicians and nurses) perceive that innovation use fosters the fulfillment of their values, and the extent to which the innovation fits with task requirements (e.g., trial feasibility). The organizational benefits of an innovation (e.g., improved patient care) depend on effective implementation (consistent, high-quality use).

Figure 3. Conceptual Model of Organizational Factors Affecting CCOP Implementation



Organizational Readiness for Change is a multi-dimensional construct that embraces recognized need for innovation, management/leadership support for implementation, organizational efficacy in innovation implementation, cultural values supporting innovation, and resource availability [79, 80]. Each dimension influences an organization's propensity and capacity to put into place organizational policies and practices that support implementation (see Appendix B for more a detailed discussion).

Implementation Policies and Practices are the strategies that an organization employs to put into use the innovation, and the actions that follow from those strategies. Examples include education and training, communication and coordination, recognition and rewards, and time to experiment with the innovation [54]. Implementation policies and practices are cumulative, compensatory, and equifinal [51]. This means that, in general, more policies and practices supporting implementation are better; yet, some high-quality policies and practices may compensate for the absence or low quality of other polices and practices. Also, organizations can achieve the same level of implementation with differing mixes of policies and practices [77, 81].

Implementation Climate refers to organizational members' "shared summary perception of the extent to which their use of a specific innovation is rewarded, supported, and expected within their organization" [51, p. 1060]. Implementation climate emerges from shared information about, observations of, and experiences with the organization's implementation policies and practices. Organizations can create a strong implementation climate by making use of a variety of policies and practices designed to enhance organizational members' means, motives, and opportunity for innovation use [77, 81].

Implementation Effectiveness refers to the consistency and quality of innovation use [51, 53, 77, 82-84]. Although individuals can vary in innovation use, implementation effectiveness is conceptualized here as an organization-level construct that describes the pooled consistency and quality of innovation use (i.e., CBPPR activity). Implementation effectiveness is necessary, but not sufficient for innovation effectiveness (see below) [51, 54, 77, 85]. Implementation effectiveness is operationally defined as accrual, or the enrollment of new patients into clinical trials. The NCI uses this objective, outcome-focused measure of CBPPR as the primary means of determining CCOP organization performance, as do several published studies [34, 42, 86-90]

Innovation-Values Fit refers to the extent to which intended users perceive that innovation use will foster the fulfillment of their values [51, 53, 81, 91]. Values refer to "generalized enduring beliefs about the personal and social desirability of models of conduct or 'end-states' of existence" [92, p.1076]. Individuals vary in their values, but emphasis here is given to values shared by groups (e.g., physicians) [93]. Innovation-values fit moderates the relationship of implementation climate and implementation effectiveness. Even in the context of a strong implementation climate, innovation use (CBPPR) use could range from non-use to compliant use to committed use depending on innovation-values fit [51].

Innovation-Task Fit refers to the extent to which the innovation is compatible with task demands, work processes, and organizational capabilities. Innovation-task fit moderates the relationship of implementation climate and implementation effectiveness. Even if a CCOP organization builds a strong implementation climate, implementation effectiveness (accrual) will suffer if the clinical interventions' design characteristics (e.g., cancers targeted, patient eligibility restrictions, data collection requirements) do not fit the CCOP organization's task performance capabilities (e.g., patient populations, workflow, specimen storage facilities).

Innovation Effectiveness refers to the organizational benefits that accrue from innovation use (i.e., CBPPR) [51, 53]. Innovation effectiveness depends on how well and how consistently intended users use the innovation (implementation effectiveness). From an organizational standpoint, innovation effectiveness exists if a business case exists. Innovation effectiveness also exists if investing entity perceives that innovation use has a positive indirect effect on organizational function (e.g., marketing value). From a CCOP perspective, innovation effectiveness exists if evidence-based clinical services more rapidly diffuse among CCOP organizations than among non-CCOP organizations. This would indicate that innovation use (CBPPR) resulted in more evidence-based clinical care even for non-trial patients.

Sustainability refers to the capacity of organizations to maintain innovation use over time. For CCOP organizations, sustainability of CBPPR depends on innovation effectiveness, continued acquisition of resources from the environment (e.g., funding, clinical trials, and study participants), and ongoing investment of resources in implementation policies and practices (e.g., training, rewards, communication systems) [59, 94].

D2. Study Setting

Several factors make the CCOP a unique opportunity to advance scientific knowledge about the value of PBRNs as a model for promoting the use of evidence-based clinical services in community-based practice settings. These factors include the program's maturity and dynamism, the number of comparable sites implementing common clinical research protocols, the availability of extensive secondary data, and the range of evidence-based clinical services disseminated through the program. Table 1 describes the study population. Appendix B offers additional information about the CCOP, including a map of CCOP organization locations.

Table 1. Description of CCOP Organizations (N = 50)

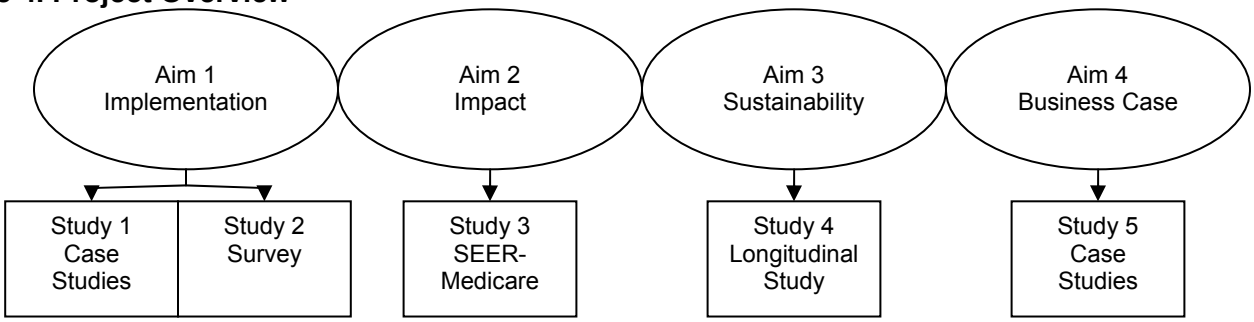
	Mean	STD	Low	High
Number of hospitals	8	6	1	28
Number of physicians	22	14	8	75
Number of open treatment trials	153	51	58	249
Number of treatment accruals	131	80	32	441
Number of open CP/C trials	17	5	4	28
Number of CP/C accruals	101	75	13	393
Number of MSAs served	2	2	1	12
MSA population	1463292	1759594	89015	9712530

Source: CCOP progress reports, Division of Cancer Prevention, National Cancer Institute. Notes: Open trials are those that the CCOP organization has activated for accrual by CCOP-affiliated physicians. Accruals are study participants enrolled in a trial. MSA refers to Metropolitan Statistical Area.

D3. Overview of the Study Design

To achieve the specific aims, we propose to conduct a series of interrelated studies employing qualitative and quantitative methods. Each study bears on one specific aim (see Figure 4).

Figure 4. Project Overview



D4. Study 1: Start-Up and Early Implementation

D4a. Purpose. Study 1 addresses the first specific aim: to identify the organizational factors associated with the effective implementation of a federally funded national PBRN in community-based practice settings. Study 1 will focus on start-up and early implementation. Research questions include: (a) how do CCOP organization leaders foster organizational readiness for change among participating provider organizations; (b) what implementation policies and practices are needed to support innovation use (i.e., CBPPR); and (c) do CCOP organizations with a stronger implementation climate show greater implementation effectiveness (i.e., greater CBPPR activity, measured as clinical trial accrual)? Answers to these questions will help NCI/DCP to assist newly funded CCOP organizations, and provide the NIH with a clearer picture of what it takes to start a PBRN.

In our preliminary studies (see Section C6), we examined the organizational adaptations that mature CCOPs have made to conduct cancer prevention and control (CP/C) research. In Study 1, we will focus on newly funded CCOP organizations and examine the implementation of cancer treatment *and* CP/C research.

D4b. Design and Sample. Study 1 employs a multiple, holistic case study design with the CCOP organization as the unit of analysis [94]. Case study methods are well-suited for studying implementation processes, which tend to be fluid, non-linear, and context-sensitive [95, 96]. In addition to permitting in-depth analysis of individual cases, case study methods offer analytic strategies for systematically comparing patterns observed across cases [94, 97]. Our prior work conducting case study research will inform our study design choices, data collection procedures, and data analysis strategies [34, 98-100].

The sample will consist of all three of the CCOP organizations that received initial CCOP program funding between 2002 and 2005 (see Appendix C for letters of support). Table 2 describes the sample.

Table 2. Description of Three Newly Funded CCOP Organizations

CCOP Organization Name	Central Office Location	First Year Funded	Number of Hospitals	Number of Physicians
Heartland Research Consortium CCOP	Saint Louis, MO	2005	1	11
Beaumont CCOP	Royal Oak, MI	2002	2	18
St Vincent Hospital Regional Cancer Center	Green Bay, WI	2002	3	14

D4c. Data Collection Strategy. A two-person research team will make one site visit to each CCOP organization each year for five years. In Year 1, the site visits will involve travel to the CCOP organizations. In Years 2-3, the site visits will take place virtually through web-based videoconferencing. During site visits, the team will conduct 8-10 one-hour individual interviews with the CCOP Principal Investigator, Associate Principal Investigator, Administrator, research nurses and clinical research associates (CRAs), oncologist and non-oncologist physicians listed as CCOP investigators, and CCOP hospital leaders such as cancer service-line executives (N= 24-30 total per year). The research team will consult with the CCOP Administrator to identify specific nurses, CRAs, and physicians for interviewing. We will use a semi-structured interview guide to gather data on organizational readiness for change, implementation policies and practices, implementation climate, user-values fit, inter-organizational relationships, and environmental conditions. Team members will alternate conducting the interviews. Interviews will be audio-taped and later transcribed verbatim.

The research team will also obtain data from CCOP grant applications and annual progress reports. The NCI requires that each CCOP organization file annual progress reports and periodic re-applications for funding. These documents include detailed data on the CCOP organization's structure, operations, and clinical trials performance. For example, they include information on CCOP governance structure, research staffing, communication procedures, coordination mechanisms, education and training activities, research base relationships, and financial and in-kind contributions from participating provider organization. They also provide accrual data for each treatment and CP/C clinical trial, sorted by CCOP research base, enrolling hospital, and enrolling physician. The NCI will make these data available for abstraction, as in previous studies [34, 71].

D4d. Data Analysis. We will employ pattern-matching logic to guide the data analysis [94]. In pattern-matching, an observed pattern is compared to a predicted one (e.g., hypothesized relationships shown in the conceptual framework). If the patterns match, the predicted pattern is said to receive support. If the patterns do not, the investigator reformulates the predicted pattern by developing and investigating alternative predictions.

Procedurally, analysis will involve three phases: data coding, within-case analysis, and between-case analysis. In the first phase, we will use qualitative data analysis software (ATLAS.ti 5.0) to code the study data. The conceptual framework will provide a starting list of codes, which we will supplement with emergent codes as analysis proceeds. Using a common codebook (See Appendix B), two investigators will conduct a pilot test

by independently coding five transcripts. Based on the pilot test, the investigators will sharpen the coding manual's definitions, decision rules, and examples. Research assistants will code the remaining documents.

In the second phase, we will conduct a within-case analysis of each CCOP organization. Using ATLAS.ti, we will generate reports of all text segments for each code. We will assess the degree to which the construct emerges in the data (its "strength"), the degree to which the construct positively or negatively affects implementation (its "valence"), and the degree to which relationships among constructs are consistent with the hypothesized model. We will assess support for the hypothesized relationships by using three criteria proposed by Trochim [101] and Miles and Huberman [97]. First, we will look for the overall covariance of the constructs (e.g., whether CCOP organizations exhibiting strong implementation climate also exhibit high implementation effectiveness, i.e., accrual). Second, we will look for explicit attributions or the identification of plausible mechanisms to link the two constructs (e.g., participants attribute a strong implementation climate to the deployment of appropriate implementation policies and practices). Third, we will look for indications of temporal precedence for the hypothesized explanatory variable. We will rely primarily on documentary evidence for establishing temporality, but we will also consider interview participants' accounts of the sequence of events.

In the third phase, we will apply the same three criteria across the cases to determine if cross-case variation in implementation is consistent with the hypothesized relationships in the model. Consistent with the organization-level focus of the model, we will aggregate and analyze quantitative data on implementation policies and practices (e.g. staffing levels), implementation effectiveness (accrual), and other study constructs using simple statistics. In addition, we will create within-case and between-case data displays that cross-tabulate the quantitative and qualitative data in order to facilitate the use of pattern-matching logic [97].

The final product of Study 1 will be a theoretically informed, empirically grounded model of organizational implementation adapted to clinical practice. The model will identify the organizational factors associated with implementation effectiveness, and describe the interplay of these factors in start-up and early implementation.

D5. Study 2: Mature Implementation

D5a. Purpose. Study 2 also addresses the first specific aim. Whereas Study 1 focuses on start-up and early implementation, Study 2 looks at implementation across the "life span" of CCOP organizations. Research questions include: (a) how do implementation policies and practices vary as a function of CCOP organization age; (b) is implementation climate positively related to implementation effectiveness; (c) does innovation-values fit or innovation-task fit moderate the relationship between implementation climate and implementation effectiveness; and (d) does implementation effectiveness mediate the relationship between implementation climate and (perceived) innovation effectiveness?

For the first question, we expect that CCOP organizations will use different implementation policies and practices as they gain experience. From a organizational life-cycle perspective [100, 102-105], we expect to see younger CCOP organizations make greater use of policies and practices that promote collective sense-making (e.g., frequent meetings), relationship building (e.g., outreach, trust building), and capacity building (e.g., hiring and training). In more mature CCOP organizations, we expect to see greater use of policies and practices that support efficient functioning (e.g., standard operating procedures) and performance management (e.g., monitoring and evaluation of individual performance). For the other research questions, Study 2 will complement Study 1 by examining quantitatively the hypothesized relationships in a larger sample.

