MULTILEVEL PREDICTORS OF CANCER CLINICAL TRIAL ENROLLMENT AMONG CCOP PHYSICIANS

Sara R. Jacobs

A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Health Policy and Management in the Gillings School of Global Public Health.

Chapel Hill
2014

Approved by:

Bryan J. Weiner

Bryce B. Reeve

Morris Weinberger

David A. Hofmann

Michael Christian

ABSTRACT

SARA R. JACOBS: Multilevel Predictors of Cancer Clinical Trial Enrollment among CCOP Physicians
(Under the direction of Bryan J. Weiner)

Despite the potential benefits, only 3-5% of American adults with cancer participate in cancer clinical trials. One intervention aimed at increasing participation in clinical trials is the Community Clinical Oncology Program (CCOP), a cancer focused provider-based research network administered by the National Cancer Institute (NCI). Although drivers of enrollment at the CCOP level are well understood, no research has exclusively examined enrollment among CCOP physicians.

The objective of this dissertation was to understand the factors that predict enrollment of patients in NCI-sponsored cancer clinical trials among CCOP physicians. Data were obtained from the 2011 Annual CCOP Progress Reports, two surveys conducted in 2011 among CCOP administrators and physicians, and the 2012 American Medical Association Physician Masterfile. The sample consisted of 485 CCOP physicians. We used structural equation modeling to analyze three models that predicted physician enrollment.

Our first analysis sought to determine the physician characteristics, attitudes, and CCOP factors associated with physician enrollment. Our results demonstrated that physicians' attitudes toward participating in CCOP, and CCOP policies and practices (e.g. trainings offered, expectations instituted, support provided) were both significant in

directly predicting enrollment, although neither physician characteristics nor CCOP factors were indirectly associated with enrollment operating through physician attitudes. In the second analysis, we included physicians' perceptions of CCOP, and tested whether fit between CCOP and physicians' values moderated the effect of physicians' perceptions of implementation climate (i.e., a climate that supports, rewards, and expects implementation) on enrollment. Our results demonstrated that both constructs were significantly associated with enrollment and including the moderator improved overall fit of the model. Lastly, we included both CCOP factors and perceptions of context in a single model. Our results confirmed that implementation climate mediated the relationship between organizational policies and practices and enrollment

Overall, the results have both theoretical and practice implications. This dissertation extends the setting and unit of analysis in which innovation implementation theories have been tested. In addition, the findings from this dissertation could be used to develop physician directed strategies aimed at increasing involvement in clinical research. These strategies will be increasingly important as the CCOP network continues to evolve.

To my family, I could not have done this without you.

ACKNOWLEDGEMENTS

First, I would like to thank my advisor, Committee Chair, and mentor, Dr. Bryan Weiner. He was an integral part of my experience at Carolina and I really appreciate his guidance and support throughout my entire tenure. I know we will continue to work together in the future. I would also like to thank Dr. Morris Weinberger for not only serving on my committee, but also for creating a supportive environment in which students can excel. In addition, I would like to thank the rest of my committee, Dr. Bryce Reeve, Dr. David Hofmann, and Dr. Michael Christian for their help in completing my dissertation. I really appreciate your insight and guidance throughout the entire process.

I also would like to thank my classmates and friends for their support. Specifically, to Marisa Morrison and Ila Broyles, I can't image completing this without the two of you. I would also like to thank Megan Roberts and Elisabeth Herron. Thank you all for your constant advice, humor, and friendship. To my parents, thank you for all of your support throughout the years. Thank you for pushing me to find a career that is both challenging and rewarding. You both are my inspiration. Thank you to my brother, Dan Rubin, my grandparents, Mike and Dolores Rubin, and all of my extended family for their love and support. Finally, I would like to thank my truly amazing husband, Todd for allowing me to be me. I could not do this without your enduring love, support, friendship, and patience.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACA	Patient Protection and Affordable Care Act
AMA	American Medical Association
CCOP	Community Clinical Oncology Program
CFI	Comparative Fit Index
ICC	Intraclass Correlations
LR	Likelihood-Ratio
MB-CCOP	Minority-Based Community Clinical Oncology Program
NCI	National Cancer Institute
NCI/DCP	National Cancer Institute Division of Cancer Prevention
NCORP	National Cancer Institute Community Oncology Research Program
IPP	Implementation Policies and Practices
PI	Principal Investigator
RMSEA	Root mean square error of approximation
SEM	Structural Equation Modeling
SRMR	Standardized root mean squared residuals
TLI	Tucker-Lewis Index

CHAPTER 1: INTRODUCTION

Cancer clinical trials are instrumental in the development of innovative cancer treatments as well as in the expansion of current diagnostic, control, and prevention techniques. Evidence demonstrates that cancer clinical trials have the potential to not only improve health outcomes for participating patients, but may also increase the quality of cancer care more generally by facilitating translation of research discoveries into clinical practice (Sorbye et al., 2009) (Grunfeld et al., 2002). Despite the potential for positive health outcomes, only 3-5% of adults with cancer in the United States actually participate in a cancer clinical trial (NCI Cancer Bulletin, 2010). In an effort to improve enrollment among all cancer patients, there has been an increasing interest in developing specific interventions to enhance patient participation in cancer clinical trials.

Patients can typically enroll in four types of cancer clinical trials. *Cancer treatment trials* test the efficacy and safety of new therapies. *Cancer prevention trials* test new interventions aimed at lowering the risk of developing cancer. Cancer prevention trials may include people who have a higher than average risk of developing cancer or are cancer survivors. *Cancer screening and diagnostic clinical trials* test new ways of detecting and/or diagnosing cancer earlier and more accurately. Screening trials often include patients with no signs of cancer while diagnostic trials often include people who have some signs or symptoms of cancer. Lastly, *cancer quality of life or symptom management trials* focus on providing comfort and improving the quality of life for

cancer patients and/or cancer survivors. Clinical trials can be sponsored by government agencies such as the National Cancer Institute (NCI) or the Veterans Health Administration, but they can also be sponsored by other organizations such as foundations, biotechnology and pharmaceutical companies, or academic medical centers (NCI, 2010).

One intervention aimed at increasing patient participation in NCI-sponsored clinical trials is the Community Clinical Oncology Program (CCOP), a cancer-focused provider-based research network administered by NCI. The goal of the CCOP network is to engage community physicians in NCI-sponsored clinical trials in order to enhance the incorporation of research results into practice (NCI, 2010). The CCOP network is a joint venture between NCI, clinical cooperative groups or research bases (which design and develop specific clinical trial protocols), and community-based physicians and hospitals (Kaluzny et al., 1994). The CCOP network is administered by NCI's Division of Cancer Prevention, which provides overall direction and funding for community hospitals and physicians to participate in clinical trials. The CCOP clinical cooperative groups support the design and execution of clinical trials, and the individual community-based physicians and hospitals assist with patient enrollment, data collection, and dissemination of study findings (Kaluzny et al., 1994) (Minasian et al., 2010).

Since its inception in 1983, the CCOP network overall has provided over 50% of the enrollment in NCI-sponsored cancer prevention and control trials and 30% of the enrollment in NCI-sponsored cancer treatment trials (Minasian et al., 2010). Although the CCOP network has clearly been successful in increasing overall cancer clinical trial enrollment, **participating physicians vary in their individual enrollment of patients**

in cancer clinical trials. It is well known that *context* is an important determinant of both organizational and individual behavior or performance (Kozlowski & Klein, 2000). Research to date has sought to identify the organizational and environmental contextual factors that drive patient clinical trial enrollment at the CCOP level (Kaluzny et al., 1995) (Carpenter et al., 2012) (Weiner et al., 2012) (Jacobs et al., 2013). However, no research has examined the individual physician characteristics and organizational contextual factors that predict CCOP physician success in enrolling patients in trials. Thus, there is a *critical need* to determine the context within which we can increase physician enrollment of cancer patients in cancer clinical trials. Context can be included in a study in three different ways. First, by including objective measures of context in a model that predicts individual performance. Second, by examining the role of perceptions of context in predicting behavior, and lastly by including both objective and perceived organizational context in a single model. In this dissertation, we examined these three ways to include organizational context. The first aim examined the impact of objectively measured organizational factors on physician enrollment of patients while the second aim explored the relationship between physicians' perceptions of context and enrollment. Lastly, the third aim expanded upon the work completed in the first two aims and examined both objective assessment of context and perceptions of context. In this setting, the data used were nested. For example, we examined individual CCOP-affiliated physicians who practiced in a CCOP organization. This dissertation does not include organizational contextual factors at the hospital or clinic level as many of the physicians that participate in CCOP practice at multiple locations. In addition, patient accrual is attributed to the individual physician or CCOP organization rather than to the

hospital or clinic.

The overall research question was to understand the role of physician characteristics and organizational context in predicting the enrollment of patients in NCI-sponsored cancer clinical trials among CCOP-affiliated physicians. The central hypothesis was that organizational contextual factors and physician characteristics would directly and indirectly determine physician performance. This central hypothesis was tested in three separate aims.

- Aim 1: To determine the physician characteristics and objective assessments of organizational context associated with higher enrollment of patients in NCI-sponsored cancer clinical trials.
- Aim 2: To examine the physician characteristics and physicians' perceptions of organizational context associated with higher enrollment of patients in NCI-sponsored cancer clinical trials.
- Aim 3: To evaluate the objective assessments of organizational context and physicians' perceptions of organizational context associated with higher enrollment of patients in NCI-sponsored cancer clinical trials.

This dissertation utilized data from four sources: 1) 2011 Annual CCOP Progress Reports; 2) 2011 CCOP Administrator Survey; 3) 2011 CCOP-Affiliated Physician Survey; and 4) 2012 AMA Physician Masterfile. The CCOP Progress Reports provide information on each CCOP's research and enrollment activities for the previous nine months and were primarily used to determine the dependent variable, patient enrollment, for all three aims. This dissertation utilized the 2011 Progress Reports submitted in March 2012, which cover the period from June 2011 to February 2012. The 2011 Progress Reports overlap in timing with the 2011 CCOP Administrator and CCOP-Affiliated Physician Surveys. The goal of CCOP Administrator Survey and Physician Survey were to learn more about how the CCOPs are organized and how they operate

as well as to better understand physician participation in the CCOP network. The CCOP Administrator Survey was primarily used for the objective assessments of organizational context in Aims 1 and 3 while the Physician Survey was used to determine physicians' attitudes (Aim 1) and perceptions of organizational context for Aims 2 and 3. The physicians who responded to the physician survey (n=485) comprised the sample for all three aims. Lastly, AMA data were used to determine the physician characteristics included in all three aims.

The analytical approach for all three aims was structural equation modeling (SEM). SEM is advantageous as it allows researchers to test latent constructs that are not directly assessed, but rather are composed of observed data (e.g., organizational context, implementation climate, innovation-values fit). Second, SEM also takes into account measurement error by including error variables in the error portions of the observed variables; therefore conclusions about relationships are not biased by any measurement error. Lastly, SEM allows researchers to test complex frameworks that include mediation and moderation in a single model (Werner & Schermelleh-Engel, 2009).

Determining the multilevel predictors of CCOP-affiliated physician success in enrolling patients in cancer clinical trials has significant policy and scientific implications. This dissertation contributes to the current knowledge base by identifying both individual physician characteristics and organizational contextual factors that predict CCOP-affiliated physician enrollment of patients in cancer clinical trials. This contribution is both innovative and significant for its potential to be used as the foundation for strategies that promote physician enrollment of patients in cancer clinical trials as well

as physician adoption of innovations more generally. These findings are particularly important as NCI builds upon the success of the CCOP program and replaces both CCOP and the NCI Community Cancer Centers Program (NCCCP) with the NCI Community Oncology Research Program (NCORP). In addition, this dissertation also examined all three ways organizational context can be incorporated into models that predict individual behavior. By using models traditionally examined in management and information systems, we extended the settings in which innovation implementation theories may be applicable. In addition, we provided evidence for adapting these theories to examine individual level innovation implementation.

The dissertation is organized as follows: Chapter 2 discusses the current literature regarding barriers to cancer clinical trial enrollment, the success of the CCOP program, known physician predictors of patient enrollment in cancer clinical trials, methods to incorporate organizational context into models that predict individual behavior, and current innovation implementation frameworks. Chapter 3 provides an overview of the methods used throughout the dissertation. It includes a discussion of study design and rationale, hypotheses, data sources, study sample, and analytical approaches. Chapters 4-6 are manuscripts corresponding to Aims 1-3, respectively, and are intended for submission for peer-reviewed publication. Chapter 7 reviews the study findings, summarizes the implications for policy, practice, and research, discusses the limitations of this dissertation, and concludes with a discussion of future research. Tables and figures are provided at the end of each chapter. References are provided in a comprehensive bibliography at the conclusion of the dissertation.

CHAPTER 2: LITERATURE REVIEW

Overview of Barriers to Clinical Trial Enrollment

As discussed, studies estimate that only 3-5% of adults with cancer participate in cancer-related clinical trials (NCI Cancer Bulletin, 2010). Specific enrollment in NCI-sponsored breast, colorectal, lung, and prostate cancer clinical trials has been shown to be as a little as 1.8% among adults with these types of cancer. Enrollment tends to be lowest among racial and ethnic minorities, women, and the elderly (Murthy et al., 2004). Research demonstrates that barriers to successful patient enrollment occur at the patient, physician, and organizational levels (Winn, 1994). Despite evidence that cancer survivors are receptive to participating in a cancer clinical trial if their physician asked them to do so, some patients are still reluctant to enroll (Comis et al., 2003) (Comis et al., 2009). Patients may have concerns over the cost and/or coverage of the trial or lack transportation to the trial site (Mills et al., 2006). In addition, some patients report discomfort with the allocation of treatment component of cancer clinical trials and/or a lack of knowledge regarding what is required of a trial participant (Mills et al., 2006) (Ellis, 2000). For example, one study found that only 13% of survey respondents reported having a clear understanding of the term “clinical trial” and 29% reported having “not much idea” (Comis et al., 2009). Patients may also prefer to be more involved in the clinical decision-making process; or, they may fear and/or distrust the medical profession, specific research or researchers involved (Mills et al., 2006) (Ellis,

2000). For example, 40% of patients of who were aware of a clinical trial, but declined to participate, noted they were concerned that the new treatment might not be as effective as the standard treatment (Comis et al., 2009).

Physician-level barriers include concerns over the potential effect on the physician-patient relationship, as well as attitude towards and knowledge of the clinical trials themselves (Winn, 1994). For example, some physicians may be concerned that they may lose contact with and control over the care of their patients once they enroll in clinical trials (Mansour et al., 1994). In addition, some physicians may not be aware of all the available trials and trial eligibility requirements for patients; they may also lack the time it takes to understand the nuances of the trial and follow-up with patients regarding the details of the specific protocol (Mansour et al., 1994). For example, in one study physicians immediately did not even consider a clinical trial for 38% of patients with cancer. The primary reason stated was no available protocol. Although the authors did confirm that for a small portion of patients no protocol was available, physicians were excluding patients even before reviewing what trials were available and the associated eligibility criteria. The authors believed that these physicians lacked the appropriate knowledge of open trials and were not even considering clinical trials for patients based on misconceptions of ideal eligible patients (Lara et al., 2001). Another important barrier to clinical trial enrollment are physician biases that the trial therapy is not as good as the standard therapy. Although rarely if ever is the trial therapy not as good as the standard therapy, some physicians may be biased to think so (Mansour et al., 1994).

At the organizational level, potential barriers include limited resources dedicated

to supporting cancer clinical trials, including the lack of support staff to help consent and enroll eligible patients (Shea et al., 1992). Other organizational barriers include having a limited number of trials available for physicians to enroll patients (Jacobs et al., 2013) (Weiner et al., 2012). Physicians also note that their organization could help facilitate patient enrollment by providing a synopsis of all open trials available at the point of care, simplifying enrollment forms, individualizing forms for each trial with specific information regarding specific tests, chemotherapy dose, and hiring additional trained staff to not only assist physicians with consenting and enrolling patients, but in the decision making process as well to help determine the appropriateness of a clinical trial for a patient (Fisher et al., 1991). Thus, successful interventions should try to alleviate barriers at the patient, physician, and organizational levels in order to increase the number of adults with cancer that enroll in a clinical trial.

Success of the CCOP Network

The CCOP started in 1983 with the goal of engaging community physicians in NCI-sponsored clinical trials to improve the incorporation of clinical research results into practice. The program is complemented by the Minority-Based CCOP network (MB-CCOP), which began in 1990 as a means to provide the infrastructure for clinical trials in those institutions, which serve communities with large minority and underserved populations (NCI, 2011). The CCOP and MB-CCOP network are administered by NCI's Division of Cancer Prevention, which provides overall direction and funding for community hospitals and physicians to participate in clinical trials. In addition, there are CCOP sites that enroll patients into NCI-approved cancer clinical trials. A CCOP site can be a single community organization or a consortium of local hospitals and private

practices. A MB-CCOP site must meet the same requirements as the CCOPs, but must also have a population that is at least 40% minority or underserved. In addition, academic institutions are permitted to be MB-CCOPs, whereas they may not serve as the lead organization for a CCOP. The CCOP and MB-CCOP sites also affiliate with Research Bases, which design and develop the specific clinical trial protocols. Each site may affiliate with multiple Research Bases (NCI, 2011). When the data were collected in 2011, there were 47 CCOPs across 28 states. The CCOPs included over 450 hospitals and physician practices, with the average CCOP comprised of about 10 hospitals and/or practice sites. CCOPs also included over 3,500 physicians, with the average CCOP composed of 48 physicians. Patient accrual to clinical trials is counted at the CCOP organizational level and at the individual physician level. CCOPs overall are required to enroll at least 100 patients per year across all types NCI-sponsored clinical trials (NCI, 2011). There is no current formal NCI requirement for individual physicians to enroll a minimum number of patients per year, although some CCOPs have instituted their own expectations for enrollment.

Physicians practicing at MB-COOPs were not analyzed in this dissertation as MB-CCOP affiliated physicians were included in the 2011 Physician Survey due to organizational differences between MB-CCOPs and CCOPs. As mentioned, academic medical centers are often the main site for MB-CCOPs. In addition, MB-CCOPs tend to be located in more urban areas as they are focused on enrolling minority and underserved patients. As expected the patient population seen at MB-CCOPs differ than those seen at CCOPs.

CCOP enrollment of adults and children with cancer provide over 30% of the

enrollment in NCI-sponsored cancer treatment trials and 50% of the enrollment in NCI-sponsored cancer prevention and symptom management trials (Minasian et al., 2010). The program was been successful due to its ability to address barriers among patients, providers, and practices. The CCOP network not only provides organizational resources and support for physicians to enroll patients, it also allows patients to enroll in clinical trials in their community, at their local hospital or physician's office, or where they most often seek care.

To date, research has focused on identifying the organizational and environmental contextual factors that explain why programs are successful at the CCOP organizational level. Significant organizational contextual factors include the number and type of locations where patients can enroll, the number of research base affiliations, the number of hours per week worked by data managers, the number of active CCOP physicians, the number of open trials, the number of support staff, policies that recognize high accruing physicians, and the volume of new cancer patients (Kaluzny et al., 1995) (Carpenter et al., 2012) (Weiner et al., 2012) (Jacobs et al., 2013). Key environmental contextual factors that predict CCOP level enrollment includes managed care penetration, hospital competition, and number of medical school affiliated hospitals in regions where CCOPs operate (Carpenter et al., 2006) (Carpenter et al., 2012). No current efforts, however, have examined the drivers of individual physicians' enrollment of patients in cancer clinical trials among CCOP physicians.

Physician Predictors of Clinical Trial Enrollment

As discussed, no studies have examined the physician characteristics associated with clinical trial enrollment exclusively among CCOP physicians. Several studies have,

however, examined physician characteristics that are generally associated with clinical trial participation. Physician characteristics associated with increased cancer clinical trial participation include medical specialty (i.e., medical oncologists compared to radiation oncologists), practice type (i.e., office-based practice compared to hospital based practice), prior participation in clinical trials, number of newly diagnosed patients seen, time spent with newly diagnosed cancer patients, training medical students or residents, and weekly tumor board participation (Klabunde et al., 2011). Research also demonstrates that foreign-trained oncologists and oncologists who had participated in *either* pharmaceutical company sponsored trials or cooperative group sponsored trials, compared to those that participated in both types of trials tend to refer less patients to cancer clinical trials. In addition, physician age, race, and gender were generally not associated with cancer clinical trial participation (Klabunde et al., 2011) (Meropol et al., 2007).

Physician knowledge and attitudes also influence patient enrollment. For example, oncologists' attitudes towards the value and importance of clinical trials directly influences whether a patient enrolls in a trial (Mansour et al., 1994). One study found that when physicians offered a cancer clinical trial to their patients and their patients understood that they were being offered a trial, 75% of patients agreed to enroll (Albrecht et al., 2008)*.* Therefore, physicians are *instrumental* in the enrollment process as they are the conduit between the healthcare organization and the patient. Ultimately if a physician does not recommend a clinical trial to a cancer patient, it is extremely unlikely that that patient will enroll in a cancer clinical trial.

Although these studies provide some initial insight into what physician

characteristics may drive patient enrollment in cancer clinical trials, notably, none of these studies were conducted exclusively among CCOP-affiliated physicians nor do they include organizational contextual factors in their analyses. Physician characteristics that influence patient enrollment in cancer clinical trials may also differ among CCOP-affiliated physicians because they elect to participate in CCOP and therefore receive resource support from NCI to assist with screening and enrolling of eligible patients. Given that the mission of the CCOP network is to facilitate cancer clinical trial participation in local communities, CCOP-affiliated physicians may have a greater level of support and interest in encouraging their patients to enroll. Although, they may be different from other oncologists, there is still considerable variation among CCOP-affiliated physicians in their enrollment of patients. For example, in 2011, approximately 40% of CCOP physicians enrolled no patients (mean: 3; range: 0-88). Variation in physician enrollment has been observed in the program since its inception, yet no studies have systematically examined the reasons why this variation may occur. Therefore this research fills a necessary gap in the current knowledge base by evaluating the predictors of CCOP physicians' enrollment of patients in NCI-sponsored cancer clinical trials.

Incorporating Organizational Context in Research

Current research indicates that both individual-level characteristics and organizational context influence individual behavior (Kozlowski & Klein, 2000). For example, factors that predict CCOP physician enrollment of patients in trials likely occurs both at the individual physician level (e.g., medical specialty, values, attitudes) as well as at the CCOP level (e.g., organizational size, organizational policies that

incentivize enrollment, minimum accrual expectations). To comprehensively assess the determinants of physician enrollment, this dissertation incorporated factors at both levels. Including individual characteristics in an analysis is relatively straightforward, organizational context, however, can be incorporated in multiple ways.

The first approach examines either objective measures of organizational context or study subjects' perceptions of organizational context. Often specific frameworks do not specify whether the organizational context should be assessed objectively or from a subject's point of view, rather the researcher decides in operationalizing the model and collecting the data. For example, in Choi's work on innovation-use behavior, the model includes both individual characteristics and organizational context (2004).

An innovation is defined as an idea, practice, or object that is perceived as new by an individual or organization (Rogers, 1983). The decision to adopt an innovation often may occur at the organizational level, but individuals within the organization also have to decide whether they are going to use (i.e., accept) the innovation. Therefore, innovation-use behavior is often defined as either the intended or continued use of an innovation by an individual. It can be measured as frequency and/or intensity of innovation use (Frambach & Schilewaert, 2002). Choi's innovation-use model suggests that personal characteristics such as personal values, attitudes and abilities mediate and/or moderate the relationship between organizational culture, norms, support and the outcome, innovation-use behavior (2004). The framework does not specifically include any perceptions of context. In operationalizing the model, however, Choi elected to use employee's perceptions of organizational climate, norms, and support instead of collecting objective measures of context. For example, instead of assessing the number

of trainings provided, he asked employees if they felt that had received enough training.

In the second approach, researchers incorporate context through a model of climate, where individual perceptions mediate the relationship between objective measures of context and personal characteristics in predicting an outcome. James and Jones suggest that objective characteristics of the organizational context are antecedents of climate, while individuals' interpretive perceptions provide meaning to the context (1974). This view proposes that individual climate perceptions are a result of both organizational objective contextual factors and personal characteristics (Kozlowski & Klein, 2000). For example, the integrative model for continually "updating" an individual's knowledge and skills as to stay current with the latest innovations (i.e., an individual-level behavior) includes both personal characteristics and contextual factors (Kozlowski & Farr, 1988). The framework suggests that individual perceptions of the climate mediate the relationship between personal characteristics (e.g., age, experience, tenure), organizational context (e.g., technology use, structure) and individual performance, including the ability to "update."

In this research, we have the unique ability to be able to test all of these approaches of incorporating context, as the data were collected from CCOP administrators and CCOP physicians and includes both types of measures of context. Specifically, Aim 1 examined the objective measures of organizational context. Aim 2 utilized the perceptions of organizational context, while Aim 3 included both objective measures of context and perceptions of context. Therefore this research is significant as we were able to comprehensively examine the impact of organizational context and personal characteristics on physician enrollment.

Innovation Implementation Frameworks

Given the objective to include organizational context in multiple ways, we required three separate conceptual frameworks to guide the research, one for each aim. Interestingly, although there are a number of models for innovation implementation or implementation effectiveness at the organizational level, overall there are very few models that examine implementation at the *individual* level. The majority of past research has either focused on the individual acceptance of technologies, such as the Technology Acceptance Model and the Unified Theory of Acceptance and Use of Technology, or has examined individual-level behavior without incorporating organizational context within the model, such as the Theory of Planned Behavior (Davis, 1989) (Venkatesh et al., 2003) (Ajzen, 1991).

One model that considers both individual- and organizational-level factors in predicting individual innovation acceptance is the Multilevel Framework of Organizational and Individual Innovation Adoption (Frambach & Schilewaert, 2002). The Multilevel Framework of Organizational and Individual Innovation Adoption suggests that individual innovation acceptance is based on objective organizational contextual factors such as trainings offered, incentives rewarded, support provided, peer usage of the innovation, and expectations as well as personal characteristics such as attitudes, values, and demographics (Frambach & Schilewaert, 2002). We used this model to guide our analysis in Aim 1. The model is based only on objective assessments of organizational context, however, and thus is not relevant for the other two aims.

There are no current models that incorporate perceptions of organizational context with individual-level determinants such as values, demographics, and

experience. Therefore in Aims 2 and 3, we adapted the theory of innovation implementation (Klein & Sorra, 1996) to explain individual level implementation effectiveness. Specifically in Aim 2, we tested whether innovation-values fit moderates the effect of perceptions of implementation climate on enrollment (i.e., implementation effectiveness). In Aim 3, we incorporated objective assessments of context and tested whether perceptions of implementation climate mediates the relationship between objective assessments of organizational policies and practices that encourage implementation and enrollment. These models are discussed in detail in Chapters 5 and 6 respectively.

CHAPTER 3: STUDY DESIGN AND METHODS

Overview and Rationale

This dissertation was a secondary analysis of data collected directly from CCOP physicians and administrators, annual CCOP Progress reports, and the AMA Physician Masterfile. The aims utilized a concurrent cross-sectional design to examine both the physician characteristics and organizational contextual factors associated with patient enrollment in NCI-sponsored cancer clinical trials. Each aim employed a separate conceptual framework. More detailed descriptions of the conceptual models are provided in Chapters 4-6 respectively. The dependent variable for all three aims is the number of patients physicians enroll in NCI-sponsored cancer clinical trials in 2011. Key physician variables included physicians' attitudes and values (Aims 1 and 2), as well as characteristics such as experience, medical specialty, and training (All three aims). Key organizational-level variables include organizational contextual factors, such as policies and practices to support implementation (e.g., trainings offered, support provided, expectations instituted) (Aims 1 and 3). In the first aim, contextual factors were incorporated by including objective measures of organizational context gathered as part of the CCOP Administrator Survey. In the second aim, organizational context was included as perceptions of organizational context as assessed by CCOP-affiliated physicians as part of the CCOP Physician Survey. Lastly, in the third aim organizational context included both objective measures and perceptions of organizational context.

Research Questions and Hypotheses

Aim 1 Research Question: *What are the physician characteristics and objective assessments of organizational context associated with higher enrollment of patients in NCI-sponsored cancer clinical trials?*

> Aim 1 Main Hypothesis: Personal characteristics (e.g., specialty, experience), attitudes towards the CCOP program, and organizational context (e.g., training, support, expectations) will directly influence physician enrollment of patients in clinical trials. In addition, personal characteristics and organizational context will have indirect effects on enrollment operating through attitudes.

Aim 2 Research Question*: What are the physician characteristics and physicians' perceptions of organizational context associated with higher enrollment of patients in NCI-sponsored cancer clinical trials?*

> Aim 2 Main Hypothesis: Physicians' perceptions of how the innovation fits with their values will moderate the role between their perceptions of innovation climate (i.e., a climate that supports, rewards, provides expectations regarding participating in CCOP) and physician enrollment of patients in clinical trials.

Aim 3 Research Question: *Are objective assessments of organizational context and physicians' perceptions of organizational context associated with higher enrollment of patients in NCI-sponsored cancer clinical trials?*

> Aim 3 Main Hypothesis: Physician perceptions of implementation climate will mediate the effect of objective assessments of organizational implementation policies and practices on physician enrollment of patients in trials.

Data

Data for this dissertation came from four sources: 1) 2011 Annual CCOP Progress Reports; 2) 2011 CCOP Administrator Survey; 3) 2011 CCOP-Affiliated Physician Survey; and 4) 2012 AMA Physician Masterfile. Data from all four sources were linked and de-identified for each respective analysis (Table 1).

2011 Annual CCOP Progress Reports. Each March, every CCOP (n=47) submits

a progress report to NCI detailing the previous nine-month's research and enrollment activities. The report includes standardized questions regarding the allocation of CCOP resources, staffing assignments, total cancer patient volume, the number of open cancer clinical trials, the total number of patients each CCOP enrolls, as well as the total number of patients each individual CCOP-affiliated physician enrolls. This study utilized the 2011 Progress Reports submitted in March 2012, which cover the period from June 2011 to February 2012. The 2011 Progress Reports overlap in timing with the 2011 CCOP Administrator and CCOP-Affiliated Physician Surveys. Specifically, the progress reports were used in all three aims to determine the dependent variable as well as to determine if a physician was the CCOP Principal Investigator (PI). Average physician enrollment by CCOP was also used in Aim 1.

2011 CCOP Administrator Survey. As part of the Implementing System Intervention to Close the Discovery-Delivery Gap Grant (5R01CA124402), we conducted a survey of CCOP administrators in Fall 2011. The goal was to learn more about how the CCOPs are organized and how they operate. All CCOP administrators participated (n=47) in the survey. The survey asked specific questions regarding the CCOP organizational structure, sponsored educational trainings, physician resources and support for screening, consenting, and enrolling patients, as well as CCOP staffing procedures. Specifically, Administrator Survey was used to assess the objective organizational context factors in Aims 1 and 3.

2011 CCOP-Affiliated Physician Survey. Also as part of the Implementing System Intervention to Close the Discovery-Delivery Gap Grant, we also conducted a survey of CCOP- physicians in Fall 2011. The goal of this survey was to learn more

about physician participation in the CCOP program. The survey did not include physicians who practice at one of the 15 MB-CCOP. The physician survey asked specific questions regarding physicians' perceptions regarding expectations for enrollment, research support provided by the CCOP, ability to provide input, how well they are kept informed of CCOP activities, recognition received from the CCOP, as well as personal beliefs, attitudes, and values regarding the importance of cancer clinical trials. Specifically, the physician survey was used to assess personal characteristics and attitudes in Aim 1. It was also used to determine innovation-values fit in Aim 2. In addition, it was used to for the physicians' perceptions of climate in Aims 2 and 3.

2012 AMA Physician Masterfile. Established by the AMA in 1906, the Physician Masterfile includes current and historical data for more than 1.4 million physicians, residents, and medical students in the U.S. This includes approximately 400,000 foreign medical graduates practicing in the U.S. A record is established when individuals enter medical school, or in the case of international medical graduates, upon entry into a post-graduate residency or when they obtain a U.S medical license. The AMA Masterfile contains demographic information, such as age and gender, as well as specialty, experience, and medical school training and residency. The Masterfile also contains information on practice location, type, and size. Specifically, the Masterfile was used to characterize the physicians in the sample. Demographics, expertise, and experience were included in the model for all three aims.

Study Sample

The sample for all three aims was comprised of physicians who responded to the 2011 CCOP-Affiliated Physician Survey. Responses were collected between October

2011 and January 2012. We surveyed a total of 817 physicians across all 47 CCOPs. We achieved a response rate of 59%, which was in the range of rates previously reported (45% to 79%) (Kellerman & Herold, 2001). Therefore, the final sample includes 485 physicians of whom, 74% were male and 26% were female (Table 2). In addition, approximately 75% were White non-Hispanic, 15% were Asian, and the remaining 10% were either African-American, Native Hawaiian/Pacific Islander, or reported multiple races. The average age was 53 years old (range 34 to 82) with an average of 26 years experience (range 8 to 57). Physicians on average enrolled approximately 5 patients a year in 2011 (range 0 to 62) with a standard deviation of 8 patients. The vast majority practiced in a group practice (78%) and trained in the U.S (80%). In addition, 40% reported hematology oncology as their primary specialty, 21% reported radiation oncology, 11% reported general non-specialized oncology, 10% reported some type of surgery, and the remaining 18% reported either general practice, gynecology oncology, pediatric oncology, or other type of specialist as their medical specialty.

In addition to generating the descriptive statistics for actual survey respondents, we also examined the descriptive statistics among non-survey respondents, the entire sample of surveyed CCOP physicians, and the population of all CCOP physicians to ensure the sample was not subject to any biases. There were two significant differences between survey respondents and non-respondents. First, in terms of specialty, respondents were less likely to be medical oncologists (11% vs. 24%) and more likely to be surgeons (10% vs. 5%). Second, responders were more likely to enroll patients in cancer trials: an average 5 patients per year (range 0 to 62; standard deviation of 8) compared to only 3 patients per year among the non-respondents (range 0 to 88;

standard deviation of 7.5).

We also tested to see if there were any significant differences between those that were sampled compared to the CCOP physician population. Our sample was slightly over representative of physicians practicing in group practices (79% v. 72%) and hospitals (12% v. 11%), and slightly under representative of physicians in solo practices (2% v. 5%) and surgeons (8% v. 10%). In addition, those that were sampled enrolled on average 4 patients per year in 2011 (range 0 to 88; standard deviation 8) compared to those that were not sampled, which only enrolled on average 2 patients per year (range 0 to 44; standard deviation 4). Although these differences were statistically significant, overall they are not likely to significantly influence the generalizability of study findings.

Overview of Statistical Analyses

Intraclass Correlations and Interrater Agreement

For each physician survey question, we tested the consistency in responses of members of the same CCOP compared to members in different CCOPs by calculating intraclass correlation coefficients, ICC(1) and ICC(2). This provided a sense of the proportion of group-level variance accounted for by group membership. In addition, we also tested the within-group interrater agreement by calculating $r^*_{WG(J)}$ indices. Overall the results indicate that there was substantial variation in responses (Table 3). The ICC(1) values were low, and the ICC(2) values which vary as a function of the ICC(1) values and the sample size, were also modest.

The interrater agreement statistics demonstrated that for some measures, such as affect ($r^*_{WG(J)}$ =0.77) and values ($r^*_{WG(J)}$ =0.82), there was strong agreement among physicians within a CCOP. There was also strong agreement for the measures that

composed the innovation-values fit construct (Want offer trials $r^*_{WG(J)}$ =0.88; Participating important $r^*_{WG(J)}$ =0.79; Value participating $r^*_{WG(J)}$ =0.82; Explore important issues $r^*_{WG(J)}$ =0.77). For other measures, however, such as beliefs regarding the complexity ($r^*_{WG(J)}$ =0.32) and exclusively ($r^*_{WG(J)}$ =0.41) of the trials there was only modest agreement. The inter-rater agreement statistics were also modest for perceived expectations for the number of patients physicians are expected to enroll ($r^*_{WG(J)}$ =0.01) and for the support needed to identify ($r^*_{WG(J)}$ =0.27) and enroll patients ($r^*_{WG(J)}$ =0.37). Physicians also disagreed as to whether they were recognized ($r^*_{WG(J)}$ =0.23) and appreciated ($r^*_{WG(J)}$ =0.21) for enrolling patients. Although many of these results indicate that several of the constructs could be assessed at the group level (i.e., innovations-value fit), we were most interested in examining enrollment at the individual physician level.

Structural Equation Modeling

For each aim, we utilized SEM to analyze the results. There are many advantages of using SEM. For example, SEM allows researchers to test latent constructs that are not directly assessed, but rather are composed of observed data (e.g., attitudes, innovation-values fit, perceptions of implementation climate, organizational context). SEM also takes into account measurement error by including error variables in the error portions of the observed variables; therefore conclusions about relationships are not biased by any measurement error. SEM is also advantageous as researchers are able to test complex frameworks that include mediation and moderation in a single model (as compared to regression that may require multiple analyses). Therefore, SEM allows researchers to easily examine

indirect and direct effects of variables on the outcome (Werner & Schermelleh-Engel, 2009).

There are five main steps involved in SEM. First, we specified each model. Second, we checked to ensure the model was identified, which means the number of parameters must be less than or equal to the number of observations (Norman & Streiner (eds), 2003). Third, we worked to fit and evaluate the model. We used maximum likelihood estimation techniques, given we had very little data missing. We also used clustered-robust standard errors as errors were likely correlated and we wanted to adjust for the 47 CCOPs. We then tested the fit of the model using the typical goodness-of-fit statistics. We examined the root mean square error of approximation (RMSEA), and the associated confidence interval and p-value. RMSEA values below 0.06 are considered acceptable with an upper bound of the confidence interval lower than 0.1. We also examined the Comparative Fit Index (CFI) and the Tucker-Lewis Index (TLI), and the standardized root mean squared residuals (SRMR). The CFI and TLI ideally should be above 0.90, and an ideal SRMR should be close to zero (lower than 0.08 is considered acceptable) (Norman & Streiner (eds), 2003) (Schreiber et al., 2006). Fourth, we modified the original models and made any necessary changes to improve fit (e.g., add covariances). Lastly, after we achieved the best fitting model, we interpreted the model and examined estimated standardized path coefficients and corresponding standard errors. The general mathematical formula for SEM is as follows:

Equation 1: $Y = BY + \Gamma X + \alpha + \zeta$

Where **Y** on the left hand side is the endogenous outcome variable, individual physician enrollment of patients in NCI-sponsored cancer clinical trials, and **Y** on the right hand

side is composed of the *observed* endogenous measures (**γ**) and *latent* endogenous constructs (**η**). **X** represents both the *observed* exogenous measures (**x**) and the *latent* exogenous constructs (**ξ**). **B** and **Γ** are the coefficient estimates for the endogenous and exogenous variables, **α** are the intercepts, and **ζ** represents the error (**e.η e.γ**) associated with the model. I can also estimate **κ**, the means of the exogenous variables, **Φ**, the variances and covariances of the exogenous variables, and **Ψ**, the variances and covariances of the error terms.

Study Size and Power

The general rule regarding sample size for SEM is that 5 to 10 subjects per parameter included in the model are needed. In SEM, the number of parameters is based on: 1) the number of pathways in the model; 2) the number of variances for the exogenous variables; 3) the number of covariances in the model; and 4) the number of disturbance terms for the endogenous variables. For Aim 1, we had 64 parameters (44 pathways, 10 variances for exogenous variables, 8 covariances, and 2 disturbance terms). For Aim 2, we had 47 parameters (33 pathways, 10 variances, 3 covariances, and 1 disturbance term). Lastly for Aim 3, we had 73 parameters (52 pathways, 12 variances, 7 covariances, and 2 disturbance terms). Thus we needed a minimum of 365 to 730 physicians in the sample. Although we only had 485 physicians in the sample, we did not encounter any problems using SEM given all three models were identified.

Model identification is critical in analyzing SEM. Identification requires that the number of observations is greater than the number of parameters. The number of observations is equal to (K*(K+1))/2, where k= number of variables. Thus, our number of observations are: 231 for Aim 1 (21 variables), 210 for Aim 2 (20 variables), and 392

for Aim 3 (27 variables). Thus the models were identified for all three aims.

- Aim 1: 231 observations > 64 parameters
- Aim 2: 210 observations > 47 parameters
- Aim 3: 392 observations > 77 parameters

Power is often assessed after a model is specified and can be based of certain fit indices, such as the RMSEA. According to the method developed by MacCallum, Browne, and Sugawara (1996) to calculate the power of a structural equation model, you need five factors: the degrees of freedom, significance level (α), sample size, a null value of RMSEA, and the alternative value of RMSEA. The null RMSEA value used tends to be 0.00, indicating a perfect fit. For Aim 1 the degrees of freedom was 165, for Aim 2 it was 139, and for Aim 3 it was 202. Using an α=0.05, a null RMSEA value of 0.00 and alternative RMSEA value of 0.05 (common values used for testing exact fit), and a sample size of at least 400, the models for all three aims were 100% powered (MacCallum et al., 1996).