D5b. Design and Sample. Study 2 will employ a cross-sectional survey design. The study population will consist of all 50 CCOP organizations (see Section D2 for a descriptive profile of the CCOP organizations). Given the organization-level focus of the conceptual model, the CCOP organization will serve as the unit of analysis. Individual CCOP members will serve as the unit of data collection. The survey sample will consist of 13-17 individuals per CCOP organization (N = 600-900 total). Sample size will vary somewhat across CCOP organizations due to organizational differences in the number of CCOP-affiliated physicians and research staff members. Table 3 describes the anticipated sample.

Table 3. Anticipated Sample Size and Composition for Implementation Survey

Role of Individual In CCOP Organization	N per CCOP Organization	Sample Total
CCOP Principal Investigator	1	50
CCOP Associate Principal Investigator	1	50
CCOP Administrator	1	50

Role of Individual In CCOP Organization	N per CCOP Organization	Sample Total
CCOP-Affiliated Physicians	8-10	400-500
CCOP Research staff members (e.g., research nurses, study coordinators, CRAs)	3-5	150-250
Total	**13-17**	**600-900**

D5c. Data Sources. Primary data collection will occur for several of the constructs in the conceptual model described in Section D1. CCOP grant applications and annual progress reports will provide supplemental data about CCOP organizational structure and operations (see Section D4d). The NCI's Cancer Therapy Evaluation Program (CTEP) clinical trials database will provide data on clinical trial accrual. The NCI will make available these secondary data sources, both of which we have used in previous studies [71].

D5d. Data Collection Strategy. We will send a mailed survey to a representative array of individuals within each CCOP organization in order to minimize single-source response bias. We will use CCOP grant progress reports to construct the sampling frame. The sampling frame will include all CCOP-affiliated physicians eligible to accrue study participants to clinical trials, including the CCOP PI and Associate PI, as well as all clinical research staff members identified in the report as supporting the CCOP organization. With the exception of the CCOP Administrator, we will exclude from the sampling frame CCOP administrative staff members (e.g., data managers). Using this list, we will select 8-10 physicians reflecting different specialties involved in the CCOP organization (e.g., medical oncology, radiation oncology, surgical oncology, and urology) and 4-5 research staff members. For larger CCOP organizations, we will randomly sample within physician and research staff strata.

We will employ several strategies developed by Dillman and others for obtaining high response rates to mailed surveys [106-108]. These include sending a letter signed by NCI/DCP officials two weeks in advance of the survey, sending the survey with a cover letter hand-signed by the Principal Investigator, using hand-placed stamps rather than metered postage, including a return address specifying the Principal Investigator, keeping the survey brief, and formatting the survey with an attractive layout. In addition, we will provide each survey respondent $50 for completing the survey. We will do three waves of mailing, each spaced four to five weeks apart. Based on the Sheps Center's experience with mailed surveys, we expect a 60% response rate to the first mailing, and a 50% response rate to the second and third mailings respectively. In sum, through intensive efforts over a four-month period, we anticipate an overall response rate of 90%. Earlier CCOP evaluations targeted similar numbers and types of respondents and achieved response rates of 86% to 100% [109].

D5e. Measures. The dependent variables will include multiple measures of implementation policies and practices, implementation effectiveness (accrual), and innovation effectiveness (perceived benefits of CCOP participation). Primary independent variables will include implementation climate, innovation-values fit, and innovation-task fit. Appendix B includes a table of sample measures and earlier surveys. In addition to surveying respondents about the implementation climate within the CCOP organization (e.g., perceived adequacy of implementation policies and practices deployed by the CCOP organization's central office), we will also survey respondents about the implementation climate for clinical research within their "home" organization (i.e., the extent to which CBPPR is expected, supported, and rewarded within their own organization). This will allow us to assess whether the implementation climate created by the CCOP organization is reinforced or undermined by the participating provider organizations.

We will measure constructs using multi-item scales to reduce the threat of mono-operational bias [110]. We will construct scales at the individual level based on exploratory principal factor analysis with orthogonal rotation. Items with factor loadings of 0.40 or more will be examined for inter-item consistency. Scale items with a Chronbach alpha coefficient of 0.70 or more will be averaged to construct individual-level scales [111, 112].

D5f. Data Analysis. The conceptual model guiding the study emphasizes organizational-level constructs. We will conduct statistical tests to assess the extent to which responses to individual-level scales constructed from factor analysis show sufficient within-CCOP agreement to justify aggregation to the CCOP organization level. Specifically, we will compute eta-squared, ICC(1), ICC(I,k), and $r_{wg(j)}$. Each statistic has its own limitations [113-115]. We will compare the values of these statistics to recommended cut-off values and values reported in other studies using individual-level variables aggregated to the organizational level [116-118]. If on balance the tests justify aggregation, we will construct CCOP-organization-level averages for implementation climate, innovation-values fit, and innovation effectiveness. If the tests do not justify aggregation, we will incorporate in our models variables that measure intra-CCOP variability of individual responses (e.g., coefficient of variation).

We will address the first research question by regressing implementation policies and practices (IPP) variables on CCOP organization age (AGE), controlling for CCOP organization characteristics, *x* (e.g., size).

$$g(E[IPP_i]) = \alpha + \beta AGE_i\ \gamma^T x_i,$$

where *g*() is a link function (identity, log, logit or cumulative logit) appropriate for the response scale.

For the remaining research questions, we will fit a series of regression models. Innovation effectiveness (InnEff) will be the dependent variable. Implementation climate (ImpCli), implementation effectiveness (ImpEff), and CCOP organization characteristics (*x*) will be the covariates. Two main models will be considered:

Model I: $g(E[InnEff_i]) = \alpha_1 + \beta_1 ImpCli_i + \delta_1^T x_i,$
Model II: $g(E[InnEff_i]) = \alpha_2 + \beta_2 ImpCli_i + \gamma_2 ImpEff_i + \delta_2^T x_i.$

Parameter β_1 reflects the effect of implementation climate on innovation effectiveness, while β_2 reflects its effect above and beyond the effect of implementation effectiveness. Thus $\beta_1 \neq 0$, $\beta_2 = 0$ implies that the effect of implementation climate is mediated totally through implementation effectiveness, while $0 < \beta_2 < \beta_1$ indicates partial mediation. In order to understand the mediation effect, we will also fit the model:

Model III: $g(E[ImpEff_i]) = \alpha_3 + \beta_3 ImpCli_i + \delta_3^T x_i,$

and test potential moderating effects of innovation-values fit (IVF) through the model

Model IV: $g(E[ImpEff_i]) = \alpha_4 + \beta_4 ImpCli_i + \gamma_4 IVF_i + \psi_4 IVF_i * ImpCli_i + \delta_4^T x_i,$

with ψ_4 as the parameter of interest. We will use a similar model to test the moderating effect of innovation-task fit (ITF).

D5g. Power Analysis. Analysis will take place at the CCOP-organization level (N = 50). Although some responses are categorical and some are counts, approximate power calculations will be done assuming a normal response with (conditional) variance σ^2. The magnitude of differences will be measured in units of σ. The structure of the covariates is not known a priori, but an approximate assessment can be made by first assuming balanced covariates and then evaluating the effect of imbalance. We consider first a regression model with two binary covariates. The main effects are contrasts between two groups. Under balance, the group size is 25 and the standard error (SE) of the contrast is $\sigma\sqrt{2/25}$. For hypothesis testing at the 5% level, this gives 80% power against a difference of 0.79σ. Allowing for multiple comparisons (five tests with overall 5% by Bonferroni's method), hypothesis testing at the 1% level gives 80% power against a difference of 0.98σ. The interaction contrast has SE equal to double that of the main effects leading to 80% power against an interaction of magnitude $2 \times 0.79\sigma = 1.58\sigma$ when testing at the 5% level. The interaction contrast appears only in Model IV, and is of secondary importance. To address covariate imbalance, we look at the case of two groups having sizes 15 and 35 instead of 25 and 25. For hypothesis testing at the 5% level, 80% power is obtained at a difference of 0.86σ compared to 0.79σ in the balanced case. Extreme imbalance is not expected in these data, and mild imbalances have little effect on power. Other published studies of the CCOP have faced similar sample size constraints, yet still observed statistically significant effects [34, 42, 43, 88, 90]. Two studies testing components of the conceptual model outlined above also possessed small sample sizes (39 manufacturing plants in one, 69 schools in another), yet observed statistically significant effects [53, 54].

Combined with Study 1, Study 2 will produce a theoretically informed, empirically grounded organizational model of implementation suitable for complex innovations and adapted to the context of clinical practice.

D5. Study 3: CCOP Impact

D5a. Purpose. Study 3 addresses the second specific aim: to examine the impact of a federally funded national PBRN in promoting the use of evidence-based clinical services in community-based practice settings. Research questions include: (a) do CCOP-affiliated hospitals and physicians more rapidly adopt evidence-based clinical services than do non-CCOP-affiliated hospitals and physicians; (b) do CCOP-affiliated hospitals and physicians adopt evidence-based clinical services more rapidly for some forms of cancer than for others

(e.g., breast versus colon), compared to their non-CCOP affiliated counterparts; and (c) do CCOP-affiliated hospitals and physicians adopt some types of evidence-based clinical services more rapidly than others (e.g., surgical versus medical therapies), compared to their non-CCOP affiliated counterparts? Based on the logic model of the CCOP (see Section B3), we expect that CCOP-affiliated hospitals and physicians will adopt evidence-based clinical services more rapidly than their non-CCOP-affiliated counterparts because they directly participate in the process of scientific discovery and follow scientific communications more closely.

Although other studies have explored similar issues, they have focused on the adoption of one of two practice changes in breast cancer (i.e., use of breast conserving surgery and adjuvant chemotherapy and/or radiation therapy) [41, 119, 120], with little attention given to other therapies and cancers. This study will build on prior research by: (1) analyzing multiple evidence-based clinical services across multiple cancers rather than a limited set of clinical services in a single cancer; (2) studying a larger sample with broader geographic distribution; and (3) incorporating a more comprehensive set of measures reflecting influential factors at multiple levels including patient, physician, hospital, network, market, and regional characteristics.

D5b. Design and Sample. Study 3 will employ a two-group, longitudinal design with two levels of analysis. At the hospital level of analysis, the two groups will consist of CCOP-affiliated and non-CCOP-affiliated hospitals. At the physician level of analysis, the two groups will consist of CCOP-affiliated and non-CCOP-affiliated physicians. The sample will consist of all CCOP-affiliated hospitals and physicians active in a SEER region during the observation period (1991-2003) along with matched comparison groups of non-CCOP-affiliated hospitals and physicians also active in a SEER region during the observation period (for a description of SEER, see Section C7). The observation period permits an analysis of 21 CCOPs in 10 SEER regions, including 100 CCOP-affiliated hospitals and approximately 415 physicians. CCOP-affiliated hospitals will be matched to non-CCOP-affiliated hospitals in the same SEER region based on academic affiliation, presence of teaching programs, total number of admissions, American College of Surgeons Oncology Group accreditation, presence of radiation therapy facilities, and other characteristics. CCOP-affiliated physicians will be matched to non-CCOP-affiliated physicians in the same SEER region based on specialty, major professional activity, type of practice, primary place of employment, board eligibility, and other characteristics.

D5c. Data Sources. The principal data source, the Surveillance Epidemiology and End Results (SEER)-Medicare, is a population-based dataset that joins the NCI's SEER program tumor registry data with Medicare beneficiaries' health insurance claims data. Data collected through the SEER program include information for each incident cancer case in the SEER registry region, including, but not limited to, diagnosis (including stage and grade), date of diagnosis, patient demographics, and type of initial surgical and radiation therapy treatment. These data are linked to Medicare claims, which include procedure-level diagnostic and treatment information for inpatient hospital stays of all beneficiaries, and for physician services, outpatient care, and durable medical equipment for the 95% of beneficiaries who subscribe to Medicare Part B [121]. The SEER-Medicare dataset also includes data on hospital organizational characteristics. The Institute of Medicine describes SEER-Medicare as one of few population-based data sources available for studying the quality of cancer care [122]. Several published studies use the data to analyze patterns of cancer care [119, 123-126] and examine the role of hospitals and providers in cancer treatment and outcomes [123, 126-130]. The SEER-Medicare dataset is readily linkable to the American Medical Association (AMA) Masterfile [131].

The American Medical Association (AMA) Physician Masterfile includes extensive information on over 805,000 active U.S. physicians, including both AMA members and non-members. Physician data is maintained beginning when they enter medical school and includes medical school information, residency activities, and finally practice information, collected from over 2,100 different resources including medical organizations, institutions and government agencies. The data is managed by Medical Marketing Services (MMS), which has added enhancements including demographic, behavioral, and psychographic information [132].

D5d. Data Collection Strategy. The primary dataset (SEER-Medicare) is available to researchers following the submission and acceptance of a study proposal and data application to the SEER-Medicare Program (see Appendix C for letter of support). In this study, there is no need to identify individual patients; however, it is necessary to identify physicians and hospitals as "CCOP affiliates" and to match them to similar non-CCOP physicians and hospitals for aggregate comparison. As such, the study proposal and data application will follow Program guidelines for requesting unencrypted data. Investigators will seek approval from each of the SEER registries to release restricted/unencrypted variables for that registry. Approximately 400 CCOP physicians and 100 hospitals and their matching non-CCOP peers (approximately 800 and 200, respectively) in SEER Regions will be identified, for whom the research team will send identifying data (UPIN and AHA identification

numbers) to the SEER-Medicare programming contractor, IMS inc. Taking the physician data as an example, IMS will un-encrypt the physician UPIN numbers, send them to the AMA's programming contractor, which will link to AMA data, and return to IMS. IMS will return to the investigator a file with re-encrypted UPINs and the selected AMA variables. In this way, anonymity is preserved: the researchers will not be able to link patient-level data to particular individual physicians or hospitals, nor be able to identify individuals in analysis.

D5e. Measures. The primary independent variable, at both levels of analysis, is CCOP participation, defined by a binary variable indicating CCOP affiliation. The dependent variables, at both levels of analyses, are the patient-level adoption of the evidence-based clinical services studied. Adoption is defined as having received the evidence-based treatment of interest among eligible patients. To enhance generalizability of findings within the cancer arena as well as to other diseases, adoption will be studied in lung, prostate, breast, colon, and pancreatic cancer. These cancers together comprise over half of the US cancer burden in terms of incidence and mortality [133]. Each is distinct in terms of the demographics of the patients that the cancer affects, the relative survival rate, the technologies available for prevention and early detection, and the risk and extent of side effects associated with treatment.