Table 1: Variables, Measures, and Data Sources for All Aims

	CCOP Progress Reports	CCOP Administrator Survey	CCOP-Affiliated Physician Survey	AMA Provider Masterfile
Measure				
Outcome: Innovation Acceptance	All Three Aims			
Attitudes: Affect			Aim 1	
Attitudes: Beliefs			Aim 1	
Attitudes: Values			Aim 1	
Objective Organizational Context: Peer Usage	Aim 1 & Aim 3			
Objective Organizational Context: Training		Aim 1 & Aim 3		
Objective Organizational Context: Expectations		Aim 1 & Aim 3		
Objective Organizational Context: Support		Aim 1 & Aim 3		
Objective Organizational Context: Incentives		Aim 1 & Aim 3		
Perceptions of Implementation Climate: Support			Aim 2 & Aim 3	
Perceptions of Implementation Climate: Incentives			Aim 2 & Aim 3	
Perceptions of Implementation Climate: Expectations			Aim 2 & Aim 3	
Innovation-Values Fit			Aim 2	
Personal Characteristic: Age				All Three Aims
Personal Characteristic: Practice Type				All Three Aims
Personal Characteristic: U.S Trained				All Three Aims
Personal Characteristic: PI	All Three Aims			
Personal Characteristic: Medical Specialty				All Three Aims
Personal Characteristic: No. Years Since Graduate Med. School				All Three Aims
Organizational Factor: Maturity	Aim 3			
Organizational Factor: Structure		Aim 3		
Organizational Factor: Size		Aim 3		

Table 2: Descriptive Statistics, All Three Aims

	CCOP Survey Respondents n=485	CCOP Survey Non-Respondents n=332	CCOP Entire Sample n=817	All CCOP Physicians n=2725
	Mean or Proportion of Sample	Mean or Proportion of Sample	Mean or Proportion of Sample	Mean or Proportion of Sample
Outcome				
	4.7*	3.4	4.2**	2.7
	(8.1)	(7.5)	(7.9)	(5.9)
2011 Patient Enrollment	Range: 0, 62	Range: 0, 88	Range: 0, 88	Range: 0, 88
Descriptive Variables				
Age	52.6	52.8	52.7	52.5
	(9.8)	(9.6)	(9.7)	(9.8)
	Range: 34,82	Range: 34, 76	Range: 34, 82	Range: 32, 90
Practice Type				
Group Practice	78%	81%	79%**	72%
Hospital	12%	12%	12%**	11%
Solo Practice	4%	5%	2%**	5%
Other/None Listed	6%	2%	7%	12%
Training Location				
U.S Trained	80%	76%	78%	79%
Non U.S Trained	20%	24%	22%	21%
Experience	25.7	26.0	28.5	25.7
	(10.1)	(10.0)	(10.1)	(10.2)
	Range: 8, 57	Range: 9,51	Range, 8,57	Range: 2,58
Medical Specialty				
General Practice	5%	5%	5%	5%
Gynecological Oncology	4%	3%	4%	3%
Hematology Oncology	40%	39%	40%	31%
Medical Oncology	11%*	24%	16%	22%
Other Specialist	4%	4%	4%	5%
Pediatric Oncology	5%	3%	5%	4%
Radiation Oncology	21%	16%	19%	19%
Surgery	10%*	5%	8%**	10%
Gender				
Male	74%	71%	72.5%	74.6%
Female	26%	29%	27.5%	25.4%

Standard deviations in parentheses

* Indicates significant difference between survey respondents and non-respondents at .05 significance

**Indicates significant difference between sample and population at .05 significance

Surgery includes abdominal surgery, colon and rectal surgery, critical care sugary, dermatologic surgery, general surgery, neurological surgery, orthopedic surgery, plastic surgery, surgical oncology, spinal cord injury, thoracic surgery, urological

General practice includes addiction medicine emergency medicine, family practice/medicine, geriatric medicine, hospice and pa

Gynecological oncology includes gynecological oncology, general gynecology, gynecological surgery

Hematology oncology includes blood banking, hematology oncology, hematology

Oncology includes medical oncology, oncology

Radiation Oncology includes diagnostic radiology, nuclear medicine, radiation oncology, radiology, vascular and interventional r

Pediatric Oncology includes child neurology, emergency medicine - pediatrics, pediatric hematology oncology, pediatrics, pedia

Other specialist includes anatomic pathology, anesthesiology, cardiovascular disease , dermatology, endocrinology, gastroenterology, neurology, otolaryngology, pain medicine, psychiatry, pulmonary disease, rheumatology, urology

Table 3: Intraclass Correlations and Interrater Agreement Statistics for Physician Survey Questions

Construct	Measure	Aim(s)	ICC(1)	ICC(2)	Average $R^*_{WG(J)}$	% Significant $R^*_{WG(J)}$
Attitudes: Affect	NCI-sponsored trials explore clinical issues that are important in my practice	1	0.00 (0.02)	-0.04	0.77	89%
Attitudes: Beliefs	NCI-sponsored trials exclude too many patients	1	0.07* (0.03)	0.44	0.41	40%
Attitudes: Beliefs	NCI-sponsored trials are too complex to do in my practice	1	0.08* (0.03)	0.46	0.32	36%
Attitudes: Values	I value participating in NCI-sponsored clinical trials	1	0.01 (0.02)	0.09	0.82	94%
Latent Construct: Attitudes		1	0.06* (0.03)	0.38	0.96	100%
Innovation-Values Fit	I want to offer NCI-sponsored clinical trials to my patients	2	0.00 (0.02)	0.00	0.88	98%
Innovation-Values Fit	Participating in NCI-sponsored clinical trials is important to me	2	0.02 (0.02)	0.18	0.79	91%
Innovation-Values Fit	I value participating in NCI-sponsored clinical trials	2	0.01 (0.02)	0.09	0.82	94%
Innovation-Values Fit	NCI-sponsored trials explore clinical issues that are important in my practice	2	0.00 (0.02)	-0.04	0.77	89%
Latent Construct: Innovation-Values Fit		2	0.01 (0.02)	0.10	0.92	100%
Perceptions of Implementation Climate: Rewards	I receive appreciation when I enroll patients in NCI-sponsored clinical trials	2 & 3	0.05* (0.03)	0.36	0.21	15%
Perceptions of Implementation Climate: Rewards	I receive recognition when I enroll patients in NCI-sponsored clinical trials	2 & 3	0.07* (0.03)	0.45	0.23	21%
Perceptions of Implementation Climate: Expectations	I am expected to help the CCOP meet its patient enrollment goals in NCI-sponsored clinical trials	2 & 3	0.03 (0.02)	0.22	0.41	47%
Perceptions of Implementation Climate: Expectations	I am expected to enroll a certain number of patients in NCI-sponsored clinical trials	2 & 3	0.14* (0.04)	0.63	0.01	11%
Perceptions of Implementation Climate: Support	I get the research support that I need to identify potentially eligible patients for NCI-sponsored clinical trials	2 & 3	0.07* (0.03)	0.44	0.27	26%
Perceptions of Implementation Climate: Support	I get the research support that I need to enroll patients in NCI-sponsored clinical trials (e.g., consenting patients)	2 & 3	0.08* (0.03)	0.48	0.37	38%
Latent Construct: Implementation Climate		2 & 3	0.08* (0.03)	0.47	0.88	100%

Standard Errors in Parenthesis

** Statistically Significant*

CHAPTER 4: ORGANIZATIONAL AND PHYSICIAN FACTORS ASSOCIATED WITH PATIENT ENROLLMENT IN CANCER CLINICAL TRIALS

Overview

Our purpose was to identify physicians' individual characteristics, attitudes, and organizational contextual factors associated with higher enrollment of patients in cancer clinical trials among physician participants in the National Cancer Institute (NCI)'s Community Clinical Oncology Program (CCOP). We hypothesized that physicians' individual characteristics, such as age, medical specialty, tenure, CCOP organizational factors (i.e., policies and procedures to encourage enrollment), and attitudes towards participating in CCOP would directly determine enrollment. We also hypothesized that physicians' characteristics and CCOP organizational factors would influence physicians' attitudes towards participating in CCOP, which in turn would predict enrollment. We evaluated enrollment in NCI-sponsored cancer clinical trials in 2011 among 481 physician participants using structural equation modeling. The data sources include CCOP Annual Progress Reports, two surveys of CCOP administrators and physician participants, and the American Medical Association Masterfile.

Physicians with more positive attitudes towards participating in CCOP enrolled more patients than physicians with less positive attitudes. In addition, physicians who practiced in CCOPs that had more supportive policies and practices in place to encourage enrollment (i.e., offered trainings, provided support to screen and enroll patients, gave incentives to enroll patients, instituted minimum accrual expectations)

also significantly enrolled more patients. Physician status as CCOP Principal Investigator (PI) had a positive direct effect on enrollment, while physician age and non-oncology medical specialty had negative direct effects on enrollment. Neither physicians' characteristics nor CCOP organizational factors indirectly influenced enrollment through an effect on physician attitudes.

We examined whether individual physicians' characteristics and attitudes, as well as CCOP organizational factors, influenced patient enrollment in cancer clinical trials among CCOP physicians. Physician attitudes and CCOP organizational factors had positive direct effects, but not indirect effects, on physician enrollment of patients. Our results could be used to develop physician-directed strategies aimed at increasing involvement in clinical research. For example, administrators may want to ensure physicians have access to support staff to help screen and enroll patients or institute minimum accrual expectations. Our results also highlight the importance of recruiting physicians for volunteer clinical research programs whose attitudes and values align with programmatic goals. Given that physician involvement is a key determinant of patient enrollment in clinical trials, these interventions could expand the overall number of patients involved in cancer research. These strategies will be increasingly important as the CCOP network continues to evolve.

Background

Cancer clinical trials are instrumental for developing innovative cancer treatments and expanding current diagnostic, control, and prevention techniques (Sorbye et al., 2009) (Grunfeld et al., 2002). Despite the potential for positive health outcomes, only 3-5% of U.S adults with cancer participate in cancer clinical trials (NCI Cancer Bulletin,

2010). To increase patient participation in trials, the CCOP, a cancer focused provider-based research network administered by the NCI, engages community physicians in clinical research to enhance the translation of research results into practice (NCI, 2010). Since its inception in 1983, the CCOP network overall has generated over 50% of the enrollment in NCI-sponsored cancer prevention and control trials and 30% of the enrollment in NCI-sponsored cancer treatment trials (Minasian et al., 2010)

Although the CCOP network has successfully increased cancer clinical trial enrollment, individual physicians vary in their enrollment of patients in clinical trials. Many participating physicians enroll no patients in a given year, while others enroll dozens. In 2011, approximately 40% of CCOP physicians enrolled no patients (mean: 3; range: 0-88). Variation in physician enrollment has occurred since the program's inception, yet the reasons have not been systematically investigated. Research to date has focused on identifying the organizational and environmental contextual factors that drive clinical trial enrollment at the CCOP, rather than the individual, level (Kaluzny et al., 1995) (Carpenter et al., 2012) (Weiner et al., 2012) (Jacobs et al., 2013). No research has examined physician and organizational contextual factors associated with physicians' success in enrolling patients. These findings are critical to determine the context within which we can increase enrollment of cancer patients in NCI-sponsored cancer clinical trials and, in turn, the pace at which we identify and disseminate innovative therapies. Understanding factors that drive physician accrual will be critical in the organizational design of the new NCI Community Oncology Research Program (NCORP), for example, by setting minimum expectations for enrollment, recognizing high enrolling physicians, or providing physicians with support (NCI, 2013). Findings can

also inform physician recruitment efforts for NCORP.

This study seeks to identify the specific CCOP-affiliated physicians' characteristics and organizational contextual factors associated with higher enrollment of patients in NCI-sponsored cancer clinical trials. The hypothesis is that organizational contextual factors, such as trainings, support to enroll patients, expectations for enrollment, physicians' attitudes towards participating in clinical trials, and individual characteristics, such as age, tenure, medical specialty will directly and indirectly affect their enrollment of patients in trials.

Methods

Theoretical Framework

The conceptual model is adapted from the Multilevel Framework of Organizational and Individual Innovation Adoption (Frambach & Schilewaert, 2002). Although this framework was developed in the marketing and management literature, it has become a common approach to address innovation implementation in health and human services research as well. For example, the framework has been integrated as part of the Consolidated Framework for Implementation Research, which seeks to advance the implementation of health services research findings into practice [12]. An attractive feature of this framework is that it includes factors at both the organizational and individual levels to predict innovation adoption (Damschroder et al., 2009). In this study we focused on adoption among individual physicians.

The original model as developed by Frambach and applied to this setting is presented in Figure 1. The model postulates that social usage of the innovation, such as social norms, expectations, peer usage, and personal disposition towards

innovativeness (i.e., tendency to accept an innovation regardless of others) directly determines individual innovation acceptance. Innovation acceptance in this study is participation in clinical trials, defined as the number of patients CCOP physicians enrolled in NCI-sponsored cancer clinical trials in 2011. The model also suggests that social usage and personal disposition towards innovativeness determines individuals' attitudes towards using the innovation, which in turn determines innovation acceptance. Also included in the model are organizational facilitators (e.g., training, support, incentives) and individual characteristics (e.g., demographics, experience) that may also indirectly influence innovation acceptance through individuals' attitudes and personal disposition towards innovativeness respectively.

The model we tested adheres to the basic structure of the framework proposed by Frambach (2002); however, based on data availability, theory, and knowledge of CCOP network operation, we made three changes to the original model before analyzing any data. The tested model is presented in Figure 2. First, we combined social usage and organizational facilitators into one construct, organizational context. We did this for two reasons: (1) it makes theoretical sense as all the data used for this construct is at the CCOP level and (2) we only had two observed variables, peer enrollment and expectations, to construct social usage, but the statistical modeling approach required we use at least three observed variables (O'Brien, 1994). The second change is that we did not include personal disposition towards innovativeness in our model because we lacked data on this construct. Lastly, we included individual values as a component of attitudes rather than an individual characteristic. We decided to do this because our survey instrument included values, along with general affect,

beliefs towards the ease of participation, and complexity of clinical trials as components of attitudes towards innovation adoption. Therefore it made theoretical sense to include values as a component of attitudes versus an individual characteristic.

Study Setting and Sample

The CCOP network is a joint venture between the NCI Division of Cancer Prevention, which provides overall direction and funding for community hospitals and physicians to participate in clinical trials, clinical cooperative groups, and community-based physicians and hospitals (Kaluzny et al., 1994). The CCOP research bases design and conduct clinical trials, and individual community-based physicians and hospitals assist with patient enrollment, data collection, and dissemination of study findings (Minasian et al., 2010) (Kaluzny et al., 1994) When the data were collected in 2011, 47 CCOPs operated in 28 states with approximately 3,000 participating community physicians.

The sample is comprised of physicians who responded to the 2011 CCOP Physician Survey. We used a stratified (by CCOP) random sample of 817 physicians across all 47 CCOPs. The final sample included 485 physicians (59.4% of the total physicians surveyed). The only significant ($p<0.05$) differences between survey responders and non-responders were that responders enrolled more patients per year (4.7 versus 3.4), were more likely to be a surgeon (10% versus 5%), and were less likely to be a non-specialized general oncologist (11% versus 24%). There were no significant differences between respondents and non-respondents regarding gender, race, age, practice type, training location, and tenure. This study was determined to be exempt from review by the Institutional Review Board at the University of North Carolina

at Chapel Hill.

Study Design and Data Sources

The data for this cross-sectional study were obtained from four sources. The 2011 CCOP Progress Reports provided data on physicians' enrollment activity from June 1, 2011 to February 29, 2012. The 2011 CCOP Administrator Survey and the 2011 CCOP Physician Survey were both administered as part of a larger NCI-funded-study (5R01CA124402). The Physician Survey supplied data on CCOP physicians' attitudes towards participation in clinical trials. Responses were collected between October 2011 and January 2012. The Administrator Survey provided information on the CCOP organizational contextual factors. The majority of responses were collected at the annual CCOP meeting in September 2011. Any remaining surveys were completed in October 2011. We achieved a 100% response rate from CCOP Administrators. Lastly, the 2012 American Medical Association Physician Masterfile provided data on CCOP physicians' individual characteristics.

Measures

Table 4 provides details on our measures. The outcome was the number of patients CCOP-affiliated physicians enrolled in NCI-sponsored cancer clinical trials in 2011. Physician attitudes, a predictor construct, was composed of questions assessing beliefs related to the complexity of trials, whether trials excluded too many patients, affect towards whether trials explored important issues, and physicians' values related to participating in clinical trials. Organizational contextual factors, also a predictor construct, included educational trainings offered, support provided by the CCOP to physicians to help screen and enroll patients, incentives provided to physicians, peer

usage (i.e., the average number of patients enrolled in NCI-sponsored clinical trials for physicians within a specific CCOP), and CCOP expectations for enrollment. Physicians' individual characteristics included age, practice type, tenure, physician training location, medical specialty, and whether or not the physician is the CCOP Principal Investigator (PI).

Statistical Analysis

SEM with maximum likelihood estimation was used to simultaneously test the effects of the latent constructs in our conceptual model (i.e., organizational contextual factors, physician attitudes) on enrollment. SEM is composed of multivariate regression models and can be used to estimate proposed causal relationships (Norman & Streiner (eds), 2003) (Schreiber et al., 2006). We used confirmatory SEM to test the hypothesized pathways among factors represented in Figure 2 by comparing how well this proposed structure fits the observed data. We elected to use SEM because it allowed us to test for constructs that are not directly assessed, but are instead composed of observed indicators representing the constructs of interest (e.g., CCOP organizational contextual factors, physician attitudes). We elected to use clustered robust standard errors to account for clustering of physicians within 47 CCOPs. We evaluated model fit using the Comparative Fit Index (CFI) and the Tucker-Lewis Index (TLI). CFI and TLI values range from 0 to 1, with values ≥ 0.90 representing adequate fit (Norman & Streiner (eds), 2003) (Schreiber et al., 2006). We also examined the root mean square error of approximation (RMSEA), and the associated confidence interval and p-value. RMSEA values < 0.05 and an upper bound of the confidence interval < 0.1 are considered acceptable (Norman & Streiner (eds), 2003) (Schreiber et al., 2006).

Next, we examined the standardized root mean squared residuals (SRMR), with values < 0.08 considered acceptable fit (Norman & Streiner (eds), 2003) (Schreiber et al., 2006). We also evaluated our model by testing the significance of all standardized estimates, including the direct and indirect effects of variables on the outcome.

Based on these fit statistics for the original model in Figure 2, we elected to re-specify the model to improve its fit. SEM is an iterative process in which model fit is improved by using theory and modifications indices either to add additional pathways between variables or to allow items to co-vary (Norman & Streiner (eds), 2003) (Schreiber et al., 2006). Modification indices are the minimum that the chi-square statistic is expected to decrease if the corresponding parameter is no longer assumed to be fixed at zero (Norman & Streiner (eds), 2003) (Schreiber et al., 2006). When revising the model, we tested whether model fit improved by comparing the baseline model with the new model using the Lagrange multiplier test and fit statistics.

Once we achieved a well-fitting model, we tested the significance of all standardized estimates, including direct and indirect effects. Standardized parameter estimates are transformations of unstandardized estimates that remove scaling and can be used for informal comparisons of parameters throughout the model (Schreiber et al., 2006). Direct effects are equal to the regression coefficients (i.e., β) while indirect effects are the product of the two regression coefficients. For example, if X predicts Y and Y predicts Z, then the indirect effect of X on Z equals the product of the two regression coefficients (X on Y and Y on Z). Lastly, to ensure the validity of our SEM results, we checked our results using negative binomial regression analysis with clustered robust standard errors. Analyses were performed using Mplus 7.

Results

Study Population

The final sample included 481 physicians with complete information. Table 5 provides descriptive statistics for the entire sample. Notably, 74% were male, 75% were White non-Hispanic, and their mean age was 53 years; they have been in practice a mean of 26 years. The vast majority practiced in group practices and trained in the U.S; 72% were oncology-based specialists, 10% were surgeons, and 18% reported another medical specialty (e.g., gynecology, pediatrics, internal medicine). Physicians enrolled a mean of 5 patients in 2011 (range: 0-62); approximately 40% of physicians enrolled no patients in the 9-month reporting period.

SEM Analysis

The fit statistics and modification indices for the fixed parameters of the original model tested in Figure 2 suggested that we re-specify the model to improve fit (CFI = 0.648; TLI = 0.560; RMSEA = 0.067; SRMR = 0.061). Therefore, we added seven post-hoc modifications that were theoretically justified and improved model fit. Figure 3 presents the final model with all post hoc modifications and standardized estimates. For these modifications, we allowed the error terms of the following measures to co-vary higher than with other variables. For example, the percentage of doctors supported in screening and enrolling patients, likely share common variation that is not explained by any of the proposed relationships in the model.

1) Peer-usage with the outcome: Peer-usage is based on the individual physicians' enrollment within a specific CCOP. We co-varied the error terms as they likely share common variation that is not explained by relationships in the model.

2) The percentage of doctors supported in screening and enrolling patients: The same support staff generally preform both functions within a CCOP.
3) Trainings offered with the percentage doctors who are supported in screening and enrolling patients: The number of trainings offered relates to the number of support staff available.
4) Incentives with expectations for enrollment: CCOPs that provide incentives may also be more likely to have expectations for enrollment.
5) Affect with values: Providers who believe that trials explore important issue are also likely to value participating.
6) Belief that trials are too complex with belief that trials exclude too many patients: These relate to an overall negative view of CCOP and may discourage participation.
7) Affect with whether physicians believe trials exclude too many patients: Providers who report that trials are important are less likely to think they exclude too many patients.

With the addition of each co-variance, we tested the baseline model against the new model for improved model fit. Overall, we achieved a final well-fitting model (CFI = 0.936; TLI = 0.914; RMSEA = 0.030; SRMR = 0.046) (Figure 3).

In general, standardized effects of less than 0.10 constitute a small effect; values greater than 0.30 indicate a medium effect; and values greater than 0.50 indicate a large effect (Suhr, 2006). Overall the effect sizes were fairly small for the latent constructs of organizational context and individual attitudes, which had significant positive direct effects on the outcome. For example, the direct effect of organizational

context on enrollment was β=0.19 (p=0.02) and for physician attitudes it was β=0.13 (p=0.04). In addition, physician's CCOP PI status, age, and non-oncologist specialty also had significant direct effects on enrollment. The most significant positive direct effect was whether the physician was the PI (β=0.35; p<0.00). Physician age (β= -0.27; p=0.02) and non-oncology specialty (β= -0.14; p=0.03) had significant negative direct effects on enrollment.

There was no evidence, however, that organizational context or any physician individual characteristics significantly influenced accrual through their effects on physician attitudes. Finally, training location, practice location, and physicians who are surgeons, hematologists, and radiological oncologists (compared to non-specialized oncologists) did not directly affect enrollment. Overall our model explained 21% of the variance in patient enrollment. The robustness check of our SEM results using negative binomial regression analysis with clustered robust standard errors confirmed our main findings that both organizational context and attitudes were significantly associated with patient enrollment, along with physician status as the CCOP PI and medical specialty.

Discussion

We hypothesized that organizational contextual factors and physicians' attitudes and individual characteristics would directly and indirectly (through attitudes) be associated with their enrollment of patients in NCI-sponsored cancer clinical trials. This hypothesis was partially supported as organizational context and physician attitudes directly influenced enrollment; however, there were no indirect effects on enrollment through attitudes. Attitudes impacted enrollment as physicians who: viewed participation as more useful and easy, had individual values aligned with CCOP goals, and had more

positive feelings were more active in enrolling patients in trials. This finding highlights the importance of recruiting physicians for volunteer research programs who value participating in clinical trials, find participating in trials important, and feel they are able to do so. Recruiting physicians whose attitudes align with the program's goals is especially important for community sites interested in participating in the new NCORP. Interestingly, organizational context did not predict physicians' attitudes. Changes in organizational context may influence overall enrollment of patients as a supportive environment assists with accrual efforts, but these contextual factors do not appear to impact the attitudes of physicians. This finding further supports recruiting physicians with positive attitudes towards participating in clinical research.

In addition, as hypothesized, contextual factors made a difference. Specifically, organizations that provided support for physicians to consent and enroll patients, offered incentives for enrollment, and mandated expectations for enrollment also increased physician enrollment, perhaps due to a strong sense of organizational commitment and social norms. Therefore CCOPs or other voluntary research programs might encourage physicians to actively participate and enroll patients. Program administrators should consider providing support for physicians' research activities, such as staff to help consent and enroll patients, incentives for enrollment goals (e.g., small tokens of appreciation, public acknowledgment), and trainings to learn about latest developments in research. Such strategies may not directly change physician attitudes, but may provide a supportive organizational context to encourage active physician participation in recruiting patients.

We were surprised that organizational context did not have an indirect effect on enrollment by influencing physicians' attitudes towards clinical trials. Perhaps physicians' attitudes were not a significant mediator of organizational context because physicians elect to participate in CCOP. Although implementation of some innovations in healthcare may be mandated, clinical trial participation, however, is not required. It may be that, specific organizational contextual factors do not influence attitudes among physicians who have already agreed to participate and recruit patients to clinical trials. Organizational context may shape attitudes towards participation in other types of settings where participation or implementation of a specific innovation is mandatory and attitudes would likely be more fluid. Therefore, organizational context would have more of an opportunity to determine attitudes towards participation.

In addition, four physician characteristics also significantly effected enrollment. Physician status (i.e., CCOP PI or not) was the strongest predictor. PIs are more likely than non-PIs to be committed to the CCOP and feel obligated to set a "good example" for their colleagues. PIs may also be more familiar with available trial protocols and receive greater assistance from support staff to consent and enroll patients. A strong negative predictor of enrollment was whether the physician was a non-oncology specialist. One reason may be that non-oncologists feel less comfortable and/or familiar with cancer protocols than oncologists. In addition, both physician age and tenure had significant total effects on outcome.

We were surprised that practice location, foreign medical training, and medical specialty (with the exception of non-oncology) did not impact enrollment. Although none of the previous studies exclusively examined enrollment among CCOP physicians, past

studies found that practice type (i.e., office-based practice compared to hospital based practice) and medical specialty (i.e., medical oncologists compared to radiation oncologists) increased physician enrollment of patients while foreign-trained oncologists enrolled fewer patients. In our study, practicing at a hospital or as a solo physician (compared to a group practice) may not have had a significant effect because it was difficult to discern a physician's main practice location. In addition, many CCOP physicians travel between different offices, which may make their primary location less relevant. We suspect that foreign medical training did not impact enrollment because we could not determine how long physicians had been practicing in the U.S., which is likely a more relevant predictor of enrollment than training location. In addition, medical specialty may not be as influential on enrollment as there are an abundance of types of cancer clinical trials, including protocols for surgery and radiological interventions. Therefore all cancer-related specialties are comfortable and willing to enroll patients in cancer trials.

Limitations

There are several limitations of our study. First, we only included physicians who participate in CCOPs. These physicians have already agreed at least on some level to participate in CCOP. Therefore our findings suggest the organizational and individual factors that are most relevant to encourage active participation in CCOP. It is important to note, however, that many organizational strategies (e.g., recognition of high achievers, expectations for enrollment) could be implemented by diverse organizations to increase physician participation in clinical research. Second, we are unable to account for variation in the number of potentially eligible patients physicians see.

Therefore, we were unable to distinguish physicians failing to offer a cancer clinical trial from patients' refusal to enroll. We also lacked the data to incorporate patient-level characteristics in the analyses. We cannot account for variations in patients' cancer stage, co-morbidities, age, or any other factors that may determine eligibility. Ultimately patients are the final decision makers regarding their participation in a cancer clinical trial. However, given that 75% of patients agree to enroll if offered we do not believe this to be a significant limitation of this study (Albrecht et al., 2008). Third, given that we were only able to explain 21% of the variance in enrollment, we were also limited in the data that was available to examine individual physician enrollment. Future studies may want to consider including additional factors, such as patient-level characteristics in the model to increase the amount of variation explained. In addition, more information on physician behaviors and personality traits (e.g., personal disposition to innovativeness, goal-orientation) may also help to explain variance in enrollment in cancer clinical trials.

We believe this study extends the literature in several important ways. First, it is the first study to evaluate physician-level predictors of their success in enrolling patients in CCOP cancer clinical trials. Second, it provides the basis of physician-directed strategies that may effectively promote enrollment of patients in cancer clinical trials. By expanding the number of patients involved in cancer clinical trials, we can accelerate the pace in which we identify promising innovative therapies and novel interventions that can ultimately improve the outcomes of cancer patients.

Conclusions

The findings from this study are important for program administrators looking to increase volunteer physician participation in clinical research as well for new NCORP

program sites. Our results suggest two strategies to increase participation. The first is to ensure physicians attitudes and values align with the programmatic goals. For example, recruiting physicians who value participating in clinical trials, find participating in trials important, and feel they are able to do so is a key determinant of a program's success. Recruitment of physicians whose values align with program goals is especially important given that CCOP organizational context did influence attitudes towards participation. Second, program administrators should consider providing support for physicians' research activities, such as staff to help consent and enroll patients, incentives for enrollment goals (e.g., small tokens of appreciation, public acknowledgment), and trainings to learn about latest developments in research. Such strategies may not directly change physician attitudes, but may provide a supportive organizational context to encourage active physician participation in recruiting patients.

Table 4: Overview of Variables and Measures for Aim 1

Model Construct	Variable	Measure	Measure Type	Data Source
Outcome Variable				
Innovation Acceptance	Enrollment	No. of patients enrolled in NCI-sponsored cancer clinical trials in 2011	Continuous	CCOP Progress Reports
Predictor Variables				
Attitudes	Affect	NCI-sponsored trials explore clinical issues that are important in my practice	Continuous	CCOP-Affiliated Physician Survey
Attitudes	Beliefs: Exclude Patients	NCI-sponsored trials exclude too many patients	Continuous	CCOP-Affiliated Physician Survey
Attitudes	Beliefs: Trials Complex	NCI-sponsored trials are too complex to do in my practice	Continuous	CCOP-Affiliated Physician Survey
Attitudes	Personal Values	I value participating in NCI-sponsored clinical trials	Continuous	CCOP-Affiliated Physician Survey
Organizational Context	Training	CCOP sponsor any events where physicians could learn about the latest developments in cancer research, treatment, prevention, or control?	Binary: 0 = N; 1=Y	CCOP Administrator Survey
Organizational Context	Support: Screening	Proportion of physicians that have CCOP staff members routinely screen patient charts for potentially eligible patients	Continuous	CCOP Administrator Survey
Organizational Context	Support: Enrolling	Proportion of physicians that have CCOP staff members routinely assist with enrollment	Continuous	CCOP Administrator Survey
Organizational Context	Incentives	CCOP provide some form of recognition to Type-A physicians with high levels of accrual to NCI-sponsored trials?	Binary: 0 = N; 1=Y	CCOP Administrator Survey
Organizational Context	Peer Usage	Average no. of patients enrolled in NCI-sponsored clinical trials by physicians in CCOP	Continuous	CCOP Progress Reports
Organizational Context	Expectations	CCOP expect Type-A physicians to enroll a minimum no. of patients in NCI-sponsored trials?	Binary: 0 = N; 1=Y	CCOP Administrator Survey
Personal Characteristics	Age	The current year minus the physicians' year of birth	Continuous	AMA Provider Masterfile
Personal Characteristics	Practice Type	Indicator of present primary employment arrangement (e.g., solo, group, hospital)	Categorical	AMA Provider Masterfile
Personal Characteristics	U.S Trained	Indicator if physician trained in the U.S.	Binary: 0 = N; 1=Y	AMA Provider Masterfile
Personal Characteristics	PI	Please indicate the PI of the CCOP	Binary: 0 = N; 1=Y	CCOP Progress Reports
Personal Characteristics	Medical Specialty	Indicator of physician self-designated primary medical specialty	Categorical	AMA Provider Masterfile
Personal Characteristics	Tenure	No. of years since graduated medical school	Continuous	AMA Provider Masterfile

Table 5: Descriptive Statistics Aim 1 Physician Level Variables

	CCOP Survey Respondents n=481	
	Mean or Proportion of Sample	Range
Outcome		
2011 Patient Enrollment	4.7* (8.1)	0, 62
Descriptive Variables		
Gender		
Male	74%	
Female	26%	
Race		
White	75%	
Asian	15%	
African-American	1%	
Other	9%	
Variables included in Model		
Attitudes		
Affect	4.6 (0.7)	2,5
Beliefs: Exclude Pts.	3.4 (1.2)	1,5
Beliefs: Complexity of Trials	2.4 (1.2)	1,5
Values	4.7 (0.6)	1,5
Personal Characteristics		
Age	52.6 (9.8)	34,82
Practice Type		
Group Practice	78%	
Hospital-Based	12%	
Solo Practice	4%	
Other/None Listed	6%	
Training Location		
U.S Trained	80%	
Non U.S Trained	20%	
Tenure (Yrs. In Practice)	25.7 (10.1)	8, 57
Medical Specialty		
Hematology Oncology	40%	
Radiation Oncology	21%	
Other Specialty	18%	
Medical Oncology	11%*	
Surgery	10%*	
Principal Investigator	9%	

Standard deviations in parentheses

*Indicates significant difference between survey respondents and non-survey respondents

Other race includes American Indian, Native Hawaiian/Pacific Islander, More than one race, or unknown

Hematology oncology includes blood banking, hematology oncology, hematology

Radiation Oncology includes diagnostic radiology, nuclear medicine, radiation oncology, radiology, vascular and interventional radiology

Other specialist includes general practice, gynecological oncology, pediatrics, pediatric hematology, cardiovascular disease etc.

Surgery includes colon and rectal surgery, critical care sugary, general surgery, neurological surgery, surgical oncology, urological surgery etc.

Figure 1: Individual Innovation Acceptance in Organizations

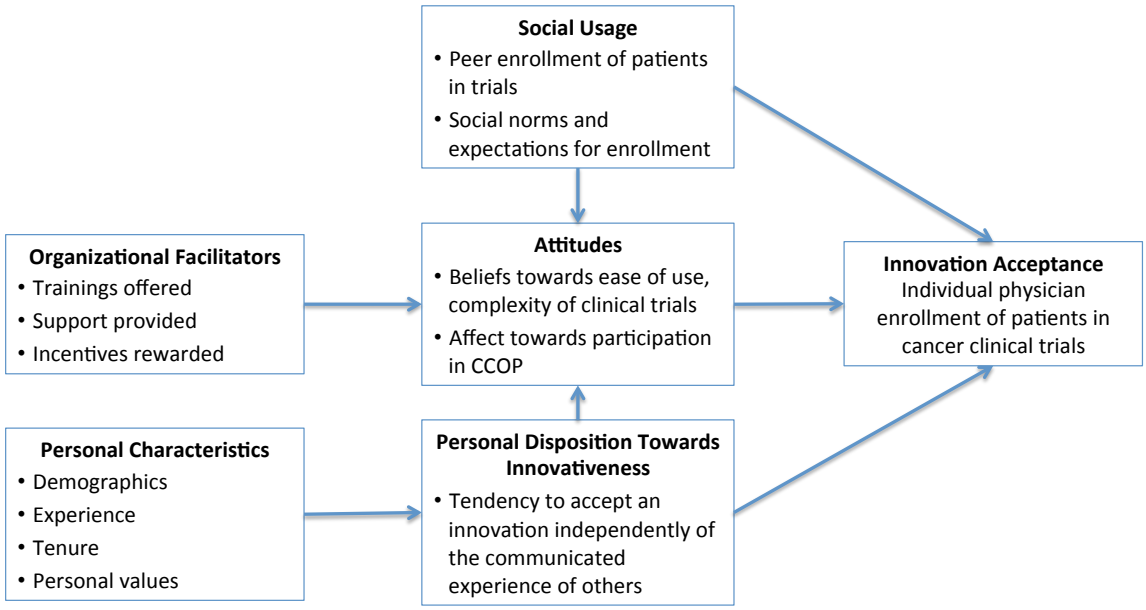


Figure 2: Tested Model of Individual Innovation Acceptance in Organizations

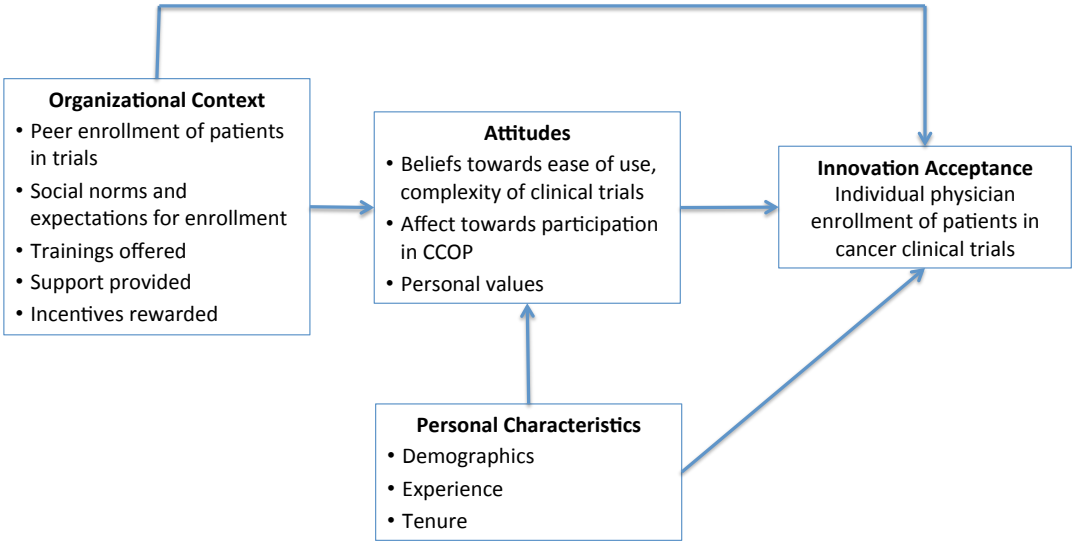
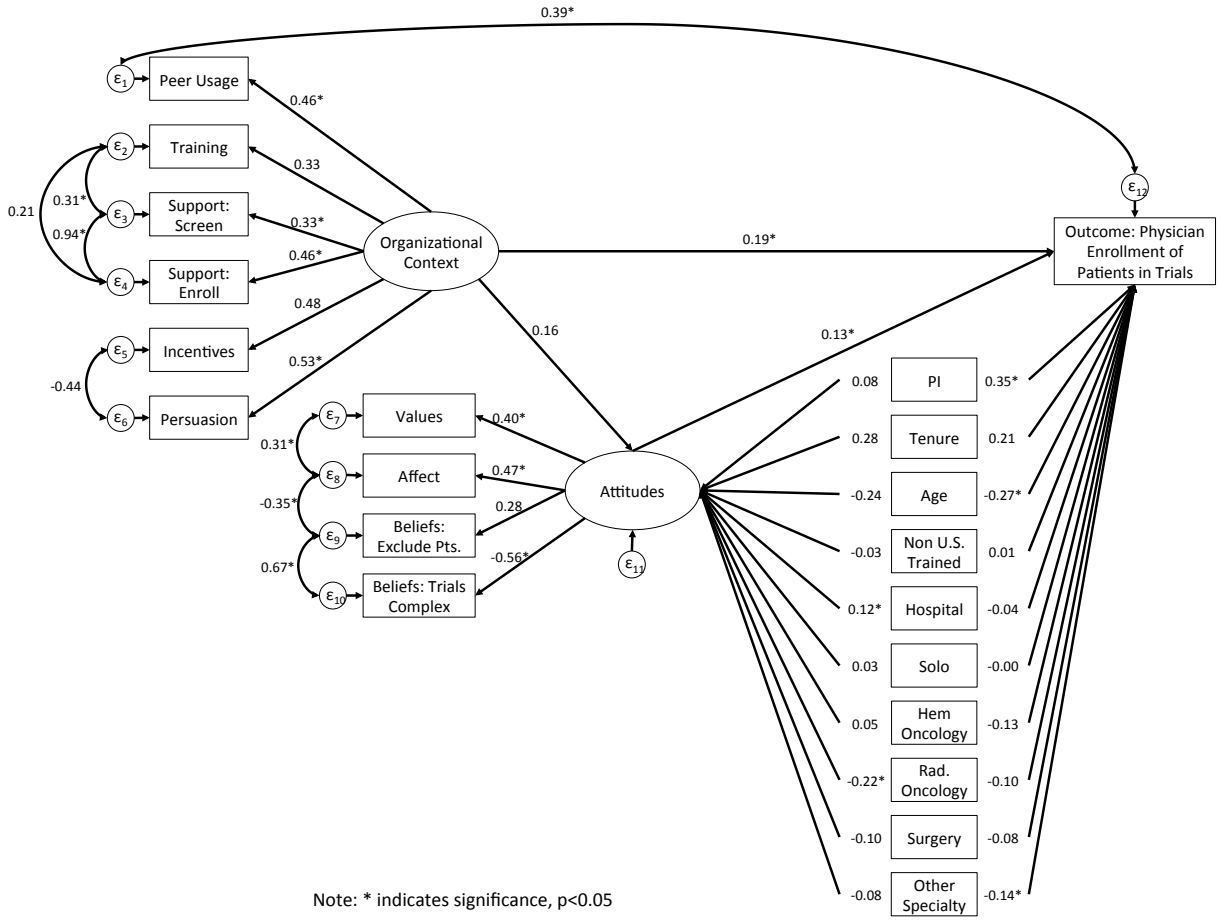


Figure 3: Standardized SEM Results Aim 1



CHAPTER 5: THE MISSING LINK: A TEST OF KLEIN AND SORRA'S PROPOSED RELATIONSHIP BETWEEN IMPLEMENTATION CLIMATE, INNOVATION-VALUES FIT AND IMPLEMENTATION EFFECTIVENESS

Overview

Klein and Sorra's theory of innovation implementation suggests that the effectiveness of implementing an innovation results from both a climate that supports, rewards, and expects implementation as well as from the fit between the innovation and the intended users' values. Although the authors propose that innovation-values fit moderates the effect of implementation climate on implementation effectiveness, this relationship is rarely tested in practice. In addition, most of the evidence supporting the use of the theory in health and human services research is from qualitative studies, while most of the quantitative tests of the theory occur in the computing or information systems environment.

Therefore, the goal of this study is to quantitatively test the proposed relationship in which innovation-values fit moderates the effect of implementation climate on implementation effectiveness in a health services setting. We tested the theory of innovation implementation using structural equation modeling (SEM) among 481 physician participants in the National Cancer Institute's Community Clinical Oncology Program (CCOP). The data sources included the CCOP Annual Progress Reports, a survey of CCOP physician participants, and the American Medical Association Physician Masterfile. Overall the hypothesized SEM model fit well. Our results demonstrated that both implementation climate and innovation-values fit were

significantly associated with implementation effectiveness among CCOP physicians (p=<0.05). In addition, including innovation-values fit as a moderator improved the overall fit of our SEM. The moderator explained 2.6% of the variation in implementation effectiveness and approached statistical significance (p=0.06).

Our study advances both innovation implementation theory as well as clinical practice. The results of this study extend the scientific literature by not only empirically examining the theory of innovation implementation in a health services setting, but also by testing whether innovation-values fit moderates the effect of implementation climate on implementation effectiveness, which has yet to be fully explored. Practically, CCOP administrators or other program directors looking to increase physician participation in clinical research should foster a strong implementation climate to encourage enrollment, as in this setting innovation-values fit did not statistically strengthen the relationship between implementation climate and implementation effectiveness.

Background

Implementation effectiveness, or the consistency and quality of organizational members' use of a specific innovation, is important because it is the key determinant regarding the benefits an organization may receive by implementing a given innovation (e.g., increased profitability, employee morale, productivity) (Klein & Sorra, 1996). Although several conceptual frameworks highlight innovation adoption and/or the effectiveness of the innovation itself, few theories focus on explaining the effectiveness of the implementation process (Davies et al., 2010) (Whitman, 2009) (VA, 2009). Klein and Sorra's theory of innovation implementation suggests that implementation effectiveness results from both a climate that encourages implementation, as well as the

fit between the innovation and the organizational members' values (Klein & Sorra, 1996). Their theory is unique in that it not only explains implementation effectiveness, but it also highlights the effectiveness of the innovation itself. Although the theory originated in manufacturing, it has become a more common approach to address innovation implementation in the field of health services research (Weiner et al., 2011).

One of the issues associated with using the theory of innovation implementation in health services research is that most evidence supporting its use in this context is qualitative in nature (Weiner et al., 2011) (Weiner et al., 2012) (Teal et al., 2012) (Damschroder et al., 2009) (Weiner et al., 2009) (Helfrich et al., 2007). Although important, qualitative studies tend to utilize smaller sample sizes, have limited external generalizability, and present challenges in standardizing the measurement of key constructs. In terms of quantitative evidence, the majority of supportive evidence is from studies examining the effectiveness of technology implementation among company employees in information systems and computing organizations (Holahan et al., 2004) (Dong et al., 2008) (Klein et al., 2001) (Osei-Bryson et al., 2008). These settings are difficult to compare to healthcare because: (1) physicians experience greater professional autonomy, and (2) the process of implementing computing technology may differ from delivering clinical care.

A second outstanding issue surrounding the use of the theory of innovation implementation in health services research is that the main relationship between implementation climate and innovation-values fit has not been empirically tested. Klein and Sorra propose that innovation-values fit (between the innovation and the organizational members' values) moderates or strengthen the effect of perceptions of

implementation climate on implementation effectiveness. So, a strong sense of innovation-values fit will intensify the relationship between implementation climate and implementation effectiveness (Klein & Sorra, 1996). Prior research testing the theory of innovation implementation has included both concepts, but whether innovation-values fit moderates the effect of implementation climate on implementation effectiveness has yet to be examined (Holahan et al., 2004) (Dong et al., 2008) (Klein et al., 2001) (Osei-Bryson et al., 2008). The lack of current studies examining innovation-values fit as a moderator may be attributable to the fact that the figure included in Klein and Sorra's seminal article detailing the theory does not depict this relationship (Figure 4) (Klein & Sorra, 1996). It is important to empirically examine innovation-values fit as a moderator between implementation climate and implementation effectiveness to provide further evidence on the utility of using this theory in health services research and to better understand the proposed relationship between implementation climate and innovation-values fit.

Therefore, the goal of this study is to draw on Klein and Sorra's theory to test whether innovation-values fit moderates the effect of implementation climate on implementation effectiveness in a health services context. We used structural equation modeling (SEM) to examine implementation effectiveness among physician participants in the National Cancer Institute's (NCI) Community Clinical Oncology Program (CCOP), a national provider-based research network aimed at engaging community physicians in NCI-sponsored clinical trials in order to advance scientific findings and facilitate the translation of research results into practice (Comis et al., 2009). The findings of this study extend the current literature by testing the proposed relationship between

implementation climate and innovation-values fit. Our results also suggest that potential administrative changes in the CCOP network and other provider-based research networks can lead to an increase in the enrollment of patients in cancer clinical trials.