Several evidence-based cancer treatments have been identified for each cancer as good candidates for study, based on strength the clinical evidence, the period of observation (1991-2003) and the availability of the necessary data. Cancer treatments generally fall into one of three categories: medical, surgical, or radiation oncology. We will explore whether differences exist between CCOP-affiliated and non-CCOP-affiliated hospitals and physicians in the adoption rates of evidence-based treatments in these three categories. Medical treatments (e.g., new chemotherapy or hormonal agents) may get adopted more rapidly than surgical treatments (e.g., nerve-sparing radical prostatectomy) or radiation treatments (e.g., addition of radiation therapy to the previous standard of care [chemotherapy] for limited-stage small cell lung cancer), because the latter two depend on local availability of harder-to-acquire skill sets or capital intensive technologies. In some cases, the combination of these different treatment modalities is itself the evidence-based treatment. The evidence-based treatments listed in Table 4 are new in the last 20 years, have received FDA approval, were eligible for Medicare reimbursement during the study period, and thus are specifically identifiable in the data through International Classification of Disease (ICD)-9-CM procedure codes for inpatient and outpatient claims, Current Procedural Terminology (CPT) codes including HCFA Common Procedural Coding System (HCPCS) in physician and outpatient claims, and revenue center codes for outpatient claims. Appendix B contains a brief discussion of the evidence and rationale for selecting each treatment described in Table 4.

Table 4: Evidence-Based Cancer Treatments Proposed for Study 3

Treatment	Summary of Patient Eligibility Criteria	Years of Focus	Primary Means of Identification in Claims*
Breast Cancer			
Trastuzumab (Herceptin)	HER2-positive Metastatic	1998-2002	H: J9355
Utilization of HER-2 Testing	Stage IV BrCa, for HER-2 overexpression (Herceptin appropriateness)	1998-2002	C: 88342
Aggressive Surgery (Mastectomy) vs. Breast Conserving Therapy (BCS) plus Radiation Therapy vs. BCS Alone	Stage I, II	1990-2002	I: 9221-9229 (RT); C: 77401-77499, 77750-77799 (RT); R: 0330-0333 (RT);
Colon/Rectal Cancer			
5-FU + Leucovorin	Stage III	1990-2002	H: J9190 + J0640
Irinotecan in Multiagent therapy; Oxaliplatin	Stage IV	1997-2002	H: J9206 (Irinotecan) H: J9263, C9205 (Oxaliplatin)
Post Surgical Chemoradiation	StageII-III rectal ca.	1990-2002	I: 9925 (Chem) + 9221-9229 (RT) C: 96400-96549, J9000-J9999, Q0083-Q0085 (Chem) + 77401-77499 (RT) R: 0331, 0332, 0335 (Chem) + 0330-0333(RT) [134]
Lung Cancer			
Addition of Radiation Therapy to use of Chemotherapy	LS-SCLC	1990-2002	I: 9925 (Chem) + 9221-9229 (RT) C: 96400-96549, J9000-J9999, Q0083-Q0085 (Chem) + 77401-77499 (RT) R: 0331, 0332, 0335 (Chem) + 0330-0333(RT) [134]
Chemotherapy and Radiation	Stage III NSCLC	1990-2002	I: 9925 (Chem) + 9221-9229 (RT) C: 96400-96549, J9000-J9999, Q0083-Q0085 (Chem) + 77401-77499 (RT) R: 0331, 0332, 0335 (Chem) + 0330-0333(RT) [134]

Treatment	Summary of Patient Eligibility Criteria	Years of Focus	Primary Means of Identification in Claims*
Pancreas Cancer			
Gemcitibine	Stage II-III	1995-2002	H: J9201
Prostate Cancer			
Lupron/Leuprolide, Goseriline; as alternative to Orchiectomy	Stage IV	1990-2002	H: (J9217, J9218, J9219) + J9202 (Rx); C: 56318, 54535, 54530, 54520 (Sx)

*H: HCPC; I: ICD-9 Procedure Code; C: CPT Code; R: Revenue Center Code

Control variables will include measures at the patient level (e.g., Charlson comorbidity index, age, race, and other measures), organizational level (e.g., total hospital beds, total discharges, medical school affiliation, referral center status, total nurses employed, the presence of therapeutic radiology services, sole community hospital status, and others), and environmental level (e.g., urban/rural [MSA], local population, local average income level, proportion of population with health insurance, geographic region of the country, among others). Appendix B provides a table of proposed measures for consideration in Study 3.

D5f. Data Analysis. Data will be received from the SEER-Medicare program in the form of compressed text files on approximately 25 CD-Roms, including SAS programming templates for data extraction into working files. Initial data files will be exceptionally large, with some individual files exceeding 6 GB. As such, experienced data managers will use specialized computers to extract and store the working files on the Sheps Center network server. Carolinas Center for Medical Excellence (CCME) staff will log in to this server remotely via a secure network protocol to build the analytic datasets. Using an algorithm based largely on clinical characteristics appropriate to the treatment of interest and necessary data management steps to assure complete claims in the data [121], CCME programmers will identify the relevant patient population (see Appendix B for an algorithm example). Once this population is identified, data will be linked to the Medicare claims files to build the primary analytic files. Because each treatment will be for a unique patient population, CCME programmers and study investigators will use a unique primary analytic file for each treatment.

The main outcome is observed at the patient level: whether the treatment in question was adopted or not for the patient. We will define the outcome Y_{ij} to be 1 if the treatment was adopted for the *j*th patient in the *i*th hospital, and 0 otherwise. Associated with Y_{ij} will be a vector x_{ij} of covariates for the patient ($x_{ij,patient}$), the attending physician ($x_{ij,physician}$), the hospital ($x_{ij,hospital}$), and time trends ($x_{ij,time}$). We will model the probability of a treatment, $pr(Y_{ij} = 1) = E[Y_{ij}] = \pi_{ij}$, as a function of the covariates x_{ij} using logistic regression as follows:

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

Hospital and physician covariates include a binary indicator of CCOP participation and other characteristics (see proposed table of measures in Appendix B). Patient covariates include clinical and demographic factors. Time covariates can be indicator variables of individual periods, such as six-month or one-year intervals, or linear, quadratic or higher-order orthogonal polynomials. These functions of time represent the diffusion curves. 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. We will also investigate whether the time trends differ between CCOP-affiliated and non-CCOP-affiliated hospitals and physicians by including interaction terms between CCOP participation and time, or by fitting models separately for CCOP-affiliated and non-CCOP-affiliated participants. We expect correlations of outcomes within a physician and a hospital. The logistic regression model described above will be estimated using generalized estimating equations (GEE) [135] to take the correlation into account. An exchangeable working correlation will be used along with the sandwich variance estimator to provide protection from misspecification of the correlation structure. General software for GEE is available in SAS PROC GENMOD, but it tends to be slow for large clusters. The exchangeable working correlation can be fitted efficiently to very large clusters using SAS/IML code developed by Investigator Bahjat Qaqish (fpt://ftp.bios.unc.edu/pub/gee/blex). In a more detailed modeling of the correlation structure, we will allow for different correlations within-physician and between-physician (within the same hospital). Special-purpose software will be developed if generally available software is impractical for this type of modeling.

D5g. Power Analysis. The anticipated sample is 100 CCOP hospitals and 300 non-CCOP hospitals, 400 CCOP physicians and 800 non-CCOP physicians. A major concern is the possible aliasing (collinearity) of hospital and physician CCOP participation. To allow an assessment of power we make some assumptions about the structure of patient, hospital and physician distributions, although we realize that this will vary by

year, cancer type and treatment. Total years of study will range from 5 to 12 depending on the treatment. The estimated average number of cases per year is 1,500. Of patients requiring any hospital care, we estimate that 10% of CCOP-affiliated physician cases will receive that care at a non-CCOP-affiliated hospital, and of patients requiring any hospital care, 10% of non-CCOP-affiliated physician cases will receive that care at a CCOP-affiliated hospital. Hence, for 1,500 annual expected cases per treatment, we anticipate a distribution of observations like the following: CCOP-physician/CCOP-hospital = 450; CCOP-physician/non-CCOP-hospital = 50; CCOP-hospital/non-CCOP-physician = 100; non-CCOP-hospital/non-CCOP-physician = 900. Assuming the above structure, we consider a regression model with main effects for hospital CCOP participation and physician CCOP participation. The response is binary; hence, variance does not exceed 1/4. Using the above structure, the standard error of both hospital and physician contrasts is at most 0.044. This gives 80% power for detecting a difference of 0.12 or more. This is based on one year of data only. Use of 5-12 years of data will increase power considerably. This analysis is very conservative except for the fact that correlation was ignored. If the 1,500 annual (expected) cases are spread uniformly across the 400 hospitals and 1200 physicians, the effect of within-hospital correlation will be small.

D6. Study 4: Sustainability

D6a. Purpose. Study 4 addresses the third specific aim: to assess the organizational, network, and environmental factors associated with the sustainability of a federally funded national PBRN in community-based practice settings. Research questions include: (a) how do organizational factors like leadership stability and research staff turnover affect CCOP organization survival and performance; (b) how do network factors like the number and types of clinical trials available and the geographic proximity of CCOP organizations to each other affect CCOP survival and performance; and (c) how do local environmental factors like provider competition and market consolidation affect CCOP organization survival and performance? Organizational sustainability depends on both an adequate, steady flow of external resources and an ongoing, predictable internal allocation of those resources to structures and practices that maintain the organization's productive capacity. Factors that reduce or disrupt external and internal resource flows are expected to have a detrimental effect on the CCOP organization survival and performance. For CCOP organizations, key resources include funding, study participants, physician referrals, willing oncologists, qualified research staff, and clinical trials.

This study will build on our earlier work [71] by (1) analyzing all CCOPs during the observational period rather than only the CCOP organizations that were continuously active, (2) incorporating additional variables shown to be associated with CCOP performance, (3) extending the study to more current years (1991-2003), and (4) refining several measures. As a result, Study 4 will provide the NIH a more comprehensive, detailed picture of how "real world" factors affect the sustainability of PBRNs like the CCOP.

D6b. Design and Sample. Study 4 will employ a single-group, longitudinal design. The CCOP organization will be the unit of observation, with data for each observation-year. The observation period begins in 1991 and ends in 2003. Data availability constrains the observation period on both ends. CCOP organizations are included in the sample if they serve an adult population and serve at least one Metropolitan Statistical Area (MSA), as determined by the location of participating provider organizations. The sample is limited by the first criterion because the cancer clinical research on pediatric populations is widely acknowledged to differ from that on adult populations [122, 136, 137]. One CCOP organization is excluded for this reason. The sample is limited by the second criterion because many environmental variables need to be paired to match the realities of CCOP operations, which see patients enrolled not only by staff in hospitals and clinical practices, but also by clinical research associates who commonly enroll participants at many locations throughout the CCOP service area, particularly for CP/C trials. Two CCOP organizations are excluded for this reason. Applying these sampling criteria, the Year 1 sample consists of 49 CCOP organizations. Fourteen CCOP organizations exited the CCOP program during the observation period. Eighteen CCOP organizations joined the CCOP program during the observation period. The sample size averages 50 CCOP organizations per year. We expect to have a total of 650 observation-years available for statistical analysis.

D6c. Data Sources. The NCI's Cancer Therapy Evaluation Program (CTEP) clinical trials database will supply data on the dependent variables: CCOP organization's clinical trials accrual. Several secondary data sources will provide data on independent and control variables:

- CCOP grant progress reports (see Section D4d) will provide data on CCOP structure, operations, pharmaceutical trials participation, and financial and in-kind support from provider organizations.

- The American Hospital Association (AHA) Annual Survey of Hospitals will provide data on market-level hospital competition and consolidation and control variables pertaining to hospital service provision and other characteristics. Administered in the fourth quarter of every year to all AHA registered and non-registered facilities, the Annual Survey contains over 600 variables regarding hospital organizational structure, facilities, services, beds, utilization, finances and staffing**.**
- The Area Resource Files (ARF) will supply data on local health resources as well as control variables pertaining to local population characteristics. Updated annually, the ARF is a rich source of county-specific information on health professions, health facilities, utilization, expenditures, population characteristics, economic data, local environment characteristics, and health professions training**.**
- Finally, the AMA Physician Masterfile (see Section D5c) will provide data on the demographic, educational, and current practice of physicians in a CCOP organization's service area.

D6d. Data Collection Strategy. The NCI will make available the CCOP grant progress reports and CTEP accrual data, both of which we have used in previous studies [34, 71]. Previously collected data from CCOP grant progress reports will be augmented with data manually extracted by two research associates. The UNC Sheps Center for Health Services Research will make available previous years of AHA Annual Survey and the ARF data. The AMA Physician Masterfile and one year of AHA Annual Survey data will be purchased. Portions of CCOP progress reports will be photocopied over by a research assistant who will travel to the NCI. Data will be extracted from these copies over a two month period and will augment previously collected data. Annual CCOP accrual activity will be mapped to counties and MSAs, and will serve as the primary determinant for linking to environmental data available electronically in secondary data sets.

D6e Measures. Sustainability will be measured in terms of CCOP organization performance (i.e., accrual) and survival (i.e., whether or not the CCOP organization exited the CCOP program and ceased operations). Two performance measures will be examined: treatment trial accrual, and CP/C trial accrual. Based on our earlier work, we suspect that the sustainability of these treatment research performance and CP/C research performance depends on differing factors. Primary independent variables will include measures of resource availability (e.g., inputs like clinical trials, study participants, and health professionals), resource predictability (e.g., changes in hospital/provider market structure), and CCOP organization productive capability (e.g., leadership stability, staffing turnover, and maintenance of implementation policies and practices). Appendix B describes the measures we propose to use. Our prior work suggests that (a) dependent variables will exhibit no missing data; (b) independent variables will demonstrate 5 to 15 percent missing data; (c) missing data will be missing-at-random. We will use multiple imputation procedures to handle missing data [138]. Environmental measures will be calculated using previously described methods [71].

D6f. Data Analysis. The main outcome is observed at the CCOP organization level and year. For the *i*th CCOP organization in the *j*th year, let Y_{ij1} be the number of treatment accruals and let Y_{ij2} be the number of CP/C accruals. Associated with Y_{ijk} will be a vector x_{ijk} of covariates representing CCOP organizational, network, and environmental characteristics, and year. X_{ij1} and x_{ij2} will be the same covariates, but can be allowed to differ. We expect 50 CCOP organizations, each with about 13 years of data. All CCOPs will enter the analysis, including those with less than 13 years of data. The general model for the mean accrual $\mu_{ijk} = E[Y_{ijk}]$ has the form, $\log\mu_{ijk} = x_{ijk}^{\mathsf{T}}\beta_k$, where the components of β_k are the effects of the different covariates on treatment ($k = 1$) and CP/C ($k = 2$) accrual. The variance will be assumed proportional to the mean $\text{var}(Y_{ijk}) = \phi_k\mu_{ijk}$, and the dispersion factors ϕ_k will be estimated. The model fit will be separate for treatment ($k = 1$) and CP/C ($k = 2$) accruals.

The models for $k = 1$ and $k = 2$ can be combined to obtain a model for how CCOP organizations allocate their resources to the different types of accrual:

$$\text{logit}\frac{\mu_{ij1}}{\mu_{ij1}+\mu_{ij2}} = \log\frac{\mu_{ij1}}{\mu_{ij2}} + x_{ij1}^{\mathsf{T}}\beta_1 - x_{ij2}^{\mathsf{T}}\beta_2$$

If $x_{ij1} = x_{ij2} = x_{ij}$, the above reduces to

$$\text{logit}\frac{\mu_{ij1}}{\mu_{ij2}} = x_{ij}^{\mathsf{T}}(\beta_1 - \beta_2)$$

We will also examine resource allocation using a model for the proportion π_{ij} where $E[Y_{ij1}|Y_{ij1} + Y_{ij2} = m] = m\pi_{ij}$. It has the logistic form $\text{logit}(\pi_{ij}) = x_{ij}^T\gamma$. Estimation will be through a logistic regression model allowing for extra-binomial variation in Y_{ij1} at each time point, and correlation across time points. The correlation of outcomes within a CCOP organization over time will be assumed to follow a first-order autoregressive, AR(1), structure and will be taken into account using GEE.

Survival analysis methods will be applied to model CCOP survival as a function of covariates. Survival time is defined as the time from CCOP organization formation to program dropout (dissolution). All CCOP organizations active at the beginning of the study will enter the risk sets at their respective "age" (not at time 0). This definition of survival time and risk sets avoids the problem of length-biased sampling (longer surviving CCOPs more likely to be observed). The risk of dropping out will be modeled by a proportional-hazards model with time-dependent covariates. Due to the small number of events, we will estimate one covariate at a time.

D6g. Power Analysis. The data for each of the 50 CCOP organizations is a short time series of length 13 (plus a few CCOP organizations with a shorter series). There are two types of covariates: between-CCOP-organization covariates and within-CCOP-organization covariates. To simplify power computations, we assume that the series have been transformed to constant variance, σ^2 (e.g., via a square root transformation). We also assume an AR(1) correlation structure with lag-1 correlation of 0.2, which is reasonable based on similar outcomes [139]. For CCOP-organization level covariates, the mean of 13 observations (which is nearly the optimal linear combination) has variance $\sigma^2/9$. With 25 CCOP organizations per group, the contrast between group means has a standard error 0.094σ, leading to power of 80% for a difference of $\sigma/4$. For within-CCOP-organization covariates the same power is attained at smaller differences because the within-CCOP-organization contrasts have smaller variance due to the positive correlation.

D7. Study 5: Business Case for CCOP Participation

D7a. Purpose. Study 5 addresses the fourth specific aim: to develop a model and produce practical tools for community-based provider organizations to evaluate the business case for participating in a federally funded national PBRN. The *model* will include a delineation of a conceptual framework, major constructs and financial and non-financial components. The *tools* will be spreadsheets that provider organizations can use to evaluate the business case for CCOP participation. Achieving this aim will require answering four questions: (1) to what extent do provider organizations subsidize CCOP operations, and how is the subsidization distributed among provider organizations; (2) what are the investment costs incurred by provider organizations during the implementation of a CCOP; (3) what are the recurrent incremental cash flows (i.e., financial benefits and operating costs) credited to individual provider organizations as a result of CCOP participation; and (4) what are the non-financial effects of CCOP participation (e.g., marketing value, physician recruitment and retention value)? Provider organizations can use the resulting model and decision making tool to measure the financial impact of CCOP implementation or continued participation, either retrospectively or prospectively.

D7b. Design and Sample. Study 5 employs a case study design. Sampling, data collection, and analysis will occur at two levels: the CCOP organization and the participating provider organization. At the CCOP organization level, the sample will consist of 5 CCOP organizations that reflect differences in CCOP age, geographic location, and degree of centralization. At the provider organization level, one hospital and one physician practice will be selected from each of the 5 CCOP organizations for in-depth analysis. The primary selection criteria for hospitals and physician practices will be willingness to participate and the ability to provide necessary financial data. Table 5 summarizes our sampling strategy. We do not anticipate any recruitment difficulties (see Appendix C for letters of support).

Table 5. Distribution of Provider Organizations by CCOP Age, Location, and Centralization

One CCOP Per Category:	Number of Hospitals	Number of Physician Practices	TOTAL
Start-up	1	1	**2**
Rural, Centralized	1	1	**2**
Rural, Decentralized	1	1	**2**
Urban, Centralized	1	1	**2**
Urban, Decentralized	1	1	**2**
TOTAL	**5**	**5**	**10**

D7c. Data Sources and Data Collection Strategy. CCOP progress reports (see Section D4d) will provide data on CCOP organization age, geographic location, and degree of centralization (e.g., distribution of CCOP research staff across provider organizations). CCOP progress reports and telephone interviews with CCOP Principal Investigators and CCOP Administrators will provide information about financial flows and non-financial benefits. Primary data collection will supply much of the data at the provider organization level. While CCOP annual progress reports provide data on certain costs incurred at the provider organization level, these reports do not routinely include data on incremental recurrent operating revenues, avoided costs, and non-financial benefits accruing to provider organizations as a result of CCOP participation.

At the provider organization level, primary data collection will occur through one site visit to each of the 5 CCOP organizations in the sample, *supplemented by follow-up telephone or e-mail communication as needed*. Twelve weeks prior to a site visit, we will first contact the CCOP PI and CCOP Administrator to identify appropriate *provider organizations and contact persons at those organizations. We will then immediately contact the provider organizations' Chief Financial Officers (CFOs) or delegates to determine their willingness and ability to provide necessary financial data. Eight weeks prior to our site visit we will mail or e-mail a set of financial data collection instruments and a list of all financial data requests so that the CFOs or their delegates can identify appropriate accounting and/or finance personnel to extract financial data. Four weeks prior to a site visit,* we will mail to each interview participant our proposed interview questions. Over a two- to three-day site visit, the team will conduct one-hour interviews with 4-5 individuals at each provider organization (N = 8-10 per CCOP organization), *and will work with finance and accounting personnel to collect financial data.* Individuals interviewed will vary somewhat across provider organizations as a function of differences in CCOP organization size and complexity, but generally will include: (a) for hospitals, the hospital's CFO, cancer service-line executives, and selected research nurses, CRAs, and data managers; and (b) for physician practices, the financial or business manager, research nurses, and physicians listed as CCOP investigators. Using a semi-structured interview guide tailored to the expertise of each individual, we will obtain information about *perceived* incremental costs and revenues, as well as non-financial benefits, accruing to provider organizations as a direct result of CCOP participation. *We will supplement interview results with actual financial data collected from the organizations' accounting and finance records. For the interviews,* one team member will conduct the interview while the other types the participant's responses into Microsoft Word. With permission, interviews will be audio-taped and later transcribed verbatim*. For financial data, each organization will be given the option of completing the financial data collection templates, or providing the necessary accounting and finance records for our research team to complete the templates. Any information that cannot be collected during the site visit will be requested through follow-up phone calls or e-mails with appropriate accounting and finance personnel.*

D7d. Data Analysis. For our CCOP-organization-level analysis, we will construct a database containing all revenues and costs reported on the most recent CCOP annual progress report and by the CCOP PI or Administrator to determine the level of support provided by NCI and the level of subsidization by provider organizations. We will compare and contrast both the total costs of CCOP operation, as well as the costs not reimbursed by NCI, across CCOPs to look for differences by CCOP age, location and degree of centralization. We will also examine CCOP operating costs by natural classification (i.e. salaries, office space, travel, etc.) in order to understand the primary cost drivers among the 5 sampled CCOPs. Using the same data, we will attempt to trace both costs and revenues back to the individual provider organizations to determine the level of subsidy provided by each participating organization. The results of this analysis will be used to construct a model that will delineate a conceptual framework, major constructs, and financial and non-financial components of the business case for CCOP participation.

For our provider-level analysis, the general method that will be used in the financial analysis is:

$$\text{Incremental } CF_t = CF_{t(\text{with CCOP intervention})} - CF_{t(\text{without CCOP intervention})}$$

The relevant cash flows (CF) in any time period, t, to consider when evaluating CCOP participation, are the incremental cash flows. Incremental cash flows are defined as the difference between the organization's cash flows in each period with CCOP participation and an estimate of what the organization's cash flows would have been in each period without CCOP participation.

We will use our estimates of the incremental revenues and costs accruing to each provider organization as a result of CCOP participation to calculate an annual "net incremental cash flow" for each organization. This

"net incremental cash flow" may be positive or negative depending on whether the financial benefits of CCOP participation exceed or are less than the costs. We will compare our "net incremental cash flow" estimates across types of provider organizations (i.e., hospital versus physician practice) and CCOP organizations (i.e., startup or existing, urban or rural, and centralized or decentralized). For each provider, Net Present Value [NPV] (a method of quantifying financial return on investment) will be calculated. NPV compares the present values of all of the net incremental cash inflows and outflows over a specified time period. A positive NPV means that the cash inflows exceed the cash outflows, which adds value to the provider. Our spreadsheet tools will include sensitivity analysis to allow users to assess the impact of various assumptions on NPV.

To construct the tools, we will use historical data about: capital expenditures; staffing and training; policy development required to support CCOP implementation; recurrent incremental operating costs and revenues; and recurrent incremental cost avoidance resulting from CCOP participation at each organization. We expect that incremental operating costs and revenues will arise from two main sources: (1) costs and revenues associated with maintaining research infrastructure, and (2) costs and revenues associated with direct patient care. Since incremental treatment costs and related reimbursement vary widely across patients and trials, and because the estimation of such costs and revenues would require complex matching of patients, our analysis will not focus on estimating (2) the incremental patient care costs associated with trial participation. Rather, the primary focus of our financial analysis will be (1) research infrastructure cash flows. However, we will consider incremental costs incurred in determining a patient's eligibility for, and enrolling a patient in a clinical trial if an organization otherwise would not have participated in clinical trials. Further, we will utilize findings in the literature [135] to estimate nonreimbursed trial-related clinical costs if our interviews suggest that this is an important financial consideration. We will also investigate providers' perceptions of the effect of CCOP participation on their competitiveness in obtaining industry-sponsored trials, and the importance of these trials as sources of subsidy. The effect of CCOP participation on incremental revenues arising from industry sources will be quantified (where possible) or included as a non-financial benefit.

Following previous business-case studies, the non-financial benefits accruing to provider organizations participating in the CCOP will not be monetized. Rather, non-financial benefits will be explored in interviews and documented with no attempt to assign a dollar value to these benefits. From interview data we will develop a comprehensive list of the non-financial benefits of participation and then look for similarities in responses across organizations and CCOPs. Also consistent with previous business-case studies, financial and/or non-financial benefits accruing to organizations or individuals outside of the provider organization will be excluded. For example, there are clearly significant benefits to patients and society of providers' participation in the CCOP; however, we are interested in the financial consequences of participation at the level of the business unit making the investment decision – in this case the individual provider organization.

A diagrammatic representation of our approach, a detailed accounting of the types of financial and non-financial information that we expect to collect, and examples of the types of data collection instruments we intend to use can be found in Appendix B. All tools and financial analyses that are developed during the course of this study will be circulated back to the provider organizations for verification of accuracy as well as to obtain comments to improve usability. Further, new knowledge obtained from the business case analyses about the flows of CCOP-related costs and revenues within provider organizations will be incorporated into the model and conceptual framework developed as part of our CCOP-level analysis.

D8. Design Issues

At the project level, the core design issue is: To what extent can the knowledge generated through this project be applied beyond the CCOP? External validity refers to the extent to which it is reasonable to apply knowledge beyond the specific people, places, settings, and times from which it was generated [101]. External validity is always a claim whose truth value can only be determined through further testing (research) or application (practice). To help others assess the reasonableness of applying project findings beyond the CCOP, we offer a "proximal similarity model" [101] that identifies two theoretically important gradients: (1) the type of clinical research conducted by the PBRN, and the strength of the science upon which it is based, and (2) the level of federal support provided to the PBRN (see Appendix B for a visual representation). The more proximal a PBRN is to the CCOP on these on these gradients, the greater the reasonableness of applying project findings.

Two factors increase our confidence in the transferability of project findings. First, as noted above, the NIH already considers the CCOP as a model for successfully developing PBRNs in other disease areas. Second,

the recently released results of the NIH-funded survey, Inventory and Evaluation of Clinical Research Networks (IECRN), indicate that many of the clinical research networks funded by the NIH share with the CCOP key organizational features with respect to funding, design, and operation [140]. This means that many NIH-funded clinical research networks are proximally similar to the CCOP.

In the remainder of this section, we discuss one or two of the key design issues facing each study.

D8a. Study 1. Study 1 will employ several strategies to minimize multiple threats to validity (see Appendix B). Case study research does not employ statistical sampling methods that permit generalization to larger populations based on probability theory. This would pose a serious problem if the objective of Study 1 was to generate a statistically representative description of the CCOP or other types of PBRNs. This is not the objective. Rather, Study 1 aims to produce a theoretically informed, empirically grounded organizational model of implementation processes that is sufficiently generic to permit further testing in future studies and, we hope, sufficiently detailed to prove useful to others as a tool for process evaluation and managerial intervention.