Methods

Theoretical Framework

Using Klein and Sorra's theory of innovation implementation (1996), we sought to test whether innovation-values fit moderates the effect of perceptions of implementation climate on implementation effectiveness (Figure 5). The authors propose that implementation effectiveness results from both a climate for implementation, or the extent to which the use of a specific innovation is rewarded, supported, and expected within an organization, and innovation-values fit, or the extent to which intended users perceive that the innovation is consistent with their current values (Klein & Sorra, 1996). Klein and Sorra suggest that all three of these constructs should be assessed at the organizational level (1996). For example, they propose that innovation-values fit and implementation climate are homogenous constructs composed of organizational members' *shared* perceptions, and are therefore not based on specific individual perceptions of climate or values fit (Klein & Sorra, 1996). In addition, they indicate that implementation effectiveness represents the *overall* consistency and quality of an organization's innovation use (Klein & Sorra, 1996) (Weiner et al., 2011). In practice, however, the theory has been empirically tested at both the organizational and individual levels (Holahan et al., 2004) (Dong et al., 2008) (Klein et al., 2001) (Osei-Bryson et al., 2008).

In this study, we were most interested in examining *individual* physician participation in CCOP because of the significant variation that occurs in enrolling patients in cancer clinical trials. Although all physicians agree to participate in CCOP at some level, the number of patients enrolled by CCOP physicians in 2011 ranged from 0 to 88 patients per physician, with over 40% of physician enrolling zero patients. In testing an organizational-level theory at the individual level, researchers should not assume that the same theoretical relationships apply (Klein & Kozlowski, 2000). Modifications to the model may be needed to ensure that the constructs are relevant at the individual level. For example, in this study we believed that individual physician characteristics (e.g., age, medical specialty, status as the CCOP Principal Investigator (PI)) would also influence implementation effectiveness. We modified the original model to include these physician characteristics in order to test the model among individual physicians (Figure 6).

Specifically, we propose that a strong implementation climate would lead to higher patient enrollment among physicians because perceptions that a CCOP institutes accrual expectations, provides support for the enrollment of patients, as well as recognizes enrollment efforts should encourage physicians to enroll more patients in cancer clinical trials. A strong implementation climate would ensure physicians have the skill and support needed to enroll patients, incentives to participate are in place, and obstacles to enroll patients are limited.

Hypothesis 1: Implementation climate will have a direct effect on implementation effectiveness.

The relationship between climate and implementation effectiveness should be strengthened if physicians also perceived that participating in clinical research aligned

with their personal values, felt participating was important, and wanted to enroll patients. For example, when innovation-values fit is good (i.e., physicians view CCOP participation as highly congruent with their values), physicians should be committed to participating in CCOP. If the CCOP's climate also encourages implementation, enrollment should be greater as physicians are also skilled and encouraged to enroll patients. If the climate is weak, however, enrollment may be more sporadic as although physicians are committed to clinical research, the CCOP climate is not providing the skills and incentives needed to enroll patients. However, when innovation-values fit is poor (i.e., physicians regard CCOP participating as highly in congruent with their values), physicians will likely resist active participation in CCOP by not enrolling patients, regardless of implementation climate. A strong climate would make participating in CCOP easier, but unless physicians are committed to enrolling patients, they are unlikely to do so.

Hypothesis 2: Innovation-values fit will moderate the relationship between implementation climate and implementation effectiveness

As discussed, we also included physician level variables in the model. We propose that physician enrollment may vary based on the physician's status as the CCOP PI, age, years in practice, medical specialty, training location, and practice location (Comis et al., 2009) (Jacobs et al., 2014). These individual characteristics may impact a physician's ability and desire to enroll patients in trials. For example, the CCOP PI would likely be more inclined to participate as they want to set a good example for other CCOP physicians regardless of their perceptions of climate, while non-oncology specialists may feel less comfortable with cancer protocols and would enroll fewer patients per year regardless of implementation climate or innovation-values fit. In addition, older

physicians and those that train outside of the United States should be included as they may negatively influence enrollment while physicians that practice in a hospital setting may have more access to resources and thus practice location may positively influence enrollment.

Hypothesis 3: Physician characteristics will have a direct effect on implementation effectiveness

Study Setting and Sample

The study was conducted in NCI's CCOP network. The CCOP network was created in 1983 with the goals of advancing the evidence-base by conducting research in clinical settings where most people receive their care, and translating results into better care (Kaluzny et al., 1994) (Kaluzny et al., 1995) (Minasian et al., 2010) (Carpenter et al., 2012) (Weiner et al., 2012) (Jacobs et al., 2013). The CCOP network is a joint venture between NCI's Division of Cancer Prevention (NCI/DCP), selected cancer centers and clinical cooperative groups (CCOP research bases), and community-based physicians and hospitals (CCOP organizations). NCI/DCP provides overall direction and funding for community hospitals and physician practices to participate in clinical trials while CCOP research bases design clinical trials and CCOP organizations assist with patient enrollment, data collection, and dissemination of study findings (Kaluzny et al., 1994) (Kaluzny et al., 1995) (Minasian et al., 2010) (Carpenter et al., 2012) (Weiner et al., 2012) (Jacobs et al., 2013). In 2011, when the study was conducted, the CCOP network consisted of 47 CCOP organizations in 28 states, the District of Columbia, and Puerto Rico and included 400 hospitals and 3,520 community physicians. CCOP organizations consisted on average of 10 community hospitals or physician practices and 48 physicians. Our specific sample included 485 CCOP

physicians who responded to the 2011 CCOP-Affiliated Physician Survey, described in detail below.

In FY 2012 the CCOP budget totaled $87.4 million. The median CCOP organization award was $705,000. NCI funds CCOP organizations through a cooperative agreement whereby participating organizations are expected to share the costs with NCI. Continued funding depends on CCOP organizations' meeting clinical trial accrual goals set by NCI. CCOP organizations are generally composed of a physician CCOP PI who provides local program leadership, a team of support staff, as well as affiliated physicians who enroll patients in NCI-sponsored cancer clinical trials (Weiner et al., 2011) (Teal et al., 2012). CCOP staff members typically include an associate PI, program administrators, research nurses or clinical research associates, data managers, and regulatory specialists who together coordinate the review and selection of clinical trial protocols for the CCOP, disseminate any trial protocol updates, collect study data, and assist affiliated physicians with enrollment (Teal et al., 2012). CCOP-affiliated physicians include specialized oncologists (e.g., hematological, surgical and radiation oncologists), general medical oncologists, and other medical specialists (e.g., urologists, gynecologists, and gastroenterologists).

Data Sources

The data for this cross-sectional study were obtained from three sources. First, this study utilizes the 2011 CCOP Annual Progress Reports submitted in March 2012, which cover the period from June 1, 2011 to February 29, 2012. Each March, every CCOP submits a progress report to NCI detailing the previous nine-month's research and enrollment activities. The report includes standardized questions regarding the

allocation of CCOP resources, staffing assignments, total cancer patient volume, the number of open cancer clinical trials, the total number of patients each CCOP enrolls, as well as the total number of patients each individual CCOP-affiliated physician enrolls.

Second, we used the 2011 CCOP Physician Survey, which was administered as part of a larger NCI-funded-study (5R01CA124402). The goal of this survey was to learn more about physician participation in the CCOP program. The physician survey included specific questions regarding physicians' perceptions regarding expectations for enrollment, research support provided by the CCOP, ability to provide input, how well they are kept informed of CCOP activities, recognition received from the CCOP, as well as personal beliefs, attitudes, and values regarding the importance of cancer clinical trials. These surveys specifically supplied data on CCOP physicians' perceptions of innovation climate as well as their perceptions of innovation-values fit.

The sampling frame included all CCOP-affiliated physicians eligible to accrue patients to clinical trials. Between October 2011 and January 2012, we surveyed 817 physicians using a random sample stratified across all 47 CCOPs. On average, 17 physicians were surveyed per CCOP, and 10 physicians responded per CCOP organization. One week after sending potential respondents a postcard announcing the survey and highlighting its importance to NCI, physicians were sent a cover letter explaining the goals of the survey, the survey itself, a self-addressed and stamped return envelope, and a $50 Visa gift card as an incentive to complete the survey. Physicians were also able to complete the survey online via a unique access code provided in the mailings. A thank you or reminder postcard was then sent the following week. Approximately three weeks after the first mailing, non-respondents received a

second copy of the survey, cover letter, and return envelope. Lastly, we contacted CCOP PIs and CCOP Administrators to email the non-responding physicians affiliated with their CCOP requesting them to complete the survey.

The 2012 American Medical Association (AMA) Physician Masterfile provided data for the individual physician control variables. Established in 1906, the Physician Masterfile includes current and historical data for more than 1.4 million physicians, residents, and medical students in the U.S.. The AMA Physician Masterfile contains demographic information, such as age and gender, as well as specialty, experience, and medical school training and residency.

Measures

The measures for this study included: implementation effectiveness, questions relating to perceptions of implementation climate, questions concerning perceptions of innovation-values fit, and physician characteristics. The outcome, *implementation effectiveness,* consistency and quality of organizational members' use of a specific innovation, was assessed as the number of patients that each individual physician enrolled in NCI-sponsored cancer clinical trials in 2011.

The *implementation climate* construct included six questions from the CCOP Physician Survey that were based on the measurement approached outlined in the literature and were consistent with how prior studies have addressed implementation climate (Klein & Sorra, 1996) (Weiner et al., 2011) (Weiner et al., 2012) (Weiner et al., 2009) (Helfrich et al., 2007) (Teal et al., 2012) (Holahan et al., 2004) (Dong et al., 2008) (Klein et al., 2001) (Osei-Bryson et al., 2008). The items were descriptive (rather than evaluative) and were direct measures of climate perceptions (rather than indirect

measures of specific implementation policies and practices). There were two questions for each of the three dimensions of implementation climate, expectations, support, and rewards (Weiner et al., 2011). Two questions addressed physician expectations and asked physicians if: 1) they are expected to enroll a certain number of patients in trials and 2) if they are expected to help the CCOP meet its patient enrollment goals. Two questions addressed whether physicians get the support they need to: 1) identify potentially eligible patients and 2) enroll patients in trials. Lastly, two questions addressed rewards by asking if physicians receive: 1) recognition and 2) appreciation when they enroll patients in trials. For all questions physicians were able to select *disagree*, *somewhat disagree*, *neither agree nor disagree*, *somewhat agree*, or *agree*

The *innovations-value fit* construct included four questions from the CCOP Physician Survey. We also developed these items based on the prior literature (Klein & Sorra, 1996) (Weiner et al., 2011). Questions asked physicians if they wanted to offer trials to patients, if participating in clinical trials was important, if clinical trials explore important clinical issues, and lastly if they valued participating in clinical trials. Physicians were also able to select *disagree*, *somewhat disagree*, *neither agree nor disagree*, *somewhat agree*, or *agree.*

Lastly*,* we also included physician characteristics such as age, if they trained in the United States, medical specialty, and whether or not the physician was the CCOP PI. We also included the practice arrangement (i.e., hospital-, group-, or solo- based) and how long the physician had been in clinical practice.

Data Analysis

SEM with maximum likelihood estimation was used to test the effect of innovation-value fit as a moderator between the implementation climate and implementation effectiveness. SEM is composed of multivariate regression models and can be used to estimate proposed causal relationships (Norman & Streiner, 2003) (Hox & Bechger, 2007) (Schreiber et al., 2006). We selected SEM because it allowed us to test for constructs that are not directly assessed, but are instead composed of observed indicators representing the constructs of interest (e.g., innovation-values fit, implementation climate).

The goal of SEM is to achieve a well-fitting model. The proposed model should be based on theory (Muthen, 2012) (Mooijaart & Satorra, 2009) (Klein & Moosbrugger, 2000). Therefore, based on our prior knowledge of implementation climate, we believed that the two questions that composed each of the three components of implementation climate (i.e., support, reward, expectations) would co-vary higher than with questions representing the other two components. For example, the two questions that compose expectations, physicians are expected to enroll a certain number of patients and physicians are expected to help the CCOP meet its goals, likely share common variation that is not explained by any of the proposed relationships in the model. Therefore we decided a priori to add three covariances, one between each of the two questions that address expectations, support, and rewards. We then used confirmatory SEM to test the hypothesized pathways among implementation factors represented in Figure 6 by comparing how well this proposed structure fits the observed data.

Specifically, to test for a moderated relationship using SEM, we created an interaction between implementation climate and the moderator, innovation-values fit.

We then followed the procedure as outlined by Muthén to evaluate models with latent variables interactions (Muthén, 2012). To test the significance of the moderation effect, we had to compare differences in model fit between the SEM with and without the moderation construct. We first fit the model without the interaction term and obtained a well-fitting model in terms of general fit statistics. Next, we added the interaction term to the model, and looked for improvements in model fit by comparing the difference between models using a Likelihood-Ratio (LR) test (Muthén, 2012) (Mooijaart & Satorra, 2009) (Klein & Moosbrugger, 2000).

We evaluated our final well-fitting model without the latent variable interaction using the Comparative Fit Index (CFI), the Tucker-Lewis Index (TLI), the root mean square error of approximation (RMSEA), and the standardized root mean squared residuals (SRMR). CFI and TLI values range from 0 to 1, with values greater than 0.90 representing adequate fit (Norman & Streiner, 2003) (Hox & Bechger, 2007) (Schreiber et al., 2006). Ideal RMSEA values should be less than 0.06 with an upper bound of the confidence interval less than 0.1 and SRMR should have values less than 0.08 (Norman & Streiner, 2003) (Hox & Bechger, 2007) (Schreiber et al., 2006). We then evaluated the final model with the interaction term by testing the significance of all standardized estimates and calculating the overall variance explained in the outcome (R^2), implementation effectiveness, as well as the percentage of variance explained by the latent variable interaction term. Lastly, to ensure the validity of our SEM results, we checked our results using negative binomial regression analysis with clustered robust standard errors. Analyses were performed using Mplus 7.

Results

Study Sample

The final sample for this study was comprised of 481 physicians with complete data who responded to the 2011 CCOP-Affiliated Physician Survey (Table 6). The majority of the sample was male (74%), White non-Hispanic (75%), with a mean age of 52.6 years. In addition, the majority of respondents practiced in a group practice (78%), trained in the U.S. (80%), and had been in practice on average almost 26 years. Over 70% were oncology-based specialists, 9% were the PI of the CCOP and physicians on average enrolled almost five patients in 2011.

The only significant ($p<0.05$) differences between survey responders and non-responders were that responders enrolled more patients per year (4.7 versus 3.4), were more likely to be a surgeon (10% versus 5%), and were less likely to be a non-specialized medical oncologist (11% versus 24%). There were no significant differences between respondents and non-respondents regarding gender, race, age, practice type, training location, and tenure.

Structural Equation Modeling

The fit statistics for the model without the interaction term as well as the modification indices did not indicate that we needed to re-specify the model or make any further adjustments (CFI = 0.967; TLI = 0.961; RMSEA = 0.032; SRMR = 0.051). Figure 7 provides a graphic version of the final SEM result. Standardized and unstandardized estimates are also provided in Table 7. The results of the SEM that included the interaction with the modifier (innovation-values fit) indicated that model fit significantly improved ($p<0.001$). Overall, we explained approximately 31% of the total

variation in the outcome, implementation effectiveness. In addition, we found that 3% of this variance is attributable to the interaction with innovation-values fit.

The latent constructs of implementation climate and innovation-values fit had significant independent effects on implementation effectiveness. Although the interaction accounted for 3% of the overall variance in implementation effectiveness, the interaction term is on the border of being significant (p=0.06). Therefore, innovation-values fit did not *statistically* strengthen the relationship between implementation climate and implementation effectiveness in this setting. The robustness check of our SEM results using negative binomial regression confirmed our main findings that implementation climate and innovation-values fit alone were each significantly associated with implementation effectiveness; however, adding in the interaction term caused all of the predictors to no longer be significant.

Discussion

Overall Significance

The findings from this study have both scientific implications for innovation implementation theory, as well as practical implications for CCOPs and other programs looking to increase volunteer physician participation. To our knowledge, this study is the first of its kind to examine whether innovation-values fit moderates the effect of implementation climate on implementation effectiveness (Klein & Sorra, 1996). Our study extends the literature surrounding the theory of innovation implementation. For example, our results are consistent with prior empirical investigations that implementation climate and innovation-values fit independently impact implementation effectiveness (Weiner et al., 2009) (Helfrich et al., 2007) (Holahan et al., 2004). In this

examination of the theory, however, we provided quantitative evidence as to the utility of the theory in a health and human services setting, where innovation implementation impacts clinical care. It is important to provide empirical evidence for the use of the theory in health services research as healthcare professionals have more professional autonomy and therefore differ from employees in a manufacturing or information systems company.

Specific Findings

Our first hypothesis was that implementation climate would have a direct effect on implementation effectiveness, or enrollment of patients in cancer clinical trials. This hypothesis was supported. Our results highlight the importance of a strong perceived implementation climate on physician enrollment of patients in clinical trials and physician participation in volunteer research more generally. Physicians who felt their organization was supportive, provided rewards, and instituted expectations enrolled more patients in clinical trials than physicians who did not view their organization as having a strong implementation climate. This was likely the case as physicians felt that they had the skills necessary to enroll patients, the support they needed, and incentives were in place to encourage enrollment. CCOPs and other voluntary research programs may want to focus their efforts on creating an environment that physicians perceive as supporting implementation. For example, there is no “magic” number regarding the number of support staff needed to help screen or enroll patients, rather physicians need to *feel* that they are supported and perceive that they get what they need to identify and enroll patients in clinical trials.

Second, we hypothesized that innovation-values fit modifies the effect of implementation climate on implementation effectiveness among CCOP physicians. This hypothesis was partially supported. Including the moderator improved model fit and explained 3% of the overall variation in implementation effectiveness, although it was just barely insignificant. Explaining 3% of the overall variance, however, is noteworthy. Moderator effects are notoriously difficult to detect that even those explaining as little as 1% of the variance can be considered important (Evans, 1985) (Champoux & Peters, 1987). In a review of the social science literature, interactions typically account for about 1-3% of the variance in outcome (Chaplin, 1991) (Hofmann et al., 2003). Perhaps innovation-values fit as a moderator was just slightly insignificant in our study because both implementation climate perceptions and innovation-values fit were strong across all physicians as indicated by high mean values for all of the innovation-values fit and climate perceptions questions (Table 6). Our results indicate that physicians in general viewed CCOP participation as aligning with their values and their CCOP as providing the necessary resources to enroll patients. Therefore, given the already strong implementation climate and sense innovation-values fit, the moderating effect of innovation-values fit itself was small. This is likely because CCOP is a voluntary program and our sample was composed of physicians who want to participate. This finding is important for programs to consider, as ensuring that clinical research aligns with physicians' values is not enough to overcome negative perceptions of implementation climate.

In addition, innovation-values fit was a significant predictor of implementation effectiveness. Physicians, who wanted to participate in CCOP, perceived that

participating in CCOP was important, and valued participating enrolled more patients in trials than physicians who did not perceive that participating in CCOP aligned with their values. Therefore, our study also demonstrates that it is important for physician-based research networks to recruit physicians who value participating in clinical research. Overall, our results indicated that both implementation climate and innovation-values fit independently determined active physician participation in clinical research.

Lastly, the hypothesis that physician characteristics (e.g., age, specialty, and practice location) would directly impact implementation effectiveness was also partially supported. Only status as the CCOP PI significantly influenced the enrollment of patients. PIs are more likely than non-PIs to be committed to the CCOP and feel obligated to set a "good example" for their colleagues. PIs may also be more familiar with available trial protocols and receive greater assistance from support staff to consent and enroll patients. Surprisingly, practice location, foreign medical training, medical specialty, age, and tenure did not impact enrollment. Practicing at a hospital or as a solo physician (compared to a group practice) may not have had a significant effect because many CCOP physicians travel between different offices, which may make their primary location less relevant. We suspect that foreign medical training did not impact enrollment because we could not determine how long physicians had been practicing in the U.S., which is likely a more relevant predictor of enrollment than training location. In addition, medical specialty may not be as influential on enrollment as there are an abundance of types of cancer clinical trials, including protocols for surgery and radiological interventions. Therefore, all specialties are comfortable and willing to enroll patients in cancer trials. Perhaps age and years in practice (tenure) were also not

significant as all physicians receive trainings now in clinical research, either through medical school or continuing medical education.

Limitations

There are several limitations of our study. First, we were limited in the data that was available to test the model of innovation implementation. We were most interested in the role of implementation climate and innovation-values fit on implementation effectiveness, but we did not have relevant data to allow us to examine some of the other model constructs (e.g., innovation effectiveness, strategic accuracy of innovation adoption). Given we were only able to explain 38% of the total variation in enrollment, there are clearly other relevant factors of implementation effectiveness that we were not able to capture in this analysis. In addition, given that we only included physicians who participate in CCOP, our findings may not be relevant for physicians practicing in other settings. CCOP physicians volunteer to participate in CCOP. Therefore, our findings are most relevant to encourage *active* participation in CCOP. Other organizations, however, that want to increase physician participation in volunteer research should consider fostering perceptions of a strong implementation climate as well as consider recruiting physicians whose values align with program's goals.

Future Research

Although innovation-values fit was not a statistically significant moderator in this context, future work should explore this proposed relationship further. Innovation-values fit may be a significant moderator in contexts where innovation implementation is mandatory and there is more variation in the perceptions regarding innovation-values fit and implementation climate. For example, if employees are forced to adopt an

innovation, those that feel that the innovation aligns with their values will be more likely to adopt and use the innovation, regardless of climate. A strong sense of innovation-values fit will also likely strengthen their perceptions of their organization's implementation climate as they are enthusiastic about the innovation and are committed to using it. If innovation-values fit is weak and users are forced to implement an innovation, they are likely unenthusiastic and unwilling to implement regardless of the organization offering incentives to adopt.

We were interested in explaining variation in enrollment among individual physicians, which led to our testing the model at the individual level. Future studies, however, should test this relationship at the organizational level to examine whether innovation-values fit moderates the effect of implementation climate on implementation effectiveness. For example, although our intraclass correlations are modest, due to low between group variance, our relatively high interrater agreement statistics indicate that we likely have enough within group agreement to aggregate our variables to the CCOP level (Hofmann & Stetzer, 1996). We could explore this further using a cross-level moderation test in multilevel modeling.