D8b. Study 2. Study 2 depends on achieving high enough intra-organizational response rates and sufficient intra-organizational homogeneity of respondents' perceptions to justify aggregation of individual responses to the organizational level. If problems arise, we will (a) include response rate as a predictor in our models, (b) include measures of variability in our models, and, if these options do not work, (c) consider estimating a two-part model to test an individual-level theory of implementation that has similar constructs (i.e., Ventakesh's Unified Theory of Technology Acceptance [141]). Given the maturity of implementation in most CCOP organizations, a second wave of data collection would not help to discount the possibility of endogeneity in the relationship of implementation climate and innovation effectiveness. Instead, we will rely on theory, literature, and longitudinal findings from the case studies (Study 1) to sort out the temporal ordering of study constructs.

D8c. Study 3. Studies suggest that the SEER-Medicare data accurately captures specific courses of treatment for cancer surgery [142] and radiation therapy [143]. Good sensitivity exists in regard to identifying chemotherapy use overall, though varied sensitivity in the ability to identify specific drugs [144]. Steps have been taken to minimize the effect of this varied sensitivity (see Appendix B). Study 3 is limited to evidence-based cancer treatments that are specifically identifiable, FDA approved, and directly reimbursed by Medicare. Not all cancer treatments meet these criteria. Study 3 is also limited to CCOP organizations practicing in SEER regions. Although SEER regions are representative of the US, they are not a random sample. Statistical methods will be applied to control for location-specific characteristics that might cause differences in adoption rates. Finally, CCOP participation is not random. Although we will match the CCOP-affiliated and non-CCOP-affiliated providers on multiple variables, the two groups might still differ systematically on unobserved characteristics. To address this concern, we will explore with NCI/DCP the feasibility of constructing comparison groups consisting of physicians and hospitals who participated but then dropped out of the CCOP, as well as physicians and hospitals who applied unsuccessfully for CCOP funding. These small, but interesting comparison groups might yield useful information about possible selection bias.

D8d. Study 4. Although Study 4 includes nearly all CCOP organizations active anytime from 1991 through 2003, the sample size places an upper limit on the statistical power of the models. This raises the risk of omitted variables bias, although statistical methods will be applied to minimize this risk. The small number of CCOP organizations that exit the program also limits the study's ability to model the factors affecting CCOP organization survival. We suspect, however, that program exit and subsequent dissolution of the CCOP organization is largely a function of poor performance. That is, CCOP organizations get de-funded and dissolve due to failure to meet the minimum performance standards set by NCI/DCP. If so, then the factors that predict program exit and dissolution are likely to be the same factors that predict poor performance.

D8e. Study 5. The principal threats to validity are: (1) the retrospective nonrandomized nature of the study, (2) the lack of a control group, and (3) the lack of a "clean" starting point for implementation. These limitations make it difficult to ensure that findings can be attributed to CCOP participation versus other market trends or conditions. We will try to minimize the risk of incorrect attribution by clearly focusing on *incremental* cash flows during data collection. Despite these limitations, the case study approach is the current state-of-the-art method for collecting the breadth and depth of financial information necessary for business case analysis.

D9 Project Management Plan and Timetable

Dr. Weiner (PI) and Dr. Godley (Co-PI) will manage the project with assistance from a full-time, *highly experienced* project manager. Dr Weiner will provide scientific leadership for Studies 1 and 2, Drs. Godley and Carpenter for Study 3, Dr. Lee for Study 4, and Drs. Pink and Reiter for Study 5. Although *conceptually*

integrated, the five studies possess few task interdependences that would affect their timing or sequencing. Work flow (see Table 6) is driven by the design characteristics of each study, the desire to minimize the burden on the study population, and the smoothing of demand on the project's resources. *Although the proposed project involves many "moving parts," several factors assure that the project will move forward at the pace described below. These factors include: (a) the dense network of working relationships that already exist among investigators (see Appendix A); (b) the full-time effort of a project manager with many years experience managing complex research projects (see budget justification); (c) the highly supportive environment of the Sheps Center for investigators managing complex research projects; (d) the use of customized project management software to monitor progress; (e) the use of monthly project meetings to increase coordination, communication, and mutual accountability; and (f) the close physical proximity of investigators' offices.*

Table 6. Timetable Overview

	Year 1				Year 2				Year 3				Year 4				Year 5			
	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4
Study 1: Startup, Early Implementation																				
Study development	■																			
Data collection	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Data analysis		■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Dissemination activity				■				■				■				■				■
Study 2: Mature Implementation																				
Study development													■	■						
Data collection															■	■	■	■		
Data analysis																■	■	■	■	
Dissemination activity																			■	■
Study 3: Impact																				
Study development	■	■																		
Data collection	■	■	■	■	■	■														
Data analysis						■	■	■	■	■	■	■	■	■	■	■	■	■		
Dissemination activity									■	■		■	■			■	■	■	■	■
Study 4: Sustainability																				
Study development	■	■																		
Data collection	■	■	■																	
Data analysis			■	■	■															
Dissemination activity					■	■														
Study 5: Business Case																				
Study development	■	■	■	■																
Data collection	■	■	■		■	■	■	■	■	■	■	■	■							
Data analysis		■	■	■	■		■	■	■	■	■	■	■	■	■	■	■			
Dissemination activity								■				■			■	■	■	■	■	■

D10. Products and Dissemination Strategy

We will disseminate templates, tools, and information to assist those seeking to close the discovery-delivery gap through PBRNs. First, we will use the within-case analyses from Study 1 to produce templates that schematically depict the activities that CCOP organizations engaged in during start-up and early implementation. The templates will describe the multiple pathways for implementing a PBRN. Second, we will produce a web-based "toolkit" to assist PBRNs with implementation. We will solicit ideas for tools from Scientific Advisory Board members and others. We will certainly include the spreadsheets developed in Study 5 that enable provider organizations to evaluate the business case for PBRN participation. We suspect that provider organizations would value tools for assessing organizational readiness for change, implementation climate, and other drivers of implementation effectiveness. We will refine our data collection instruments and transform them into practical tools [145]. We will disseminate these templates and tools by posting them on the Sheps Center's website. Also, we will describe the templates and tools and present regular updates of study findings at meetings with NCI/DCP officials, meetings of the Society for Clinical Trials, and other venues.

E. HUMAN SUBJECTS

Each of the studies in the proposed project has its own human-subjects considerations. Therefore, we discuss each study separately.

E1. Study 1

E1a. Risks to Subjects

E1a1. Human Subjects Involvement and Characteristics. Study 1 will involve interviews with 24-30 individuals from three CCOP organizations per year over the five-year study period. The exact number and type of individuals interviewed will vary somewhat across CCOP organizations due to differences in organizational size and complexity. However, we anticipate conducting 8-10 individual interviews per CCOP organization. Interview participants will include the CCOP Principal Investigator, Associate Principal Investigator, Administrator, research nurses and Clinical Research Associates, oncologist and non-oncologist physicians listed as CCOP investigators, and CCOP hospital leaders such as cancer service-line executives.

E1a2. Sources of Materials. Data for this project will be obtained through individual interviews and CCOP grant applications and annual progress reports.

E1a3. Potential Risks. The primary risk to subjects participating in this research project is a breach of confidentiality. Protection against this risk is discussed below.

E1b. Adequacy of Protection against Risks

E1b1. Recruitment and Informed Consent. The PI will send a letter to the Principal Investigator of each participating CCOP organization to confirm his or her organization's willingness to participate in the research study. Upon receiving an affirmative response, the PI will contact by telephone the CCOP PI or the CCOP Administrator to discuss site visit logistics and selection criteria for interview participants. The PI will provide the CCOP PI and/or the CCOP Administrator with a draft email (or letter) that he or she may use to obtain the permission of potential interview candidates for the Principal Investigator to contact them. The PI will explicitly encourage the CCOP PI and/or CCOP Administrator to include women and people of color in the list of potential interview candidates. Upon receiving permission to contact them, the PI (or a designated research staff member) will telephone or email the potential interview candidates to describe the study in more detail and schedule an interview. Two weeks prior to the interview, the PI will ask the interview participant to read and sign an informed consent letter. For the virtual site visits, the PI will conduct the interviews using EduFolio, a web-based videoconferencing software application, currently used by the Department of Health Policy and Administration in its distance learning courses. To initiate an interview, interview participants will access the EduFolio web-page set up for this research project using an authorized user-name and password. EduFolio will enable the PI and the interview participant to see and hear each other. The PI will electronically restrict access to the interview session to the interview participant alone.

E1b2. Protection against Risk. The primary risk to subjects participating in this research project is a breach of confidentiality. The risk of such a breach will be minimized through appropriate training of all study personnel regarding confidentiality. All study personnel will complete training and obtain certification in human-subjects protection. In addition, all research personnel will submit to the PI a signed copy of the UNC IRB-approved "Responsibilities of Staff in Human Subjects Research" form. In doing so, research personnel agree to abide by the informed consent process approved by the Institutional Review Board. They also agree not to divulge, publish, or otherwise make known to unauthorized persons or to the public any information obtained in the course of this study that could identify the persons who participated in the study. Tape recordings of interviews will be erased upon completion of the project. Electronic and hard copies of interviewer notes and other data will be stored without personal identifiers on password-protected laptops, on secure computer servers, and in locked filing cabinets. Each study participant will be assigned a unique identification number. A master list linking names and identification numbers will be stored separately from project data. Only the PI will possess the master list. Access to electronic and hard copies of notes and other data will be restricted to project members only. Oral presentations and written reports drawing on the data will contain no identifying information linking individuals to specific comments.

E1c. Potential Benefits of Proposed Research to Subjects and Others

Study participants can expect to benefit from this research project to the extent that the knowledge gained facilitates the implementation the CCOP. At an organizational level, the three participating CCOP organizations will receive a written report each year summarizing the case study findings to date. Although the report will

describe study findings at aggregate level, it will include recommendations tailored to each CCOP organization for enhancing the implementation of the CCOP intervention. Each participating CCOP organization will receive $500 per year to offset the administrative costs associated with study participation and to recognize the value of people's time. At an individual level, the study may generate information and recommendations that help some interview participants to perform their organizational roles (e.g., help the CCOP Administrator to develop more effective communication procedures and coordination mechanisms to manage CCOP operations).

E1d. Importance of Knowledge to be Gained

To achieve large-scale improvements in the public's health and substantial reductions in health disparities, the NIH has embarked on a fundamental restructuring of the national clinical research enterprise [1]. Through its Roadmap initiative, "Reengineering the Clinical Research Enterprise," the NIH aims to develop a national system of clinical research networks involving partnerships between academic centers and community-based providers (PBRNs). Developing this national system will entail integrating and expanding PBRNs as well as building new ones [2, 3]. The CCOP has already served as a model for other NIH-supported PBRNs [8], and NCI/DCP officials continue to provide advice to Roadmap steering committees. This study will provide the NIH with much needed information about what it takes to implement successfully a PBRN.

E1e. Women and Minority Inclusion in Clinical Research

Organizational roles determine the types of potential interview candidates for this study (e.g., CCOP PI, CCOP Administrator, research nurses and CRAs, oncologist and non-oncologist physicians listed in CCOP grant progress reports as CCOP investigators). The PI will explicitly encourage the CCOP PI and CCOP Administrator to include women and people of color in the list of potential interview candidates who fill these organizational roles within the CCOP organization.

E1f. Inclusion of Children

Not applicable.

E1g. Data Safety and Monitoring

Although this research involves human subjects, it does not meet the criteria that require specific Data and Safety Monitoring beyond the protection against risks described above. The Institutional Review Board of University of North Carolina at Chapel Hill will be apprised of any untoward events affecting human subjects resulting from this project.

E2. Study 2

E2a. Risks to Subjects

E2a1. Human Subjects Involvement and Characteristics. Study 2 will involve a survey of 13-17 individuals from each of the 50 CCOP organizations (N = 600-900 individuals total). The exact number and type of individuals surveyed will vary somewhat across CCOP organizations due to differences in organizational size and complexity. However, we anticipate that our sample will include: 50 CCOP Principal Investigators, 50 Associate Principal Investigators, 50 CCOP administrators, 400-500 CCOP-affiliated physicians, and 150-250 clinical research staff members (e.g., nurses and Clinical Research Associates).

E2a2. Sources of Materials. Primary data will be collected through a cross-sectional survey. Secondary data sources will include CCOP grant applications and annual progress reports.

E2a3. Potential Risks. The primary risk to subjects participating in this research project is a breach of confidentiality. Protection against this risk is discussed below.

E2b. Adequacy of Protection against Risks

E2b1. Recruitment and Informed Consent. CCOP grant progress reports to construct the sampling frame. The sampling frame will include all CCOP-affiliated physicians eligible to accrue study participants to clinical trials, including the CCOP PI and Associate PI, as well as all clinical research staff members identified in the report as supporting the CCOP organization. With the exception of the CCOP Administrator, we will exclude from the sampling frame CCOP administrative staff members (e.g., data managers). Using this list, we will select 8-10 physicians reflecting different specialties involved in the CCOP organization (e.g., medical oncology, radiation oncology, surgical oncology, and urology) and 4-5 research staff members. For larger CCOP organizations, we will randomly sample within physician and research staff strata.

Contact information for survey respondents will be extracted from the CCOP progress reports. Two weeks prior to the survey mailing, NCI/DCP officials will send a letter to potential survey respondents announcing the impending survey and highlighting its importance to the NCI. For the survey itself, we will seek a waiver of written informed consent from the Institutional Review Board of UNC. Instead, the survey will contain an IRB-

approved cover-page that describes the survey as a research study, outlines the survey respondent's rights and responsibilities with respect to research participation, and informs the respondent that returning the survey is an indication of informed consent. Second and third waves of mailing will include the same cover page.

E2b2. Protection against Risk. The primary risk to subjects participating in this research project is a breach of confidentiality. The risk of such a breach will be minimized through appropriate training of all study personnel regarding confidentiality. All study personnel will complete training and obtain certification in human-subjects protection. In addition, all research personnel will submit to the Project Leader a signed copy of the UNC IRB-approved "Responsibilities of Staff in Human Subjects Research" form. In doing so, students agree to abide by the informed consent process approved by the Institutional Review Board. They also agree not to divulge, publish, or otherwise make known to unauthorized persons or to the public any information obtained in the course of this study that could identify the persons who participated in the study. Electronic copies of data will be stored in password-protected files on secure computer servers, access to which also is network password protected. Hard copies of data will be stored in locked filing cabinets in locked offices. Each study participant will be assigned a unique identification number. A master list linking names and identification numbers will be stored separately from project data. Only the PI will possess the master list. Access to electronic data and hard copies of the completed surveys will be restricted to project members only. Oral presentations and written reports drawing on the data will contain no identifying information linking individuals to specific comments.