Conclusion

Through this analysis we were able to extend both the literature regarding the theory of innovation implementation and individual CCOP physician implementation effectiveness variation. In this study, we were able to add to the theoretical literature by not only empirically examining the theory of innovation implementation in a health and human services setting, but also by testing if innovation-values fit moderates the effect of implementation climate on implementation effectiveness, as suggested by Klein and

Sorra (1996). We also offered suggestions for CCOPs and other volunteer provider-based research networks about how to engage physicians in clinical research through fostering a strong implementation climate as well as ensuring physicians' values align with programmatic goals.

Table 6: Descriptive Statistics, Aim 2

CCOP Survey Respondents n=481		
	Mean or Proportion of Sample	Range
Outcome		
2011 Patient Enrollment	4.7* (8.1)	0, 62
Descriptive Variables		
Gender		
Male	74%	
Female	26%	
Race		
White	75%	
Asian	15%	
African-American	1%	
Other	9%	
Predictor Variable: Perceived Implementation Climate		
Expectations: Enroll Patients	3.4 (1.5)	1,5
Expectations: Help CCOP	4.2 (1.1)	1,5
Support: Identify Patients	3.8 (1.3)	1,5
Support: Enroll Patients	4.1 (1.2)	1,5
Rewards: Recognition	3.2 (1.3)	1,5
Rewards: Appreciation	3.3 (1.3)	1,5
Moderator: Innovation-Values Fit		
Want to Offer Trials	4.8 (0.5)	1,5
Participation in Important	4.7 (0.6)	1,5
Trials Explore Important Issues	4.6 (0.7)	2,5
Value Participating	4.7 (0.6)	1,5
Control Variables: Individual Physician Characteristics		
Age	52.6 (9.8)	34,82
Practice Type		
Group Practice	78%	
Hospital-Based	12%	
Solo Practice	4%	
Other/None Listed	6%	
Training Location		
U.S Trained	80%	
Non U.S Trained	20%	
Tenure (Yrs. In Practice)	25.7	8, 57
Medical Specialty		
Hematology Oncology	40%	
Radiation Oncology	21%	
Other Specialty	18%	
Medical Oncology	11%*	
Surgery	10%*	
Principal Investigator	9%	

Standard deviations in parentheses

*Indicates significant difference between survey respondents and non-survey respondents

Other race includes American Indian, Native Hawaiian/Pacific Islander, More than one race, or unknown

Hematology oncology includes blood banking, hematology oncology, hematology

Radiation Oncology includes diagnostic radiology, nuclear medicine, radiation oncology, radiology, vascular and interventional radiology

Other specialist includes general practice, gynecological oncology, pediatrics, pediatric hematology, cardiovascular disease etc.

Surgery includes colon and rectal surgery, critical care sugary, general surgery, neurological surgery, surgical oncology, urological surgery etc.

Table 7: SEM Results, Aim 2

Factor	Unstandardized Estimates	Standard Error	Standardized Estimates	Standard Error
Outcome: Enrollment in NCI-Sponsored Cancer Clinical Trials in 2011				
Implementation Climate	3.12*	1.15	0.29*	0.10
Innovation-Values Fit	4.42*	1.26	0.18*	0.05
Latent Variable Interaction	5.19	2.73	0.16	0.09
Age	-0.13	0.10	-0.16	0.12
*Hospital-Based^*	-1.47	0.89	-0.06	0.04
*Solo Practice^*	0.86	1.32	0.02	0.04
Non U.S. Trained	-0.30	0.97	-0.01	0.05
PI	8.95*	2.14	0.31*	0.07
Tenure	0.09	0.09	0.12	0.12
*Hematologist Oncology^^*	-1.44	1.40	-0.09	-0.08
*Radiation Oncology^^*	-2.01	1.57	-0.10	0.08
*Surgery^^*	-2.13	1.78	-0.08	0.07
*Other Specialty^^*	-2.68	1.46	-0.13	0.07
Latent Variable: Implementation Climate				
Expectations: Enroll Patients	0.56*	0.14	0.10*	0.03
Expectations: Help CCOP	0.75*	0.16	0.10*	0.02
Support: Identify Patients	1.04*	0.12	0.16*	0.02
Support: Enroll Patients	0.94*	0.12	0.14*	0.02
Rewards: Recognition	1.00	0.00	0.16*	0.01
Rewards: Appreciation	0.89*	0.06	0.14*	0.01
Latent Variable: Innovation-Values Fit				
Want to Offer Trials	1.00	0.00	0.06*	0.01
Participation is Important	1.83*	0.14	0.15*	0.01
Trials Explore Important Issues	1.02*	0.14	0.08*	0.01
Value Participating	1.63*	0.13	0.12*	0.01

Model Fit Statistics: CFI=0.967; TLI= 0.961; RMSEA=0.032; SRMR=0.051

**Statistically Significant at p<0.05*

^Compared to Group Practice

^^Compared to General Non-Specialized Oncology

Figure 4: Determinants and Consequences of Implementation Effectiveness, as

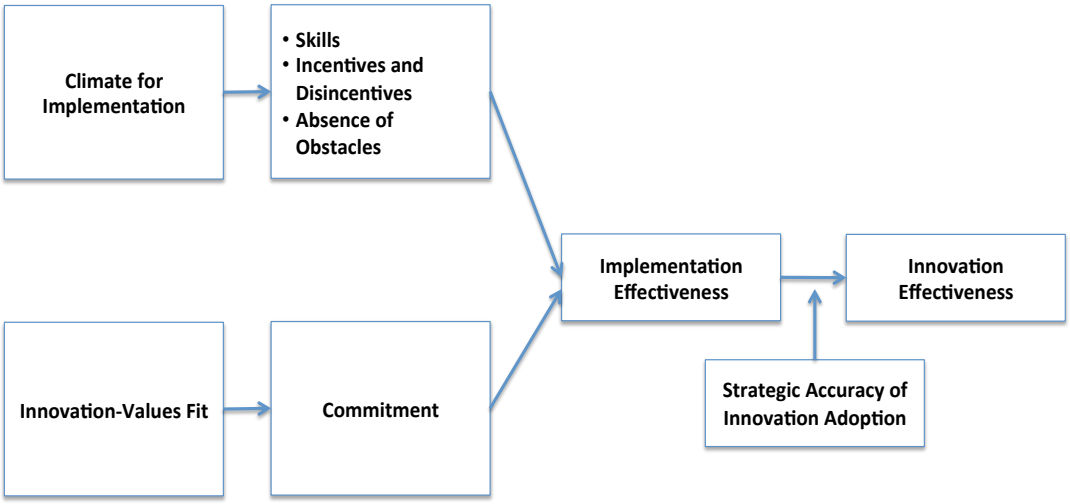


Figure 5: Determinants, Consequences, and Modifiers of Implementation Effectiveness, as Articulated in Klein & Sorra, 1996; Weiner, 2011

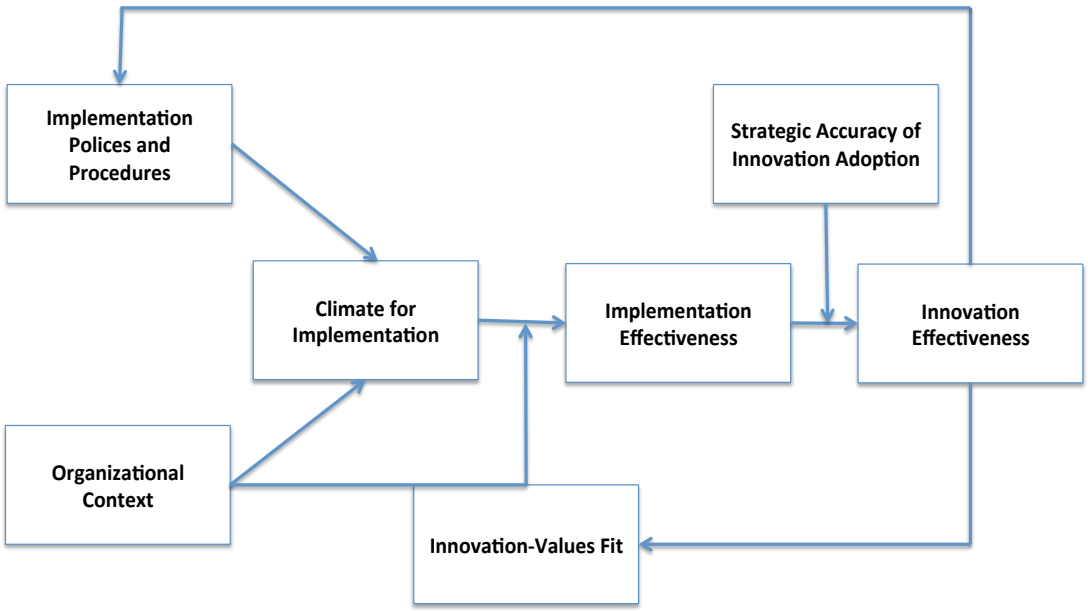


Figure 6: Determinants and Modifiers of Implementation Effectiveness Model, as Tested

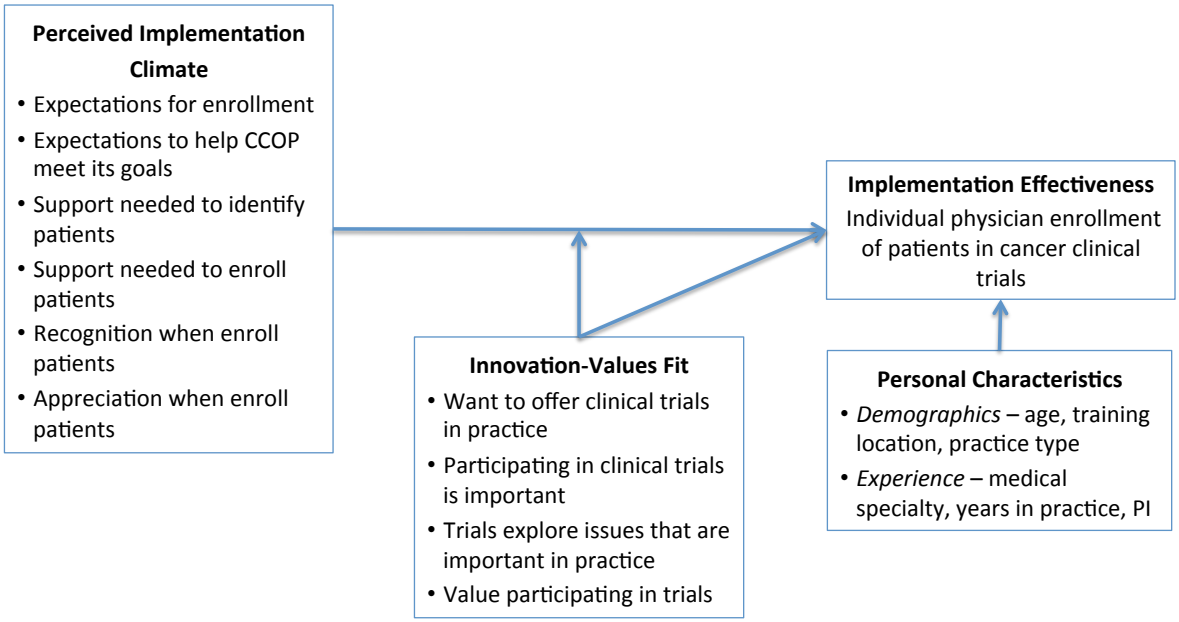
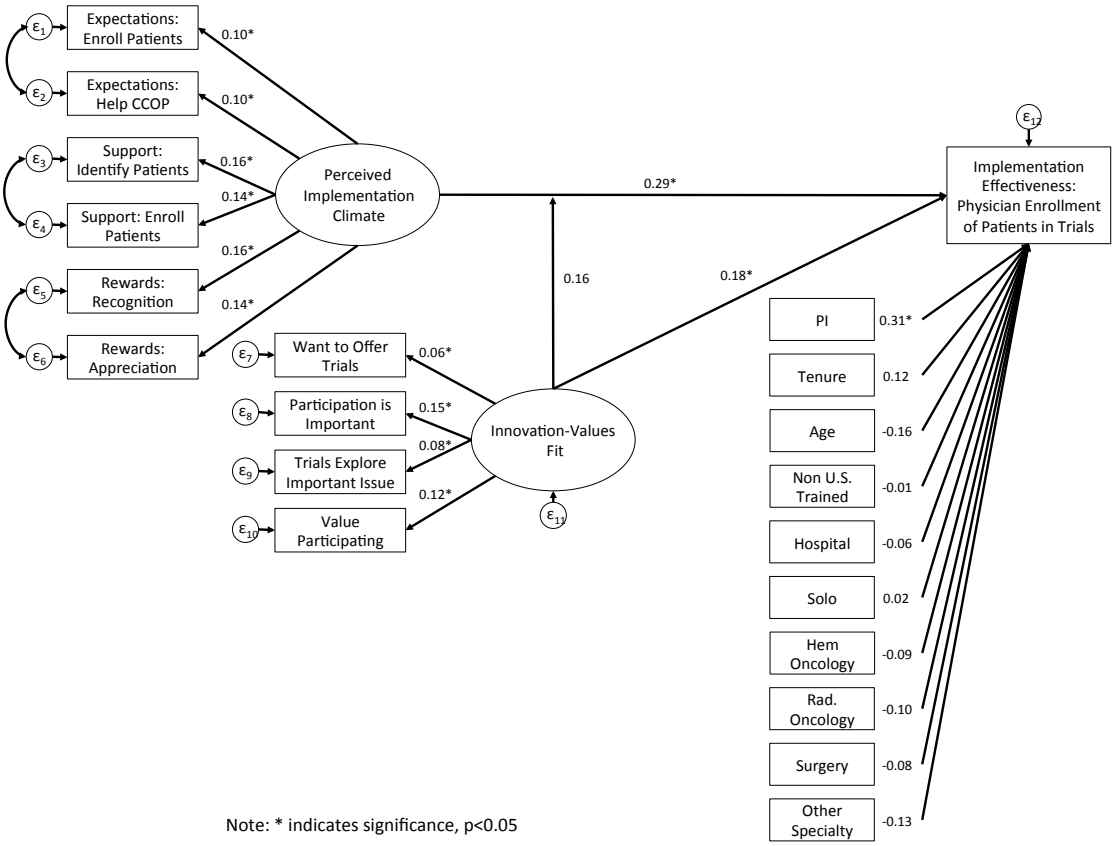


Figure 7: Standardized SEM Results, Aim 2



CHAPTER 6: DETERMINING THE PREDICTORS OF INNOVATION IMPLEMENTATION IN HEALTHCARE: A QUANTITATIVE ANALYSIS OF IMPLEMENTATION EFFECTIVENESS

Overview

With healthcare reform, healthcare organizations will need to implement innovations. Unfortunately, the failure rate for implementing innovations is high, with upwards of 50% of failures due in part to the high uncertainty, risk, and clinical discretion required to practice medicine. Klein and Sorra's (1996) innovation implementation framework offers a promising approach to examine the organizational factors that determine effective implementation. To date, the utility of this framework in a healthcare setting has been limited to qualitative studies and/or group level analyses. To enhance this models' usefulness in explaining innovation implementation among individuals, further research is needed to examine whether key relationships can be supported quantitatively. Therefore, the goal of this study was to examine this framework among individual participants in the National Cancer Institute's Community Clinical Oncology Program using structural equation modeling. Our results have implications for both the implementation of innovations in clinical practice and for innovation implementation theory.

Background

Healthcare organizations continuously need to implement complex innovations. This is truer now than ever, as the Patient Protection and Affordable Care Act (ACA) introduces innovative payment and delivery arrangements such as Accountable Care

Organizations, bundled payments, patient-centered medical homes, and value-based purchasing (ACA, 2010). Unfortunately the failure rates for implementing complex innovations are high. Estimates range from 30% to 90% depending on the scope of the organizational change involved, the definition of failure, and the criteria to judge it. (Alexander & Hearld, 2011) (Alexander et al., 2006) (Berlowitz et al.,2003). Innovations in healthcare often fail due in part to poor implementation (Alexander & Hearld, 2011) (Nembhard, et al., 2009), which can result from the high uncertainty, risk, and clinical discretion required to practice medicine, stronger professional identification among physicians compared to organizational identification, and perceived conflict of goals between leaders and workforce (Nembhard et al., 2009). Additional reasons for failure include misaligned incentives for adoption, unsustained leadership, lack of support and/or training, competing priorities, and resistance to change (Alexander & Hearld, 2011) (Shortel et al., 1998) (Rivera, 1999). Implementation failure may not only result in the loss of time and money for the organization, but can also impact the quality of care patients receive.

Theories of innovation implementation offer a promising approach to examine organizational factors that influence effective implementation (Klein & Sorra, 1996). Although the framework was developed in manufacturing contexts, it has been increasingly applied to innovation implementation in healthcare (Klein & Sorra, 1996) (Weiner et al., 2011) (Helfrich et al., 2007) (Naveh & Marcus, 2004). To date, most of the evidence supporting its use in healthcare is qualitative in nature (Weiner et al., 2011) (Weiner et al., 2012) (Teal et al., 2012) (Weiner et al., 2009) (Helfrich et al., 2007). Although important, qualitative studies tend to use small sample sizes, have

limited external generalizability, and present challenges in standardizing the measurement of key constructs. Currently, the majority of quantitative studies testing this framework have examined the effectiveness of technology implementation among company employees in information systems and computing organizations (Dong et al., 2008) (Holahan et al., 2004) (Klein et al., 2001) (Osei-Bryson et al., 2008) (Sawang & Unsworth, 2011) (Leiva et al., 2011) (Mollaoglu-Korkmaz et al., 2013). These settings are difficult to compare to healthcare because: (1) physicians experience greater professional autonomy, and (2) the process of implementing computing technology offers greater standardization than delivering clinical care or implementing innovative care delivery models.

It is important to quantitatively examine Klein and Sorra's framework as it will allow for a more precise examination of proposed hypotheses as well as allow researchers to compare results across settings, samples, and innovations. A quantitative analysis also allows researchers to control for other explanatory variables that may predict implementation effectiveness, which is difficult to do with qualitative research. Therefore, we quantitatively tested Klein and Sorra's innovation implementation framework in the National Cancer Institute (NCI)'s Community Clinical Oncology Program (CCOP), a provider-based research network focused on the enrollment of patients in cancer clinical trials (Minasian et al., 2010). Using both survey and archival data, we examined the hypothesized relationship among core constructs of the model using structural equation modeling (SEM). Specifically we sough to investigate the role of implementation climate and organizational implementation policies and practices (IPP) in determining effectiveness of innovation implementation.

Our research not only extends the literature surrounding innovation implementation theory, but it also has important practice implications for implementing innovations in complex, rapidly changing healthcare organizations.

New Contribution

This study is one of first to quantitatively test Klein and Sorra's (1996) innovation implementation framework in a healthcare context. As such, it will provide important evidence regarding the utility of this framework in explaining innovation implementation in healthcare. In addition, the framework tested in this paper focuses on implementation among individual physicians, rather than at the organizational or group level which is common when testing innovation implementation models (Dong et al., 2008) (Holahan et al., 2004) (Klein et al., 2001) (Sawang & Unsworth, 2011) (Muilenburg et al., 2013). This is a critical advancement because many innovations in healthcare are implemented voluntarily by individual physicians. Therefore, it is important to understand the organizational determinants of innovation implementation among physicians. Overall, study findings will allow researchers and managers to have a better understanding regarding the role of implementation climate and organizational policies and practices in determining the effectiveness of an innovation in clinical practice.

Methods

Conceptual Framework

The conceptual model for this study is based on Klein and colleagues' framework of innovation implementation which specifics the antecedents of complex innovation implementation (Klein & Sorra, 1996) (Klein et al., 2001). The framework postulates that implementation effectiveness, or the consistency and quality of innovation use, results

from both organizational implementation policies and practices (IPP) and individual climate perceptions (Figure 8). IPP are the formal strategies organizations use to put the innovation into use, while implementation climate is the extent to which organizational members perceive that an innovation is expected, supported, and rewarded by their organization (Klein & Sorra, 1996) (Helfrich et al., 2007) (Klein et al., 2001). Specifically, the authors suggest that IPP are the antecedents of climate, while individuals' interpretive perceptions of climate ascribe meaning to the policies and practices (James & Jones, 1974). Therefore, how physicians view their organization in terms of encouraging innovation implementation is determined by IPP. In addition, these perceptions predict the number of patients each physician enrolls in a cancer clinical trial (i.e., implementation effectiveness).

> Hypothesis 1: IPP will have a positive indirect effect on implementation effectiveness operating through implementation climate perceptions.

A strong implementation climate ensures organizational members, or in this case physicians, have the skill and support needed to implement the innovation, incentives to participate are in place, and obstacles to implement are limited. In this setting, strong perceptions of implementation climate should directly lead to stronger implementation effectiveness (higher patient enrollment among physicians). This is because perceptions that a CCOP institutes accrual expectations, provides support for the enrollment of patients, as well as recognizes enrollment efforts should encourage physicians to enroll more patients in cancer clinical trials.

> Hypothesis 2: Perceptions of implementation climate will have a direct positive effect on implementation effectiveness.

Given our interest in examining innovations that do not require interdependent use by multiple individuals, we needed to modify the Klein & Sorra model to ensure that the constructs were relevant at the individual level (Klein & Kozlowski, 2000). For example, we were interested in examining *individual* physician participation in CCOP because of the significant variation that occurs in enrolling patients in cancer clinical trials. Thus, we added control variables such as physician characteristics (e.g., physician age, years of experience, specialty, practice type, training location, and CCOP Principal Investigator (PI) status), as we believed these characteristics would both influence physicians' perceptions of climate and their ability to enroll patients in cancer clinical trials. For example, experience and age may influence perceptions, as older and more experienced physicians may perceive they have access to more resources, as well as enrollment, as more experienced physicians or CCOP PIs may be more familiar with clinical trials and enroll more patients.

> Hypothesis 3: Physician characteristics will have both direct and indirect effects, operating through perceptions of implementation climate on implementation effectiveness.

Lastly, we included organizational control factors, such as structure, years in existence, and size in our model. For example, we believed larger organizations that are part of a cancer center or research institute may have more resources to encourage innovation implementation compared to smaller, non-profit independent organizations. In addition, we believed that CCOPs that had been in existence longer would likely have more resources and thus provide more trainings and offer greater incentives for physicians to enroll patients.

> Hypothesis 4: Organizational factors will have an indirect effect on implementation effectiveness operating through IPP and perceptions of

implementation climate.

Study Setting

The study was conducted in NCI's CCOP network. In brief, the goals of the CCOP network are to advance the evidence-base by conducting research in clinical settings where most people receive their care, and translate results into better care (Kaluzny et al., 1994) (Minasian et al., 2010). The CCOP network is a joint venture between NCI's Division of Cancer Prevention, who provides overall direction and funding for community hospitals and practices to participate in clinical trials, selected cancer centers and clinical cooperative groups (CCOP research bases), who design the trials, and community-based physicians and hospitals (CCOP organizations) care, who assist with patient enrollment, data collection, and dissemination of study findings (Kaluzny et al., 1994) (Minasian et al., 2010). CCOP organizations are generally composed of a physician CCOP PI who provides local program leadership, a team of support staff, as well as affiliated physicians who enroll patients in NCI-sponsored cancer clinical trials (Weiner et al., 2011) (Teal et al., 2012). CCOP-affiliated physicians include specialized oncologists (e.g., hematological, surgical and radiation oncologists), general medical oncologists, and other medical specialists (e.g., urologists, gynecologists, and gastroenterologists).

In 2011, when the study was conducted, the CCOP network consisted of 47 CCOP organizations across 28 states, the District of Columbia, and Puerto Rico and included 400 hospitals and 3,520 community physicians. CCOP organizations consisted on average of 10 community hospitals or physician practices and 48 physicians.

Data Sources and Data Collection Procedures

The data for this cross-sectional study were obtained from four sources. First, the 2011 CCOP Annual Progress Reports, submitted in March 2012, provided data on physicians' enrollment activities during the period from June 1, 2011 to February 29, 2012. The reports were mainly used in determining the outcome, physician enrollment of patients in trials. Each March, every CCOP submits a progress report to NCI detailing the previous nine-month's research and enrollment activities. The report includes standardized questions regarding the allocation of CCOP resources, staffing assignments, total cancer patient volume, the number of open cancer clinical trials, the total number of patients each CCOP enrolls, as well as the total number of patients each individual CCOP-affiliated physician enrolls.

This study also used the 2011 CCOP Physician Survey and the 2011 CCOP Administrator Survey, which were both designed and administered as part of a larger NCI-funded-study (5R01CA124402). The goal of the physician survey was to learn more about physician participation in the CCOP program, while the administrator survey collected information regarding CCOP policies and procedures. The physician survey included specific questions regarding their perceptions surrounding expectations for enrollment, research support provided by the CCOP, ability to provide input, how well they are kept informed of CCOP activities, recognition received from the CCOP, as well as attitudes regarding the importance of cancer clinical trials. The survey specifically supplied data on CCOP physicians' perceptions of implementation climate.

The sampling frame for the physician survey included all CCOP-affiliated physicians eligible to accrue patients to clinical trials. Between October 2011 and

January 2012, we surveyed 817 physicians using a random sample stratified across all 47 CCOPs. One week after sending potential respondents, a postcard announcing the survey and highlighting its importance to NCI, physicians were sent a cover letter explaining the goals of the survey, the survey itself, a self-addressed and stamped return envelope, and a $50 Visa gift card as an incentive to complete the survey. Physicians were also able to complete the survey online via a unique access code provided in the mailings. A thank-you or reminder postcard was then sent the following week. Approximately three weeks after the first mailing, non-respondents received a second copy of the survey, cover letter, and return envelope. Lastly, we contacted CCOP PIs and administrators to email the non-responding physicians affiliated with their CCOP requesting them to complete the survey. On average, 17 physicians were surveyed per CCOP, and 10 physicians responded per CCOP organization.

The administrator survey included questions relating to the CCOP's organizational structure and size, performance management, education and trainings, protocol selection practices, research support, and staffing. The survey specifically supplied data on CCOP's IPP and the organizational control factors. The survey was completed by 100% of CCOP administrators. The vast majority of administrators completed the survey at the 2011 annual CCOP meeting, held each September at NCI. We followed up via email with administrators that did not complete the survey in person. Any remaining surveys were completed between October 2011 and January 2012.

Lastly, the 2012 American Medical Association (AMA) Physician Masterfile provided data for the physician characteristics. Established by the AMA in 1906, the Physician Masterfile includes current and historical data for more than 1.4 million

physicians, residents, and medical students in the U.S, including data on demographics, specialty, experience, medical school training, and residency.

Measures

The outcome of this study was implementation effectiveness, which was operationally defined as the number of patients that each physician enrolled in cancer clinical trials in 2011. The NCI uses this objective, outcome-focused measure as the primary means of determining CCOP physician performance, as do several other studies (Jacobs et al., 2014).

Key Constructs

The organizational implementation policies and practices (IPP) construct included five measures from the CCOP Administrator Survey. To measure expectations for enrollment, administrators were asked whether their CCOP expects physicians to enroll a minimum number of patients in clinical trials. Three measures addressed CCOP support for enrollment activities: 1) proportion of physicians for whom CCOP staff members routinely screen patient charts for potentially eligible patients; 2) proportion of physicians for whom CCOP staff members routinely assist with enrollment; and 3) whether or not CCOP sponsor any events where physicians could learn about the latest developments in cancer research, treatment, prevention, or control. Lastly, to assess rewards, administrators were asked whether the CCOP provides some form of recognition to physicians with high levels of accrual to NCI-sponsored trials.

The perceptions of implementation climate construct included six measures from the CCOP Physician Survey that were consistent with prior studies examining perceptions of implementation climate (Klein & Sorra, 1996) (Weiner et al., 2011) (Teal

et al., 2012). Two measures addressed whether physicians were: 1) expected to enroll a certain number of patients in trials and 2) expected to help the CCOP meet its patient enrollment goals. Two measures addressed whether physicians get the support they needed to: 1) identify potentially eligible patients and 2) enroll patients in trials. Lastly, two measures addressed whether physicians received: 1) recognition and 2) appreciation when they enroll patients in trials. For all measures, physicians could respond *disagree*, *somewhat disagree*, *neither agree nor disagree*, *somewhat agree*, or *agree*

Control Variables

We also included both physician characteristics and CCOP organizational factors as controls. Physician characteristics included age, whether or not they trained in the United States, self-designated medical specialty (e.g., hematologist oncologist, surgeon, radiological oncologist, general oncologist, non-oncologist specialist), and whether or not the physician was the CCOP PI. We also included the practice arrangement (i.e., hospital-, group-, or solo- based) and how long the physician had been in clinical practice. The organizational factors included CCOP organizational structure (e.g., hospital cancer center or cancer service line, research institute, department or center, separate non-profit organization), size (i.e., number of locations patients can enroll in a clinical trial), and how long the CCOP has been in existence.

Data Analysis

SEM with maximum likelihood estimation was used to simultaneously test whether perceptions of implementation climate mediates the relationship between IPP and implementation effectiveness. SEM is composed of multivariate regression models

and can be used to estimate proposed causal relationships (Norman & Streiner, 2003) (Hox & Bechger, 2007) (Schreiber et al., 2006). We used confirmatory SEM to test the hypothesized pathways among implementation factors represented in Figure 9 by comparing how well this proposed structure fits the observed data. We selected SEM because it allowed us to test for constructs that are not directly assessed, but are instead composed of observed indicators representing the constructs of interest (e.g., IPP, perceptions of implementation climate).

The goal of SEM is to achieve a well-fitting model based on theory (Norman & Streiner, 2003) (Hox & Bechger, 2007) (Schreiber et al., 2006). Therefore, a priori, we believed that the two measures that composed each of the three components of perceptions of implementation climate (i.e., support, reward, expectations) would co-vary higher than with measures representing the other components. For example, the two measures that compose expectations, physicians are expected to enroll a certain number of patients and are expected to help the CCOP meet its goals, likely share common variation that is not explained by any of the proposed relationships in the model. Therefore we decided a priori to add three covariances, one between each of the two measures that address expectations, support, and rewards. We also elected to use clustered robust standard errors to account for clustering of physicians within 47 CCOPs.

We then evaluated model fit using the Comparative Fit Index (CFI) and the Tucker-Lewis Index (TLI). CFI and TLI values range from 0 to 1, with values ≥ 0.90 representing adequate fit (Norman & Streiner, 2003) (Schreiber et al., 2006). We also examined the root mean square error of approximation (RMSEA) and the associated

confidence interval and p-value. RMSEA values < 0.06 and an upper bound of the confidence interval < 0.1 are considered acceptable. Next, we examined the standardized root mean squared residuals (SRMR), with values < 0.08 considered acceptable fit (Schreiber et al., 2006).

Based on these fit statistics for the original model, we elected to re-specify our original model to improve its fit. SEM is an iterative process in which model fit is improved by using theory and modifications indices either to add additional pathways between variables or to allow items to co-vary (Norman & Streiner, 2003) (Hox & Bechger, 2007) (Schreiber et al., 2006). Modification indices are the minimum that the chi-square statistic is expected to decrease if the corresponding parameter is no longer assumed to be fixed at zero (Norman & Streiner, 2003). Therefore, we added four additional co-variances to the original model. With the addition of each error-term co-variance, we tested whether model fit improved by examining the baseline model against the new model using the Lagrange multiplier test and fit statistics.

Once we achieved a well fitting SEM model, we evaluated our model by testing the significance of all standardized estimates. To examine standardized direct and indirect effects, we used bootstrapping with 95% confidence intervals on 1,000 bootstrap estimates. We elected to use bootstrapping to correct for non-normality, given the power of the joint test of two pathways in mediation analysis is larger than the power of the test of their product when using the usual z test and the associated confidence intervals for the product (MacKinnon, 2008). This appears to be due to the non-normality of the product. Specifically, indirect effects are the product of the two regression coefficients. For example, if X predicts Y and Y predicts Z, then the indirect

effect of X on Z equals the product of the two regression coefficients (X on Y and Y on Z). Lastly, to ensure the validity of our SEM results, we checked our results using negative binomial regression analysis with clustered robust standard errors. Analyses were performed using Mplus 7.

RESULTS

Descriptive Statistics

The final sample for this study included 481 physicians with complete data on the 2011 CCOP-Affiliated Physician Survey (Table 8). The vast majority of the sample was male (74%), White non-Hispanic (75%), practiced in a group practice (78%), and trained in the U.S (80%). The mean age was approximately 53 years old and physicians on average had been in practice approximately 26 years. Over 70% were oncology-based specialists and 9% were the CCOP PI. Physicians on average enrolled close to five patients in a cancer clinical trial in 2011. In addition, physicians generally agreed that their CCOP encouraged implementation. The average response on all six questions relating to implementation climate was 3.6 on a scale of one to five. Physicians on average rated the two reward items the lowest (Item 1: 3.2; Item 2: 3.4) and the expectation and support items more favorably (Expectations item 1 & 2: 3.4 and 4.2; support items 1 & 2: 3.8 and 4.1). The only significant ($p<0.05$) differences between survey responders and non-responders were that responders enrolled more patients per year (4.7 versus 3.4), were more likely to be a surgeon (10% versus 5%), and were less likely to be a non-specialized general oncologist (11% versus 24%).

For the CCOPs (n=47), the average number of years in existence was over 25 (Table 9). The average size, as determined by the number of locations a patient could

enroll in a clinical trial, was 14 and the majority of CCOPs were a hospital cancer center or cancer service line (40%), although 30% were a separate non-profit organization and 24% were a research institute, department, or center. The majority of CCOPs did not institute a minimum number of patients physicians should enroll per year (65%), did not offer trainings or events where physicians could learn about the latest developments in cancer research (58%), but did provide some form of recognition to physicians with high levels of accrual (62%). In addition, about 50% of physicians within a CCOP had support staff members help screen patient charts for potentially eligible patients and assist with enrollment.

SEM Measurement Analysis

The fit statistics and modification indices for the fixed parameters of the original model suggested that we re-specify the model to improve fit (CFI = 0.846 TLI = 0.815; RMSEA = 0.068; SRMR = 0.052) (Figure 9). Therefore, we added four post-hoc modifications that were theoretically justified and improved model fit (Figure 10). For these modifications, we allowed the error terms of the following measures to co-vary higher than with other variables. For example, the percentage of doctors supported in screening and enrolling patients, likely share common variation that is not explained by any of the proposed relationships in the model.

1) The percentage of doctors supported in screening and enrolling patients: The same support staff generally preform both functions within a CCOP.
2) Trainings offered with the percentage doctors who are supported in screening patients: The number of trainings offered relates to the number of support staff available.

3) Trainings offered with the percentage doctors who are supported in enrolling patients: The number of trainings offered relates to the number of support staff available.
4) Rewards with expectations for enrollment: CCOPs that provide incentives may also be more likely to have expectations for enrollment.

With the addition of each error-term co-variance, we tested whether model fit improved by examining the baseline model against the new model using the Lagrange multiplier test and fit statistics. Figure 10 provides a graphic version of the final standardized bootstrapped SEM results. Standardized bootstrapped total, direct, and indirect effects are provided in Table 10. Overall, we achieved a final well-fitting model (CFI = 0.933; TLI = 0.918; RMSEA = 0.045; SRMR = 0.048) and explained approximately 24% of the total variation in implementation effectiveness.

Regarding the IPP construct, the majority of the construct was determined by expectations for enrollment (β=0.82), although all five measures were statistically significant ($p<0.05$). In addition, regarding the perceived implementation climate construct, all six measures were statistically significant determinants of the construct ($p<0.05$). The largest determinants were perceptions regarding the organization's recognition and appreciation of enrollment activities (β= 0.62; β=0.56) as well as perceptions regarding support provided to screen and enroll eligible patients (β= 0.61; β=0.59) (Figure 10).

SEM Structural Analysis

Hypothesis one was supported, as physicians' perceptions of implementation climate mediated the relationship between IPP and enrollment. This means there was a

significant indirect effect between IPP and enrollment operating through perceptions of implementation climate (indirect effect = 0.069; p=0.01) (Table 10). Although our final model suggested that implementation climate fully mediated the relationship between IPP and implementation effectiveness, we could also envision scenarios where IPP directly influenced implementation effectiveness. For example, in addition to helping to shape perceptions of implementation climate, the number of staff available at each CCOP to screen and enroll patients might also directly determine the number of patients a physician was able to enroll in a clinical trial. Therefore, we also tested an alterative model (Figure 11) where there was a direct pathway between IPP and implementation effectiveness. This alternative model fit the data well (CFI = 0.934; TLI = 0.918; RMSEA = 0.045; SRMR = 0.047). The results demonstrated that there also was a significant direct effect of IPP on implementation effectiveness (direct effect = 0.10; p=0.04). Therefore, perceptions of implementation climate only partially mediated the relationship between IPP and implementation effectiveness, as there was also a direct relationship between the two constructs.

Hypothesis two was also supported as perceptions of implementation climate had a statistically significant direct effect on implementation effectiveness (direct effect = 0.285; p<0.00). Hypothesis three was partially supported given CCOP PI status, age, radiological oncologists, and non-oncologist specialists significantly influenced enrollment while training location, tenure, practice location, and physicians who are surgeons, and hematologists (compared to non-specialized oncologists) did not directly influence implementation effectiveness. There was no evidence, however, that any of the physician characteristics significantly influenced implementation effectiveness

through their effect on perceptions of implementation climate. Lastly, hypothesis four was also partially supported as organizational size and structure indirectly influenced implementation effectiveness through IPP and implementation climate. However, organizational maturity did not significantly influence implementation effectiveness through its effect on IPP and perceptions of implementation climate. The robustness check of our SEM results using negative binomial regression analysis with clustered robust standard errors confirmed our main findings.

DISCUSSION

Overall Significance

Overall, our results quantitatively confirmed the main relationship postulated by Klein and Sorra (1996) between IPP, implementation climate, and implementation effectiveness among individual physicians. It is often difficult to test this theory quantitatively given the large sample of participants and organizations required. Although the model has been discussed within healthcare organizations before, the studies have been predominately qualitative in nature. For example, Helfrich and colleagues (2007) demonstrated the relationship between IPP, implementation climate, and effectiveness using comparative case studies of four cancer clinical research networks implementing new programs in cancer prevention and control research. Similar results have also been confirmed in other settings. Sawang and Unsworth (2011) confirmed a similar model where implementation climate mediated the role of IPP and implementation effectiveness among small and medium businesses implementing different innovations in Australia. Both of these analyses, however, were conducted at the organizational level. Our results demonstrate the potential for using

the model in healthcare to explain *individual* level innovations. Although the model still must be tested at the organizational level in a healthcare setting, our results might have broad implications given that many innovations and evidence-based practices in healthcare are implemented by individual physicians on a voluntary basis. For example, the use of novel therapies often only require implementation by a single physician, not collective, coordinated implementation among multiple individuals in an organization.

Our findings are also relevant to other implementation theories and frameworks. For example, our results can be used in conjunction with the Consolidated Framework For Implementation Research (CFIR). The CFIR offers guidance as to the possible predictors of implementation effectiveness, such as intervention characteristics, factors at the system and organizational levels, and characteristics of the individuals implementing the innovation (Damschroder et al., 2009). The CFIR does not, however, provide rationale as to *why* some domains may be more relevant than others and *how* they are related in certain circumstances. Therefore our results could be useful in selecting relevant constructs from the CFIR to examine implementation effectiveness of individually driven innovations in a healthcare setting. For example, as part of the inner setting or organizational level construct, the CFIR includes organizational characteristics, such as size and structure, which we found to be important determinants of organizational IPP. The inner setting also includes policies and practices related to implementation climate, such as organizational incentives and rewards, clearly communicated goals and feedback, available resources, and access to information through trainings, all of which were included in our model as IPP and/or in physicians' perceptions of implementation climate. Lastly, the CFIR also includes

characteristics of the individual such as tenure, age, and experience. Our research indicates how these constructs not only relate to one another, but how they also impact implementation effectiveness.

Specific Findings

Our results demonstrated that implementation climate perceptions partially mediated the relationship between IPP and implementation effectiveness. Therefore, the policies and practices an organization has in place to encourage innovation implementation may be most effective if the intended users *perceive* these policies and practices as supportive. Although there was a significant direct effect between IPP and implementation effectiveness, over a third of the total effect of IPP on implementation effectiveness resulted from the *indirect* effect of IPP on implementation effectiveness operating through perceptions of implementation climate. Therefore, even with supportive IPP in place, implementation could still fail if the intended users do not feel the effects of these IPP as encouraging implementation. In addition, the direct relationship between *implementation climate* and implementation effectiveness was almost three times greater than the relationship between *IPP* and implementation effectiveness. Thus, managers looking to increase implementation effectiveness of an innovation should focus on creating an environment that physicians perceive as encouraging implementation. For example, ensuring physicians *feel* that they are supported and perceive that they get what they need to effectively implement an innovation is more important than having a certain number of staff available or offering trainings in terms of encouraging implementation.

In addition, our results also confirmed that implementation climate should be composed of measures relating to expectations, support, and rewards, as suggested in Klein and Sorra's (1996) theory of innovation implementation. Although, the authors suggest that implementation climate should be assessed at the group level as an aggregation of shared perceptions, our results demonstrate that implementation climate can also be measured at the individual level using the same theoretical construct. Managers should consider instituting specific organizational IPP aimed at increasing positive perceptions of climate in all three areas. For example, IPP should include specific expectations, support, and rewards for innovation use.

Given the goal was to examine an innovation in healthcare implemented by individual physicians on a voluntary basis, we needed to adapt our model by including personal characteristics. We proposed that personal characteristics would have both direct effects on implementation effectiveness as well as indirect effects on implementation effectiveness operating through climate perceptions. However, we only found direct effects for some of the personal characteristics. Although we did find that status as the CCOP PI had a significant effect on climate perceptions, the indirect effect operating through climate perceptions on implementation effectiveness was not significant. Therefore intended users that are leaders or innovation champions may have more positive perceptions of climate compared to non-leaders. Overall, however, these results indicate that climate perceptions were mostly determined by IPP. Our findings suggest that there may be alternative ways in which personal characteristics relate to implementation effectiveness. For example, personal characteristics may have an influence on fit between the innovation and the organizational members' values

(Klein & Sorra, 1996). Perhaps, more experienced physicians or physicians that have been at the organization longer perceive the innovation as more congruent with their individual values and therefore use the innovation in a more consistent and high-quality way. This should be tested in future studies. In addition, it is possible that personal characteristics *moderate* the relationship between implementation climate and implementation effectiveness. For example, experience, or status as an innovation leader may strengthen the effect of perceptions of implementation climate on implementation effectiveness. So, experience or status as a leader would intensify the relationship between implementation climate and implementation effectiveness. Therefore, future studies should examine other potential relationships between personal characteristics and implementation effectiveness.

Our findings are also consistent with Klein and Sorra's equifinality argument in that IPP have an indirect effect on implementation effectiveness through climate perceptions. Although implementation climate perceptions were the key determinant of implementation effectiveness, there are potentially multiple combinations of specific organizational IPP that may result in positive perceptions of implementation climate. More research is needed to demonstrate that different combinations of IPP can produce equivalent perceptions of implementation climate. Our study, however, presents one possible parsimonious model of climate and its role in determining implementation effectiveness.

Limitations and Future Directions

There are several limitations of our study. First, we only included physicians who participated in CCOP in our study. In addition, CCOP Physician Survey respondents

significantly enrolled more patients per year than survey non-respondents. Thus, we need to be careful in generalizing our results to all CCOP physicians as well other types of physicians. Our findings might be most relevant to encourage *active* participation where innovation use is voluntary. We believe, however, that our findings are still relevant for administrators wanting to increase implementation of individual-focused innovations given our high response rate and overall there were few significant differences between survey respondents and non-respondents The study should be tested in other settings with a variety of innovations especially where participation or implementation is mandatory. Second, our study is cross-sectional and represents a single point in time. Future studies should consider examining implementation climate over the course of implementation to better understand how climate may vary over time or among different groups within a single organization. Third, our study only explained 24% of the variance in enrollment. Therefore, future studies may want to explore additional factors, such as patient characteristics that may influence enrollment in cancer clinical trials. Lastly, although many innovations in healthcare are focused on the individual, it is important to also test this theory at the intended unit of analysis. Therefore future work should also consider investigating this framework at the organizational or practice level by aggregating implementation climate perceptions if possible.