E2c. Potential Benefits of Proposed Research to Subjects and Others

Study participants may benefit from this research project to the extent that the knowledge gained facilitates the implementation the CCOP. Each survey respondent will receive $50 compensation for his or her time.

E2d. Importance of Knowledge to be Gained

To achieve large-scale improvements in the public's health and substantial reductions in health disparities, the NIH has embarked on a fundamental restructuring of the national clinical research enterprise [1]. Through its Roadmap initiative, "Reengineering the Clinical Research Enterprise," the NIH aims to develop a national system of clinical research networks involving partnerships between academic centers and community-based providers (PBRNs). Developing this national system will entail integrating and expanding PBRNs as well as building new ones [2, 3]. The CCOP has already served as a model for other NIH-supported PBRNs [8], and NCI/DCP officials continue to provide advice to Roadmap steering committees. This study will provide the NIH with much needed information about what it takes to implement successfully a PBRN.

E2e. Women and Minority Inclusion in Clinical Research

Organizational roles determine the types of individuals included in the sampling frame (e.g., CCOP PI, CCOP Administrator, research nurses and CRAs, and physicians listed in CCOP grant progress reports as CCOP investigators). For smaller CCOP organizations, obtaining the desired number of survey respondents may require surveying all listed CCOP personnel filling these organizational roles. For larger CCOP organizations, survey respondents will be selected through random sampling within physician and research staff strata. The gender and minority distribution of individuals filling the organizational roles listed above is not known at this time.

E2f. Inclusion of Children

Not applicable.

E2g. Data Safety and Monitoring

Although this research involves human subjects, it does not meet the criteria that require specific Data and Safety Monitoring beyond the protection against risks described above. The Institutional Review Board of University of North Carolina at Chapel Hill will be apprised of any untoward events affecting human subjects resulting from this project.

E3. Study 3

E3a. Risks to Subjects

E3a1. Human Subjects Involvement and Characteristics. Study 3 will not directly involve human subjects, instead utilizing a secondary dataset made available to the research community by the NCI's SEER-Medicare Program. The study will involve the analysis of patterns of care of CCOP hospitals and physicians in SEER regions. Individual physicians and hospitals will only be identified for the purposes of determining their participation or non-participation in the CCOP program, for which a binary indicator variable will be constructed. Beyond this point, study hospitals and physicians will be identified through an encrypted unique identifier variable preventing the identification of study hospitals and physicians, including to the research

team. Reporting the results of analysis will be made at a level which not will allow the identification of individual physicians or hospitals. Individual patient identities are strictly protected by the SEER-Medicare Program – individual patients will never be identifiable. There are an estimated 100 CCOP hospitals and 400 CCOP physicians. These will be matched to approximately 300 hospitals and 800 physicians, based on criteria described earlier.

E3a2. Sources of Materials. Secondary data will be purchased from the NCI's SEER-Medicare Program.

E3a3. Potential Risks. The primary risk to subjects of this research project is a breach of confidentiality. Protection against this risk is discussed below.

E3b. Adequacy of Protection against Risks

E3b1. Recruitment and Informed Consent. Secondary data in the form of SEER registry data and Medicare claims have already been collected and are available to the researchers in the form of a secondary data set. The consent of the SEER-Medicare program and each of the SEER Regions' Principal Investigators will be obtained before CCOP participation is determined among physicians and hospitals whose data will be coded in the data and analyzed, as per standard SEER-Medicare Program procedures.

E3b2. Protection against Risk. The primary risk to subjects participating in this research project is a breach of confidentiality. The risk of such a breach will be minimized through appropriate training of all study personnel regarding confidentiality. All study personnel will complete training and obtain certification in human-subjects protection. In addition, all research personnel will submit to the Project Leader a signed copy of the UNC IRB-approved "Responsibilities of Staff in Human Subjects Research" form. In doing so, they agree to abide by the informed consent process approved by the Institutional Review Board. They also agree not to divulge, publish, or otherwise make known to unauthorized persons or to the public any information obtained in the course of this study that could identify the individual physicians and hospitals under study. Each study participant (hospital or physician) has already been assigned a unique identification number. Only the SEER-Medicare Program will be able to identify participants following the determination of their CCOP Program. Oral presentations and written reports drawing on the data will contain no information that would allow the identification of individual hospitals or physicians.

E3c. Potential Benefits of Proposed Research to Subjects and Others

Study participants can expect to benefit from this research project to the extent that the knowledge gained will facilitate the diffusion of cutting-edge cancer care modalities at participant clinics, practices, and hospitals. Future cancer patients and individuals at risk for cancer will benefit through greater health care industry understanding of factors that contribute to the more rapid translation of research into practice.

E3d. Importance of Knowledge to be Gained

To achieve large-scale improvements in the public's health and substantial reductions in health disparities, the NIH has embarked on a fundamental restructuring of the national clinical research enterprise [1]. Through its Roadmap initiative, "Reengineering the Clinical Research Enterprise," the NIH aims to develop a national system of clinical research networks involving partnerships between academic centers and community-based providers (PBRNs). Developing this national system will entail integrating and expanding PBRNs as well as building new ones [2, 3]. The CCOP has already served as a model for other NIH-supported PBRNs [8], and NCI/DCP officials continue to provide advice to Roadmap steering committees. This study will provide the NIH with much needed information regarding the clinical benefits of such PBRN participation.

E3e. Women and Minority Inclusion in Clinical Research

Women and minorities will be included in this research. The research data will be drawn from a dataset of all individuals who were a) diagnosed with cancer in a SEER region, and b) participating in the Medicare program. With the exception of some gender-specific cancers (i.e., breast cancer and prostate cancer), the study will analyze all data on as many individuals as possible, not discriminating on the basis of gender or race.

E3f. Inclusion of Children

Medicare is a government-sponsored health insurance program primarily for the aged. As such, the overwhelming majority of the study population is over the age of 65. The overwhelming majority of the burden of cancer is borne by adults, particularly for the 5 cancers proposed for study. As such, children are not included in the study.

E3g. Data Safety and Monitoring

Although this research involves human subjects, it does not meet the criteria that require specific Data and Safety Monitoring beyond the protection against risks described above. The Institutional Review Board of

University of North Carolina at Chapel Hill will be apprised of any untoward events affecting human subjects resulting from this project.

E4. Study 4

E4a. Risks to Subjects

E4a1. Human Subjects Involvement and Characteristics. Study 4 involves an analysis of secondary data from multiple sources. The study sample consists of all CCOP organizations active between 1991 and 2003. To complete this study, there is no need to identify individuals. However, two of the data sources will contain information about individuals, including their names: CCOP grant progress reports and the AMA Physician Masterfile, which will identify physician participants in the CCOP Program. Moreover, it may be possible to deductively identify individuals through the combination of datasets employed in this study.

E4a2. Sources of Materials. Study 4 will draw upon secondary data from several sources: the NCI's Cancer Therapy Evaluation Program (CTEP) clinical trials database, CCOP grant progress reports, American Hospital Association (AHA) Annual Survey of Hospitals, Area Resource Files (ARF), Group Health Association of America's Managed Care Penetration Dataset, InterStudy Competitive Edge Regional Market Analysis Dataset, and the AMA Physician Masterfile.

E4a3. Potential Risks. The primary risk to human subjects is a breach of confidentiality. Protection against this risk is discussed below.

E4b. Adequacy of Protection against Risks

E4b1. Recruitment and Informed Consent. No recruitment or consent procedures will be employed since the study draws exclusively on existing, secondary data sources.

E4b2. Protection against Risk. A breach of confidentiality is the primary risk to the individuals identified or identifiable through the secondary data used in this study. The risk of such a breach will be minimized through appropriate training of all study personnel regarding confidentiality. All study personnel will complete training and obtain certification in human-subjects protection. In addition, all research personnel will submit to the PI a signed copy of the UNC IRB-approved "Responsibilities of Staff in Human Subjects Research" form. In doing so, research personnel agree to abide by the informed consent process approved by the Institutional Review Board. They also agree not to divulge, publish, or otherwise make known to unauthorized persons or to the public any information obtained in the course of this study that could identify the persons who participated in the study. Electronic copies of data will be stored in password-protected files on secure computer servers, access to which also is network password protected. Hard copies of data will be stored in locked filing cabinets in locked offices. Access to electronic and hard copies of data will be restricted to project members only. Oral presentations and written reports drawing on the data will contain no information permitting the identification of specific individuals.

E4c. Potential Benefits of Proposed Research to Subjects and Others

Study 4 participants can expect to benefit from this research project to the extent that the knowledge gained will help improve future research operations, potentially facilitating their future work..

E4d. Importance of Knowledge to be Gained

To achieve large-scale improvements in the public's health and substantial reductions in health disparities, the NIH has embarked on a fundamental restructuring of the national clinical research enterprise [1]. Through its Roadmap initiative, "Reengineering the Clinical Research Enterprise," the NIH aims to develop a national system of clinical research networks involving partnerships between academic centers and community-based providers (PBRNs). Developing this national system will entail integrating and expanding PBRNs as well as building new ones [2, 3]. The CCOP has already served as a model for other NIH-supported PBRNs [8], and NCI/DCP officials continue to provide advice to Roadmap steering committees. This study will provide the NIH with much needed information about what it takes to sustain a PBRN over a 13-year period.

E4e. Women and Minority Inclusion in Clinical Research

Not applicable.

E4f. Inclusion of Children

Not applicable.

E4g. Data Safety and Monitoring

Although this research involves human subjects, it does not meet the criteria that require specific Data and Safety Monitoring beyond the protection against risks described above. The Institutional Review Board of

University of North Carolina at Chapel Hill will be apprised of any untoward events affecting human subjects resulting from this project.

E5. Study 5

E5a. Risks to Subjects

E5a1. Human Subjects Involvement and Characteristics. Study 5 will involve interviews with 40-50 individuals from five CCOP organizations. The exact number and type of individuals interviewed will vary somewhat across CCOP organizations due to differences in organizational size and complexity. However, we anticipate conducting 8-10 interviews per CCOP organization. Interview participants will include the CCOP Principal Investigator, Associate Principal Investigator, Administrator, research nurses and CRAs, data managers, oncologist and non-oncologist physicians listed as CCOP investigators, and CCOP hospital and physician group leaders such as cancer service-line executives, Chief Financial Officers, and business managers.

E5a2. Sources of Materials. Data for this project will be obtained through individual interviews, examination of providers' financial and utilization records, and CCOP grant applications and annual progress reports.

E5a3. Potential Risks. The primary risk to subjects participating in this research project is a breach of confidentiality. Protection against this risk is discussed below.

E5b. Adequacy of Protection against Risks

E5b1. Recruitment and Informed Consent. The PI will send a letter to the Principal Investigator of each participating CCOP organization to confirm his or her organization's willingness to participate in the research study. Upon receiving an affirmative response, the PI will contact by telephone the CCOP PI or the CCOP Administrator to discuss site visit logistics and selection criteria for interview participants. The PI will provide the CCOP PI and/or the CCOP Administrator with a draft email (or letter) that he or she may use to obtain the permission of potential interview candidates for the Principal Investigator to contact them. The PI will explicitly encourage the CCOP PI and/or CCOP Administrator to include women and people of color in the list of potential interview candidates. Upon receiving permission to contact them, the PI (or a designated research staff member) will telephone or email the potential interview candidates to describe the study in more detail and schedule an interview. The PI will send in advance, to each interview candidate, a copy of the proposed interview questions and data requirements. During the site visit, the PI will ask the interview participant to read and sign an informed consent letter.

E5b2. Protection against Risk. The primary risk to subjects participating in this research project is a breach of confidentiality. The risk of such a breach will be minimized through appropriate training of all study personnel regarding confidentiality. All study personnel will complete training and obtain certification in human-subjects protection. In addition, all research personnel will submit to the PI a signed copy of the UNC IRB-approved "Responsibilities of Staff in Human Subjects Research" form. In doing so, research personnel agree to abide by the informed consent process approved by the Institutional Review Board. They also agree not to divulge, publish, or otherwise make known to unauthorized persons or to the public any information obtained in the course of this study that could identify the persons who participated in the study. Tape recordings of interviews will be erased upon completion of the project. Electronic and hard copies of interviewer notes and other data will be stored without personal identifiers on password-protected laptops, on secure computer servers, and in locked filing cabinets. Each study participant will be assigned a unique identification number. A master list linking names and identification numbers will be stored separately from project data. Only the PI will possess the master list. Access to electronic and hard copies of notes and other data will be restricted to project members only. Oral presentations and written reports drawing on the data will contain no identifying information linking individuals to specific comments.

E5c. Potential Benefits of Proposed Research to Subjects and Others

Study participants can expect to benefit from this research project to the extent that the knowledge gained increases understanding of, and provides a tool for evaluating, the financial implications of CCOP participation. The five participating CCOP organizations will receive: (1) a written report summarizing our conceptual model and aggregate case study findings, and (2) a toolkit composed of a series of spreadsheets that can be used to evaluate the business case for CCOP participation. In addition, each participating provider organization will receive the toolkit described above and a written report detailing the findings of our business case analysis. Each participating CCOP organization will receive $500 to offset the administrative costs associated with study participation and to recognize the value of people's time. At an organizational level, the study may generate

information and recommendations that help increase the financial value to provider organizations of participating in the CCOP (e.g., information about organizational characteristics that reduce costs).

E5d. Importance of Knowledge to be Gained

To achieve large-scale improvements in the public's health and substantial reductions in health disparities, the NIH has embarked on a fundamental restructuring of the national clinical research enterprise [1]. Through its Roadmap initiative, "Reengineering the Clinical Research Enterprise," the NIH aims to develop a national system of clinical research networks involving partnerships between academic centers and community-based providers (PBRNs). Developing this national system will entail integrating and expanding PBRNs as well as building new ones [2, 3]. The CCOP has already served as a model for other NIH-supported PBRNs [8], and NCI/DCP officials continue to provide advice to Roadmap steering committees. This study will provide the NIH with much needed information about what it costs to implement successfully a PBRN.

E5e. Women and Minority Inclusion in Clinical Research

Organizational roles determine the types of potential interview candidates for this study (e.g., CCOP PI, CCOP Administrator, research nurses and CRAs, data managers, oncologist and non-oncologist physicians listed in CCOP grant progress reports as CCOP investigators, hospital and physician group leaders). The PI will explicitly encourage the CCOP PI and CCOP Administrator to include women and people of color in the list of potential interview candidates who fill these organizational roles within the CCOP organization.

E5f. Inclusion of Children

Not applicable.

E5g. Data Safety and Monitoring

Although this research involves human subjects, it does not meet the criteria that require specific Data and Safety Monitoring beyond the protection against risks described above. The Institutional Review Board of University of North Carolina at Chapel Hill will be apprised of any untoward events affecting human subjects resulting from this project

G. LITERATURE CITED

1. Zerhouni, E.A., *Translational and clinical science--time for a new vision.* N Engl J Med, 2005. **353**(15): p. 1621-3.
2. Zerhouni, E.A., *US biomedical research: basic, translational, and clinical sciences.* Jama, 2005. **294**(11): p. 1352-8.
3. Zerhouni, E., *Medicine. The NIH Roadmap.* Science, 2003. **302**(5642): p. 63-72.
4. Kutner, J.S., et al., *The practice-based research network as a model for end-of-life care research: challenges and opportunities.* Cancer Control, 2005. **12**(3): p. 186-95.
5. Wasserman, R., E. Slora, and A. Bocian, *Current status of pediatric practice-based research networks.* Curr Probl Pediatr Adolesc Health Care, 2003. **33**(4): p. 115-23.
6. Lindbloom, E.J., B.G. Ewigman, and J.M. Hickner, *Practice-based research networks: the laboratories of primary care research.* Med Care, 2004. **42**(4 Suppl): p. III45-9.
7. LeBailly, S., et al., *The origin and evolution of a regional pediatric practice-based research network: practical and methodological lessons from the Pediatric Practice Research Group.* Curr Probl Pediatr Adolesc Health Care, 2003. **33**(4): p. 124-34.
8. Lamb, S., M.R. Greenlick, and D. McCarty, eds. *Bridging the Gap Between Practice and Research*. ed. Institute of Medicine. 1998, National Academy Press: Washington, DC.
9. Lenfant, C., *Shattuck lecture--clinical research to clinical practice--lost in translation?* N Engl J Med, 2003. **349**(9): p. 868-74.
10. Lenfant, C., *Claude Lenfant, MD: retiring NHLBI director looks ahead. Interviewed by Brian Vastag.* Jama, 2003. **290**(8): p. 1017-8.
11. Clanton, M. *Moving Discovery through to Delivery: A Critical Opportunity for Leadership and Partnership*. Dialogue on Dissemination [Powerpoint Presentation] 2005 [cited 2005 December 1]; Available from: http://cancercontrol.cancer.gov/d4d/info_dod.html.
12. *Designing for Dissemination Conference Summary Report*. 2002 [cited 2005 December 1]; Available from: http://cancercontrol.cancer.gov/d4d/info_dod.html.
13. *Making Cancer Health Disparities History--Report of the Trans-HHS Cancer Health Disparities Progress Review*. 2004 [cited 2005 December 1]; Available from: www.hhs.gov/chdprg/pdf/chdprg.pdf.

14. Warnecke, R.B. and A.D. Kaluzny, *The Challenges of Improving Cancer Care*, in *Managing a Health Care Alliance: Improving Community Cancer Care*, A.D. Kaluzny and R.B. Warnecke, Editors. 2000, Beard Books: Fredrick, MD.
15. Bodenheimer, T., et al., *What are the facilitators and barriers in physician organizations' use of care management processes?* Jt Comm J Qual Saf, 2004. **30**(9): p. 505-14.
16. Rothman, A.A. and E.H. Wagner, *Chronic Illness Management: What Is the Role of Primary Care?* Ann Intern Med, 2003. **138**(3): p. 256-261.
17. Institute of Medicine, *Reducing Risks for Mental Disorders: Frontiers for Preventive Intervention Research*. 1994, Washington, DC: National Academy Press.
18. Crump, C.E., et al., *Effect of organization-level variables on differential employee participation in 10 federal worksite health promotion programs.* Health Educ Q, 1996. **23**(2): p. 204-23.
19. Bero, L.A., et al., *Closing the Gap Between Research and Practice: An Overview of Systematic Reviews of Interventions to Promote the Implementation of Research Findings. The Cochrane Effective Practice and Organization of Care Review Group.* British Medical Journal, 1998. **317**(7156): p. 465-8.
20. Grimshaw, J.M. and I.T. Russell, *Effect of Clinical Guidelines on Medical Practice: A Systematic Review of Rigorous Evaluations.* Lancet, 1993. **342**(8856): p. 1317-1322.
21. Grimshaw, J.M., et al., *Changing Provider Behavior: An Overview of Systematic Reviews of Interventions.* Medical Care, 2001. **39**(8 Suppl 2): p. II2-45.
22. *Practice-Based Research Networks*. 2005 [cited 2006 January 18]; Available from: http://www.nidcr.nih.gov/Research/Extramural/ClinicalResearch/GeneralPracticeBasedResearchNetworks.htm.
23. *Fact Sheet: Primary Care Practice-Based Research Networks*. 2001 [cited 2006 January 18]; Available from: http://www.ahrq.gov/research/pbrnfact.htm.
24. Shine, B. (2004) *Blending Reseach and Practice: CTN Update*. NIDA Notes **Volume**,
25. *Executive Summary NHLBI Working Group Clinical Heart Failure Research Network*. 2004 [cited 2006 January 18]; Available from: http://www.nhlbi.nih.gov/meetings/workshops/chf_execsum.htm.
26. *NIAIA-Funded Research Networks and Programs*. 2004 [cited 2006 January 18]; Available from: http://www.niaid.nih.gov/daids/fundedresearch.htm.
27. Health Resources and Services Administration. *R60: Maternal and Child Health Research Network on Pregnancy-Related Care (MCHPRC)*

HRSA-05-082. 2005 [cited 2006 January 18]; Available from: http://www.hrsa.gov/grants/preview/guidancemch/hrsa05082.htm.

28. Genel, M. and A. Dobs, *Translating clinical research into practice: practice-based research networks--a promising solution.* J Investig Med, 2003. **51**(2): p. 64-71.
29. Alexander, G. and C. Clancy, *Practice-based research: laboratories for health care reform.* J Fam Pract, 1994. **38**(4): p. 428-30.
30. Warnecke, R.B., et al., *The community clinical oncology program: its effect on clinical practice.* Jt Comm J Qual Improv, 1995. **21**(7): p. 336-9.
31. Miller, V.D., J.R. Johnson, and J. Grau, *Antecedents to Willingness to Participate in Planned Organizational Change.* Journal of Applied Communications Research, 1994. **22**: p. 59-60.
32. Johnson, T.P., R.B. Warnecke, and M.J. Aitken, *Changing Practice Patterns*, in *Managing a Health Care Alliance: Improving Community Cancer Care*, A.D. Kaluzny and R.B. Warnecke, Editors. 2000, Beard Books: Fredrick, MD.
33. Division of Cancer Prevention, *Decades of Progress, 1983-2003: The Community Clinical Oncology Program*. 2003, The National Cancer Institute, National Institues of Health, US Department of Health and Human Services.
34. Helfrich, C.H., et al., *Determinants of Implementation Effectiveness: Exploring an Adapted Model for Complex Innovations.* Medical Care Research and Review, 2005. **(revise and resubmit)**.
35. Weiner, B.J., M.M. McKinney, and W. Carpenter, *Adapting Clinical Trials Networks to Conduct Cancer Prevention and Control Research.* Cancer, 2006. **106**(1): p. 180-187.
36. Greenwald, P., J.W. Cullen, and J.W. McKenna, *Cancer prevention and control: from research through applications.* J Natl Cancer Inst, 1987. **79**(2): p. 389-400.
37. Hunter, C.P., A.R. Bavier, and L.G. Ford, *Cancer control research for community programs: the National Cancer Institute initiative.* Cancer Detect Prev, 1990. **14**(6): p. 633-7.

38. Klabunde, C.N., A.D. Kaluzny, and R.B. Warnecke, *Bringing Cancer Prevention and Control Protocols to the Community*, in *Managing a Health Care Alliance: Improving Community Cancer Care*, A.D. Kaluzny and R.B. Warnecke, Editors. 1996, Jossey-Bass: San Francisco. p. 147-170.
39. Moulton, G., *Community Clinical Oncology Program Celebrates 20 Years of Trials and a Few Tribulations.* Journal of the National Cancer Institute, 2003. **95**(4): p. 1822-1924.
40. Fiegl, P., *Community Cancer Care Evaluation (CCCE) Final Report, Volume 5*. 1987, Fred Hutchinson Cancer Research Center: Seattle, WA.
41. Laliberte, L., M.L. Fennell, and G. Papandonatos, *The relationship of membership in research networks to compliance with treatment guidelines for early-stage breast cancer.* Med Care, 2005. **43**(5): p. 471-9.
42. Kaluzny, A.D., et al., *Predicting the performance of a strategic alliance: an analysis of the Community Clinical Oncology Program.* Health Serv Res, 1993. **28**(2): p. 159-82.
43. Kaluzny, A.D., et al., *Accrual of patients to randomized clinical trials. Factors affecting cancer prevention and control research.* Int J Technol Assess Health Care, 1994. **10**(3): p. 506-16.
44. Oxman, A.D., et al., *No Magic Bullets: A Systematic Review of 102 Trials of Interventions to Improve Professional Practice.* Canadian Medical Association Journal, 1995. **153**(10): p. 1423-31.
45. Lorenzi, N.M. and R.T. Riley, *Organizational issues = change.* International Journal of Medical Informatics, 2003. **69**(2-3): p. 197-203.
46. Lorenzi, N.M., et al., *Antecedents of the people and organizational aspects of medical informatics: review of the literature.* Journal of the American Medical Informatics Association, 1997. **4**(2): p. 79-93.
47. Markus, M.L., *Power, Politics, and MIS Implementation.* Communications of the ACM, 1983. **26**(6): p. 430-444.
48. Southon, F.C., C. Sauer, and C.N. Grant, *Information technology in complex health services: organizational impediments to successful technology transfer and diffusion.* Journal of the American Medical Informatics Association, 1997. **4**(2): p. 112-24.
49. Peggy Leatt, C.S.M.S.a.V.W., *IT Solutions for Patient Safety - Best Practices for Successful Implementation in Healthcare.* Electronic Healthcare, 2006: p. 94-104.
50. Rogers, E.M., *The Diffusion of Innovations*. Fifth Edition ed. 2003, New York: Free Press. 517.
51. Klein, K.J. and J.S. Sorra, *The Challenge of Implementation.* Academy of Management Review, 1996. **21**(4): p. 1055-1080.
52. Gallivan, M.J., *Information Technology Diffusion: A Review of Empirical Research.* Database for Advances in Information Systems, 2001. **32**: p. 51-85.
53. Holahan, P.J., et al., *Implementing Computer Technology: A Multi-Organizational Test of Klein and Sorra's Model.* Journal of Engineering and Technology Management, 2004. **21**: p. 31-50.
54. Klein, K.J., A.B. Conn, and J.S. Sorra, *Implementing Computerized Technology.* Journal of Applied Psychology, 2001. **86**(5): p. 811-824.
55. O'Loughlin, J., et al., *Correlates of the sustainability of community-based heart health promotion interventions.* Prev Med, 1998. **27**(5 Pt 1): p. 702-12.
56. Goodman, R.M., et al., *Development of Level of Institutionalization Scales for Health Promotion Programs.* Health Education Quarterly, 1993. **20**(2): p. 161-178.
57. Patterson, R.E., et al., *Durability and diffusion of the nutrition intervention in the Working Well Trial.* Prev Med, 1998. **27**(5 Pt 1): p. 668-73.
58. Pluye, P., et al., *Program sustainability: focus on organizational routines.* Health Promot Int, 2004. **19**(4): p. 489-500.
59. Goodman, R.M. and A. Steckler, *A Model for the Institutionalization of Health Promotion Programs.* Family & Community Health, 1989. **11**(4): p. 63-78.
60. Bracht, N., et al., *Community ownership and program continuation following a health demonstration project.* Health Educ Res, 1994. **9**(2): p. 243-55.
61. Jackson, C., et al., *The capacity-building approach to intervention maintenance implemented by the Stanford Five-City Project.* Health Educ Res, 1994. **9**(3): p. 385-96.
62. Lichtenstein, E., et al., *Durability of tobacco control activities in 11 north American communities: life after the Community Intervention Trial for Smoking Cessation (COMMIT).* Health Educ Res, 1996. **11**(4): p. 527-34.

63. Thompson, B., et al., *Durability of tobacco control efforts in the 22 Community Intervention Trial for Smoking Cessation (COMMIT) communities 2 years after the end of intervention.* Health Educ Res, 2000. **15**(3): p. 353-66.
64. Alexander, J.A., et al., *Sustainability of Collaborative Capacity in Community Health Partnerships: A Proposed Model and Empirical Test.* Medical Care Research and Review, 2003. **60**(4): p. 130S-161S.
65. Kilpatrick, K.E., et al., *The insufficiency of evidence to establish the business case for quality.* Int J Qual Health Care, 2005. **17**(4): p. 347-55.
66. Emanuel, E.J., et al., *The costs of conducting clinical research.* J Clin Oncol, 2003. **21**(22): p. 4145-50.
67. Roche, K., et al., *Factors affecting workload of cancer clinical trials: results of a multicenter study of the National Cancer Institute of Canada Clinical Trials Group.* J Clin Oncol, 2002. **20**(2): p. 545-56.
68. Evans, W.K., et al., *An estimate of the cost of conducting phase II trials in lung cancer.* Lung Cancer, 2000. **28**(2): p. 85-95.
69. McKinney, M.M., B.J. Weiner, and W. Carpenter, *Building Community Capacity to Participate in Cancer Prevention Research.* Cancer Control: Journal of the Moffitt Cancer Center, (in press).
70. McKinney, M.M., B.J. Weiner, and V. Wang, *Recruiting Participants to Cancer Prevention Clinical Trials: Lessons from Successful Community Oncology Networks.* Oncology Nursing Forum, (in press).
71. Ash, J.S., et al., *A diffusion of innovations model of physician order entry.* Proc AMIA Symp, 2001: p. 22-6.
72. Rycroft-Malone, J., et al., *Ingredients for change: revisiting a conceptual framework.* Quality & Safety in Health Care, 2002. **11**(2): p. 174-180.
73. Godley, P.A., et al., *Racial differences in mortality among Medicare recipients after treatment for localized prostate cancer.* J Natl Cancer Inst, 2003. **95**(22): p. 1702-10.
74. Cohen, J.H., et al., *Racial differences in clinical progression among Medicare recipients after treatment for localized prostate cancer (United States).* Cancer Causes Control, 2006. **17**(6): p. 803-11.
75. Cohen, J.H., et al., *Racial differences in disease-free survival in a Medicare population after treatment for clinically localized prostate cancer.* Lancet Oncology, Under Review.
76. Emmons, K.M., *The Relationships Between Organizational Characteristics and the Adoption of Workplace Smoking Policies.* Health Education & Behavior, 2000. **27**: p. 483-501.
77. Nord, W.R. and S. Tucker, *Implementing Routine and Radical Innovations.* 1987, Lexington, MA: Heath and Company.
78. Greer, A.L., *The State of the Art Versus the State of the Science: The Diffusion of New Medical Technologies into Practice.* International Journal of Technology Assessment in Health Care, 1988. **4**: p. 5-26.
79. Lehman, W.E.K., J.M. Greener, and D.D. Simpson, *Assessing Organizational Readiness for Change.* Journal of Substance Abuse Treatment, 2002. **22**(3): p. 197-209.
80. Holt, D.T., *Readiness for Change: The Development of a Scale*. 2002: Paper presented at Academy of Managment Annual Meeting, Denver Colorado.
81. Leonard-Barton, D., *Implementation as Mutual Adaptation of Technology and Organization.* Research Policy, 1988. **17**: p. 251-267.
82. Cooper, R.B. and R.W. Zmud, *Information Technology Implementation Research - a Technological Diffusion Approach.* Management Science, 1990. **36**(2): p. 123-139.
83. Fichman, R.G. and C.F. Kemerer, *The assimilation of software process innovations: An organizational learning perspective.* Management Science, 1997. **43**(10): p. 1345-1363.
84. Fichman, R.G. and C.F. Kemerer, *The Illusory Diffusion of Innovations: An Examination of Assimilation Gaps.* Information Systems Research, 1999. **10**: p. 255-275.
85. Griffith, T.L. and G.B. Northcraft, *Cognitive elements in the implementation of new technology: Can less information provide more benefits?* Mis Quarterly, 1996. **20**(1): p. 99-110.
86. Cobau, C.D., *Clinical Trials in the Community: The Community Clinical Oncology Program Experience.* CANCER, 1994. **74**(9): p. 2694-2700.
87. Schopler, J.H., *Ecological analysis of the first generation of community clinical oncology programs.* Health Serv Res, 1993. **28**(1): p. 69-95.
88. Klabunde, C., A. Kaluzny, and L. Ford, *Community Clinical Oncology Program participation in the Breast Cancer Prevention Trial: factors affecting accrual.* Cancer Epidemiol Biomarkers Prev, 1995. **4**(7): p. 783-9.

89. Klabunde, C.N. and A.D. Kaluzny, *Accrual to the Breast Cancer Prevention Trial by participating Community Clinical Oncology Programs: a panel data analysis.* Breast Cancer Res Treat, 1995. **35**(1): p. 43-50.
90. Kaluzny, A.D., et al., *Using a community cancer treatment trials network for cancer prevention and control research: challenges and opportunities.* Cancer Epidemiol Biomarkers Prev, 1994. **3**(3): p. 261-9.
91. Leonard-Barton, D., *Implementation Characteristics of Organizational Innovations.* Communication Research, 1988. **15**: p. 603-631.
92. Kabanoff, B., R. Waldersee, and M. Cohen, *Espoused Values and Organizational Change Themes.* Academy of Management Journal, 1995. **38**: p. 1075-1104.
93. Guth, W.D. and I.C. Macmillan, *Strategy Implementation Versus Middle Management Self-Interest.* Strategic Management Journal, 1986. **7**(4): p. 313-327.
94. Yin, R.K., *Changing Urban Bureaucracies*. 1979, Lexington, MA: DC Heath and Company.
95. Van De Ven, A.H. and D.E. Polley, *The Innovation Journey*. 1999, New York: Oxford University Press.
96. Ferlie, E., et al., *The Nonspread of Innovations: The Mediating Role of Professionals.* Academy of Management Journal, 2005. **48**(1): p. 117-134.
97. Miles, M.B. and A.M. Huberman, *Qualitative Data Analysis: An Expanded Sourcebook, Second Edition.* 1994, Thousand Oaks, CA: Sage Publications. 338.
98. Weiner, B.J., et al., *How Do Integrated Delivery Systems Adopt and Implement Clinical Information Systems?* Health Care Management Review, 2004. **29**(1): p. 1-16.
99. Weiner, B.J. and J.A. Alexander, *The Challenges of Governing Public-Private Community Health Partnerships: Lessons from the Community Care Networks Demonstration Program.* Health Care Management Review, 1998. **23**(2): p. 39-55.
100. Weiner, B.J., J.A. Alexander, and H.S. Zuckerman, *Strategies for Effective Management Participation in Community Health Partnerships.* Health Care Management Review, 2000. **25**(3): p. 48-66.
101. Trochim, W.M.K., *The Research Methods Knowledge Base, First Edition*. 2001, Cincinnati, OH: Atomic Dog Publishing.
102. Daunno, T.A. and H.S. Zuckerman, *A Life-Cycle Model of Organizational Federations - the Case of Hospitals.* Academy of Management Review, 1987. **12**(3): p. 534-545.
103. Shortell, S.M., et al., *Evaluating partnerships for community health improvement: Tracking the footprints.* Journal of Health Politics Policy and Law, 2002. **27**(1): p. 49-91.
104. Leatt, P., et al., *Downsizing, Reengineering, and Restructuring: Long-Term Implications for Healthcare Organizations.* Frontiers of Health Services Management, 1997. **13**(4): p. 3-37.
105. Kaluzny, A.D., H.S. Zuckerman, and D.J. Rabiner, *Interorganizational factors affecting the delivery of primary care to older Americans.* Health Services Research, 1998. **33**(2): p. 381-401.
106. Dillman, D.A., *Mail and Internet Surveys: The Tailored Design Method*. 2000, New York:: John Wiley & Sons, Inc.
107. Jepson, C., et al., *In a mailed physician survey, questionnaire length had a threshold effect on response rate.* J Clin Epidemiol, 2005. **58**(1): p. 103-5.
108. Kellerman, S.E. and J. Herold, *Physician response to surveys. A review of the literature.* Am J Prev Med, 2001. **20**(1): p. 61-7.
109. Survey Research Lab of the University of Illinois, Sheps Center for Health Services Research at the University of North Carolina, and D. Gillings, *Assessment of the Implementation and Impact of the Community Clinical Oncology Program - Phase II. Appendix A Evaluation Methodology*. 1992: Chicago, IL.
110. Cook, T.D. and D.T. Campbell, *Quasi-Experimentation: Design & Analysis Issues in Field Settings*. 1979, Boston: Houghton Mifflin Company.
111. Kim, J.-O. and C.W. Meuller, *Introduction to Factor Analysis: What It Is and How to Do It.* 1978, Beverly Hills, CA: Sage Publications, Inc.
112. Kim, J.-O. and C.W. Mueller, *Factor Analysis: Statistical Methods and Practical Issues*. 1978, Beverly Hills, CA: Sage Publications, Inc.
113. Gresham, F.M., et al., *Treatment Integrity of School-Based Behavioral Intervention Studies - 1980-1990.* School Psychology Review, 1993. **22**(2): p. 254-272.

114. Bliese, P.D. and R.R. Halverson, *Group size and measures of group-level properties: An examination of eta-squared and ICC values.* Journal of Management, 1998. **24**(2): p. 157-172.
115. Bliese, P.D., *Within-Group Agreement, Non-Independence, and Reliability: Implications for Data Aggregation.*, in *Multilevel Theory, Research, and Methods in Organizations*, K.J. Klein and S.W.J. Kozlowski, Editors. 2000, Jossey-Bass: San Francisco. p. 349-381.
116. Liao, H. and D.E. Rupp, *The impact of justice climate and justice orientation on work outcomes: A cross-level multifoci framework.* Journal of Applied Psychology, 2005. **90**(2): p. 242-256.
117. Zohar, D., *Safety Climate in Industrial-Organizations - Theoretical and Applied Implications.* Journal of Applied Psychology, 1980. **65**(1): p. 96-102.
118. Moertel, C.G., et al., *Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma.* N Engl J Med, 1990. **322**(6): p. 352-8.
119. Du, X. and J.S. Goodwin, *Patterns of use of chemotherapy for breast cancer in older women: findings from Medicare claims data.* J Clin Oncol, 2001. **19**(5): p. 1455-61.
120. Woodard, S., et al., *Older women with breast carcinoma are less likely to receive adjuvant chemotherapy: evidence of possible age bias?* Cancer, 2003. **98**(6): p. 1141-9.
121. Warren, J.L., et al., *Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population.* Med Care, 2002. **40**(8 Suppl): p. IV-3-18.
122. Hewitt, M. and J. Simone, *Enhancing Data Systems to Improve the Quality of Care*. 2000, Washington DC: National Academy Press.
123. Fehrenbach, S.N., et al., *Physician characteristics and the initiation of beta-adrenergic blocking agent therapy after acute myocardial infarction in a managed care population.* Am J Manag Care, 2001. **7**(7): p. 717-23.
124. Bach, P.B., et al., *Racial differences in the treatment of early-stage lung cancer.* N Engl J Med, 1999. **341**(16): p. 1198-205.
125. Klabunde, C.N., et al., *Trends and black/white differences in treatment for nonmetastatic prostate cancer.* Med Care, 1998. **36**(9): p. 1337-48.
126. Warren, J.L., et al., *Trends and outcomes of outpatient mastectomy in elderly women.* J Natl Cancer Inst, 1998. **90**(11): p. 833-40.
127. Begg, C.B., et al., *Impact of hospital volume on operative mortality for major cancer surgery.* Jama, 1998. **280**(20): p. 1747-51.
128. Potosky, A.L., et al., *Breast cancer survival and treatment in health maintenance organization and fee-for-service settings.* J Natl Cancer Inst, 1997. **89**(22): p. 1683-91.
129. Potosky, A.L., et al., *Prostate cancer treatment and ten-year survival among group/staff HMO and fee-for-service Medicare patients.* Health Serv Res, 1999. **34**(2): p. 525-46.
130. Schrag, D., et al., *Influence of hospital procedure volume on outcomes following surgery for colon cancer.* Jama, 2000. **284**(23): p. 3028-35.
131. Baldwin, L.M., et al., *Linking physician characteristics and medicare claims data: issues in data availability, quality, and measurement.* Med Care, 2002. **40**(8 Suppl): p. IV-82-95.
132. Medical Marketing Services (MMS). *AMA Physician Masterfile*. [MMS Internet Web Site] 2005 [cited 2005 December 5, 2005]; Available from: http://www.mmslists.com/category_drilldown.asp?nav=category&subnav=physicians&item=ama#.
133. (ACS) American Cancer Society, *Cancer Facts and Figures - 2004*. 2004: Atlanta, GA.
134. Du, X., J.L. Freeman, and J.S. Goodwin, *Information on radiation treatment in patients with breast cancer: the advantages of the linked medicare and SEER data. Surveillance, Epidemiology and End Results.* J Clin Epidemiol, 1999. **52**(5): p. 463-70.
135. Diggle, P., *Analysis of longitudinal data*. 2nd ed. Oxford statistical science series ; 25. 2002, Oxford ; New York: Oxford University Press. xv, 379.
136. Benson, A., 3rd, et al., *Oncologists' reluctance to accrue patients onto clinical trials: an Illinois Cancer Center study.* Journal of Clinical Oncology, 1991. **9**(11): p. 2067-75.
137. Shochat, S., et al., *Childhood Cancer: Patterns of Protocol Participation in a National Survey.* CA Cancer J Clin., 2001. **51**(2): p. 119-30.
138. Newman, M. and R. Sabherwal, *Determinants of commitment to information systems development: A longitudinal investigation.* Mis Quarterly, 1996. **20**(1): p. 23-54.

139. Kinsinger, L.S., et al., *Using an office system intervention to increase breast cancer screening.* J Gen Intern Med, 1998. **13**(8): p. 507-14.
140. Westat. *Inventory and Evaluation of Clinical Research Networks*. 2006 [cited 2006 22 August]; Available from: http://www.clinicalresearchnetworks.org/documents/Reports.pdf.
141. Venkatesh, V., et al., *User acceptance of information technology: Toward a unified view.* Mis Quarterly, 2003. **27**(3): p. 425-478.
142. Cooper, R.B. and R.W. Zmud, *Information Technology Implementation Research: A Technological Diffusion Approach.* Management Science, 1990. **36**: p. 123-139.
143. Virnig, B.A., et al., *Studying radiation therapy using SEER-Medicare-linked data.* Med Care, 2002. **40**(8 Suppl): p. IV-49-54.
144. Warren, J.L., et al., *Utility of the SEER-Medicare data to identify chemotherapy use.* Med Care, 2002. **40**(8 Suppl): p. IV-55-61.
145. Kerner, J. *Overview: The State of the Art and Science of Dissemination of Evidence-Based Interventions*. in *Paper presented at Dissemination: Putting Evidence into Action*. 2005. University of North Carolina at Chapel Hill, North Carolina.

H. CONSORTIUM/CONTRACTUAL ARRANGEMENTS

Medical Review of North Carolina, dba The Carolinas Center for Medical Excellence, is an independent non-profit corporation. MRNC will support this grant through the subcontract mechanism by providing technical assistance during the data analyses of the SEER Medicare part of the study. Dr. Anna Schenck will also work in an advisory role to researchers at the University of North Carolina.