CONCLUSION

Through this analysis we were able to extend the literature concerning the use of innovation implementation theories as well as provide practical suggestions for managers considering implementing an innovation. Our study not only provides

quantitative evidence that implementation climate mediates the relationship between IPP and implementation effectiveness, but it also demonstrates the utility of adapting an implementation framework to explain individually focused innovations. The majority of our hypotheses were supported, thus demonstrating the importance of physicians' perceptions of implementation climate in determining implementation effectiveness. Therefore, managers looking to increase innovation implementation effectiveness should consider fostering a strong implementation climate through supportive IPP to encourage innovation use.

Table 8: Descriptive Statistics CCOP Physicians

CCOP Physician Survey Respondents n=481			
	Mean or Proportion of Sample	Standard Deviation	Range
Outcome			
2011 Patient Enrollment	4.7*	8.1	0, 62
Descriptive Variables			
Gender			
Male	74%		
Female	26%		
Race			
White	75%		
Asian	15%		
African-American	1%		
Other	9%		
Perceptions of Implementation Climate			
Expectations: Enroll Patients	3.4	1.5	1,5
Expectations: Help CCOP	4.2	1.1	1,5
Support: Identify Patients	3.8	1.3	1,5
Support: Enroll Patients	4.1	1.2	1,5
Rewards: Recognition	3.2	1.3	1,5
Rewards: Appreciation	3.3	1.3	1,5
Physician Characteristics Included in Model			
Age	52.6	9.8	34,82
Practice Type			
Group Practice	78%		
Hospital-Based	12%		
Solo Practice	4%		
Other/None Listed	6%		
Training Location			
U.S Trained	80%		
Non U.S Trained	20%		
Tenure (Yrs. In Practice)	25.7	10.1	8, 57
Medical Specialty			
Hematology Oncology	40%		
Radiation Oncology	21%		
Other Specialty	18%		
Medical Oncology	11%*		
Surgery	10%*		
Principal Investigator	9%		

*Indicates significant difference between survey respondents and non-survey respondents
Other race includes American Indian, Native Hawaiian/Pacific Islander, More than one race, or unknown
Hematology oncology includes blood banking, hematology oncology, hematology
Radiation Oncology includes diagnostic radiology, nuclear medicine, radiation oncology, radiology, vascular and interventional radiology
Other specialist includes general practice, gynecological oncology, pediatrics, pediatric hematology, cardiovascular disease etc.
Surgery includes colon and rectal surgery, critical care sugary, general surgery, neurological surgery, surgical oncology, urological surgery etc.

Table 9: Descriptive Statistics CCOP Organizations

CCOP Administrator Survey Respondents n=47			
	Mean or Proportion of Sample	Standard Deviation	Range
Organizational Implementation Context			
Expectations: Enroll Patients			
Yes	35%		
No	65%		
Support: Identify Patients	0.51	0.32	0,1.5
Support: Enroll Patients	0.50	0.32	0,1.5
Support: Training			
Yes	32%		
No	68%		
Rewards: Recognition			
Yes	62%		
No	38%		
Organizational Factors included in Model			
Organizational Maturity	25.5	6.2	8,30
Organizational Size	14.3	15.6	2,87
Organizational Structure			
Cancer Center	41%		
Research Institution	24%		
Separate Organization	30%		
Other	5%		

Table 10: Standardized Total, Direct, and Indirect Effects, Aim 3

	Total Effect	Direct Effect	Indirect Effect
Outcome: Enrollment in NCI-Sponsored Cancer Clinical Trials in 2011			
Perceptions of Implementation Climate	0.285*	0.285*	N/A
Organizational Implementation Policies and Practices (OIPP)	0.069*	N/A	0.069*
Age	-0.264*	-0.179	-0.085
*Hospital-Based^*	-0.043	-0.066	0.023
*Solo Practice^*	-0.001	0.034	-0.035
Non U.S. Trained	-0.035	-0.011	-0.024
PI	0.356*	0.322*	0.034
Tenure	0.224	0.117	0.107
Hematologist Oncology+	-0.097	-0.075	-0.022
Radiation Oncology+	-0.162*	-0.120	-0.042
Surgery+	-0.114	-0.077	-0.037
Other Specialty+	-0.147*	-0.120	-0.027
Organizational Size	0.028*	N/A	0.028*
Structure: Hospital Cancer Center++	0.047*	N/A	0.047*
Structure: Research Institute++	0.016*	N/A	0.016*
Structure: Other++	0.024*	N/A	0.024*
Organizational Maturity	0.000	N/A	0.000

Model Fit Statistics: CFI=0.933; TLI= 0.918; RMSEA=0.045; SRMR=0.048

Note: Total effects is the sum of direct and indirect effects

*Note: Indirect effects are the product of the regression coefficients leading to the outcome. For example for OIPP, OIPP predicts perceptions and perceptions predicts enrollment. The indirect effect and subsequently the total effect of OIPP on enrollment equals the product of the two regression coefficients (From Figure 3) 0.243*0.285=0.069*

**Statistically Significant (p<0.05)*

^Compared to Group Practice

+Compared to General Non-Specialized Oncology

++Compared to Separate Non-Profit Structure

Figure 8: The Impact of Implementation Climate on Physician Enrollment

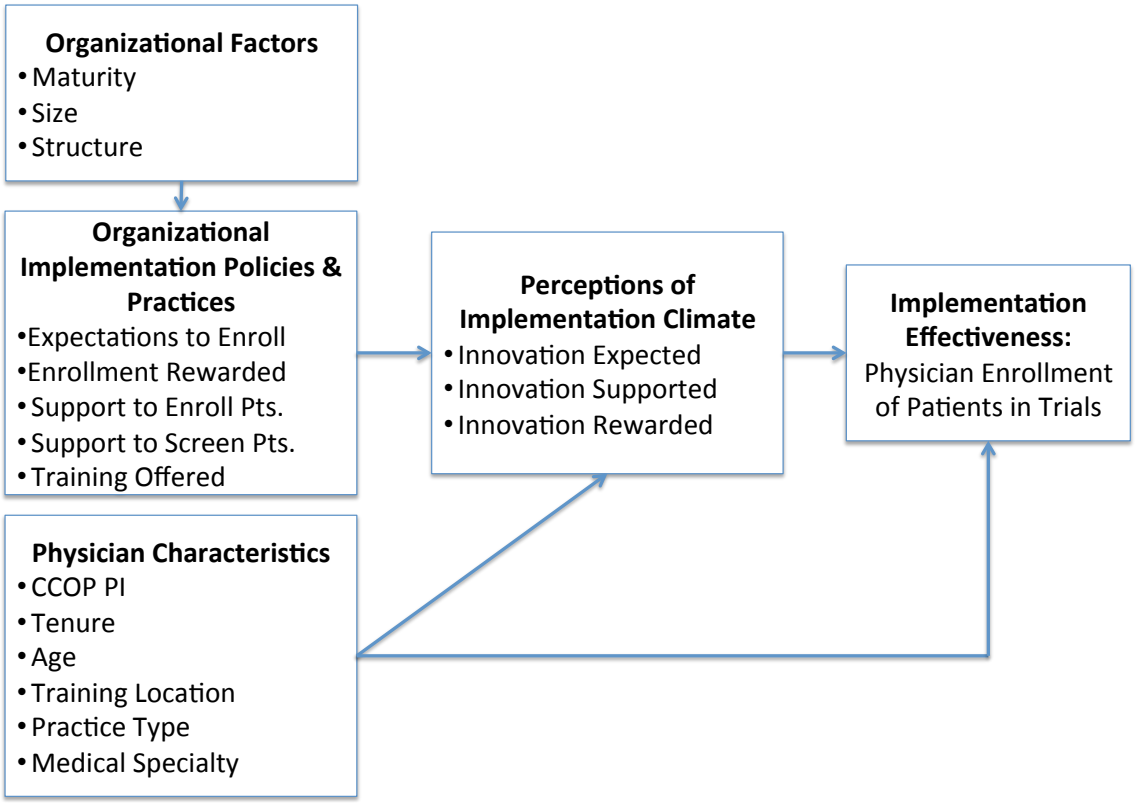


Figure 9: Original Proposed SEM Model, Aim 3

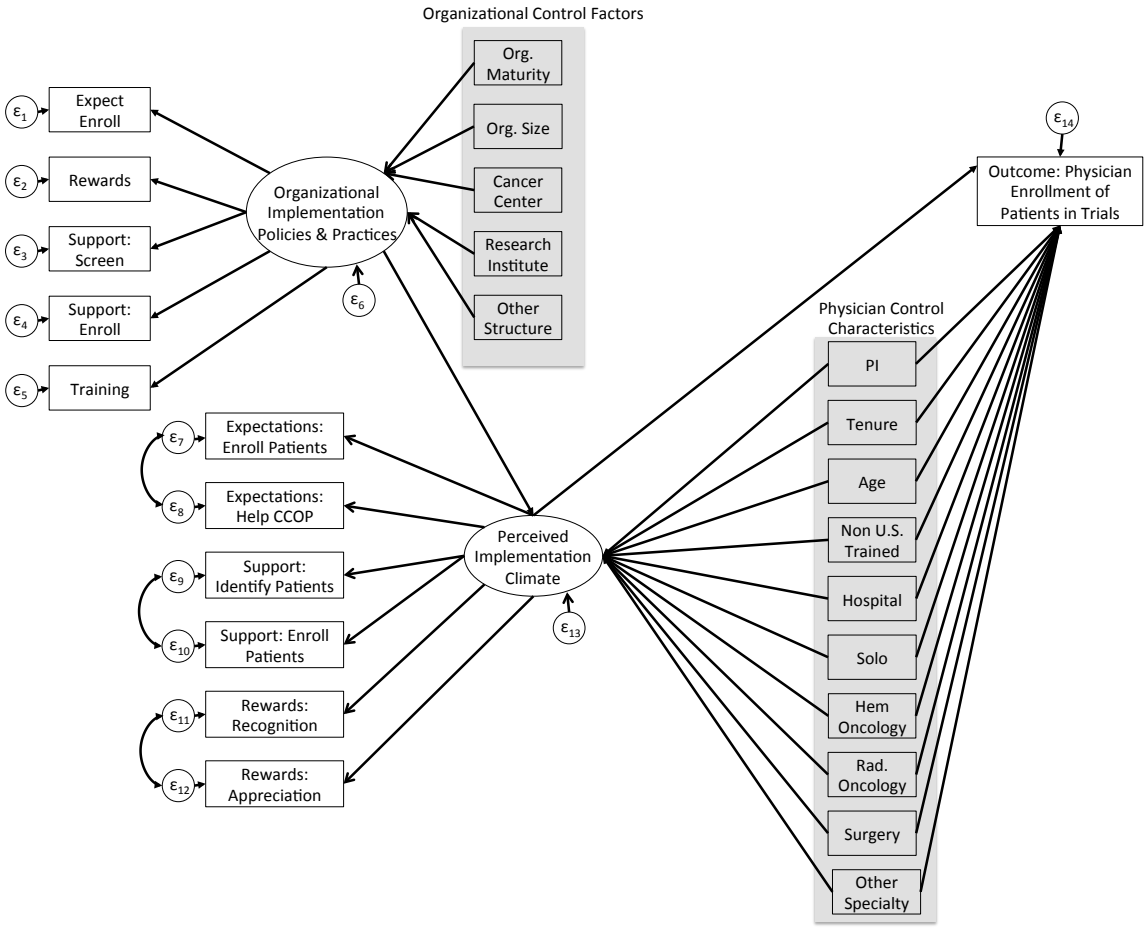


Figure 10: Final SEM Model with Standardized Estimate, Aim 3

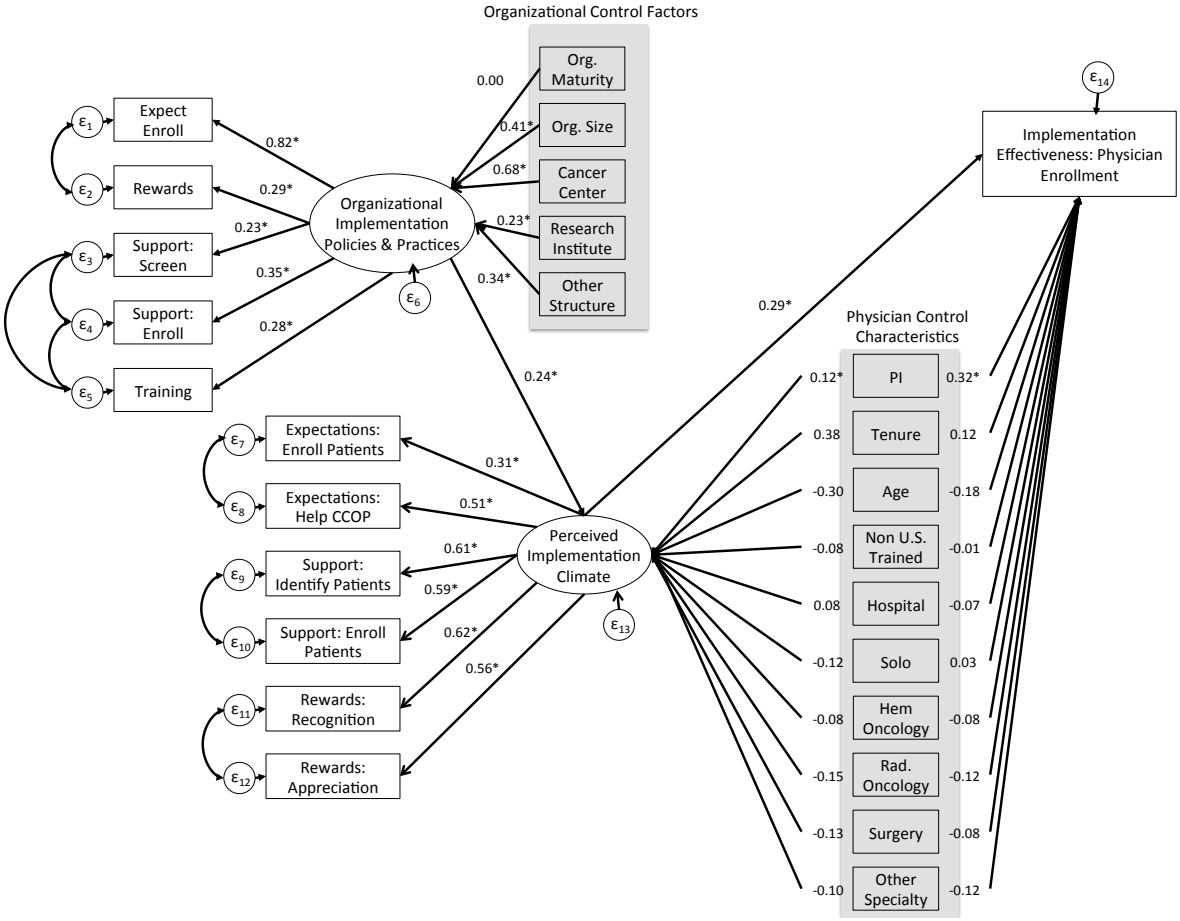
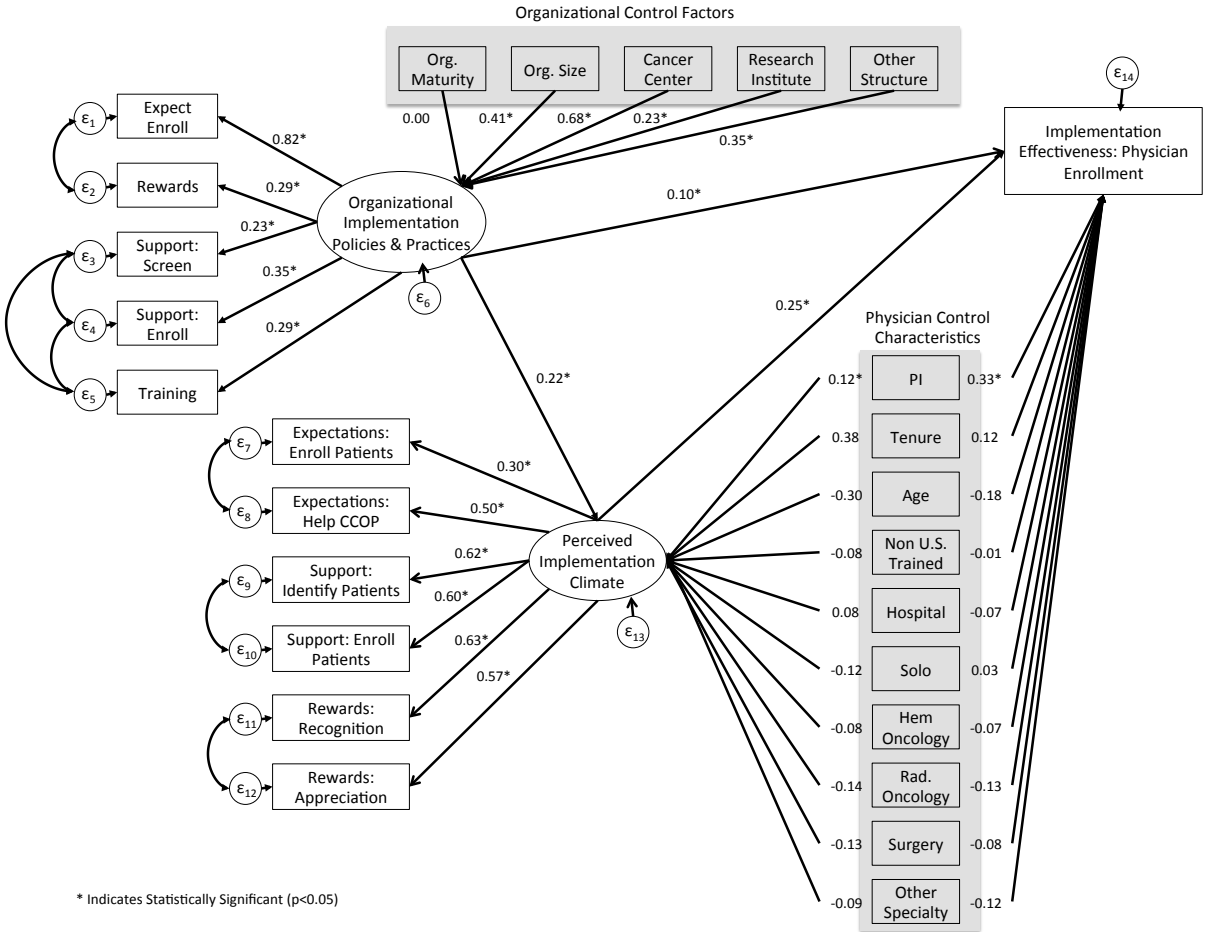


Figure 11: Alternative SEM Model with Standardized Estimates, Aim 3



CHAPTER 7: SUMMARY OF FINDINGS AND IMPLICATIONS FOR POLICY, PRACTICE, AND RESEARCH

Summary of Findings

The objective of this dissertation was to examine physician characteristics and organizational contextual factors that predict CCOP physician enrollment of patients in cancer clinical trials. Overall, there were several key findings across all aims. First, physicians' attitudes, values, and perceptions were strong predictors of enrollment. In Aim 1, our results demonstrated that physicians' attitudes towards participating in CCOP were a key determinant of enrollment (β=0.13; p=0.04). In Aim 2 we showed that physicians' perceptions of a climate that encourages implementation (β=0.29; p=0.01) and perceived fit between CCOP goals and physicians' values (β=0.18; p<0.00) were both significant determinants of enrollment. We also found that including innovation-values fit as a moderator between perceptions of implementation climate and enrollment significantly improved model fit and explained 3% of the total variation in enrollment, although it was on the border of being statistically significant (p=0.06). Lastly, in Aim 3, we also demonstrated that physicians' perceptions of implementation climate were a significant direct determinant of enrollment (β=0.29; p<0.00).

Second, regarding physician characteristics, we only found significant direct effects on enrollment. In Aim 2, we found that only status as the CCOP PI had a significant effect on enrollment (β=0.31; p<0.00). In Aims 1 and 3, we tested whether physician characteristics such as status as the CCOP PI, age, tenure, medical specialty, practice

type, and training location directly impacted enrollment and indirectly impacted enrollment operating through either attitudes towards participating in CCOP (Aim 1) or perceptions of implementation climate (Aim 3). In both aims we found significant effects on enrollment for: status as the CCOP PI (both aims: β=0.36; p<0.00), age (Aim 1: β=-0.30; p<0.00; Aim 3: β=-0.26; p=0.03), and non-oncology specialists (Aim 1: β=-0.15; p=0.02; Aim 3: β=-0.15; p=0.03). In addition, we found significant effects for tenure in Aim 1 (β=0.25; p=0.01) and for radiological oncologists in Aim 3 (β=-0.16; p=0.03). We found no significant direct or indirect effects across all three aims for training location (U.S. versus foreign trained), practice type (hospital or solo versus group), hematologist oncologists, or surgeons (compared to non-specialized generalist oncologists).

Lastly, we achieved mixed results regarding the importance of organizational context on physician enrollment. In Aim 1, we used objective assessments of organizational context, such as trainings offered, support staff provided, incentives rewarded, and expectations instituted. Although we found that organizational context had a significant direct effect on enrollment (β=0.19; p=0.02), it did not significantly influence enrollment indirectly operating through physician attitudes (p=0.32). Therefore, we only observed direct effects of objective assessments of organizational context on enrollment. In Aim 2, we incorporated organizational context through physicians' perceptions. In this case, as discussed, physicians' perceptions of implementation climate significantly impact enrollment. In Aim 3, we included both objective assessments of organizational context (i.e., IPP) and physicians' perceptions of implementation climate. In this aim, we found that perceptions of organizational context mediated the relationship between IPP and enrollment. IPP had a significant indirect effect on enrollment operating through climate

perceptions (β=0.07; p=0.01). In this aim we also included organizational control measures such as organizational maturity, size, and structure. We tested to see if these organizational factors influenced organizational IPP, and ultimately enrollment operating through physician perceptions of implementation climate. We found that although organizational maturity had no indirect effect on enrollment (p=0.97), organizational size (i.e., number of locations) did have an indirect effect on enrollment (β=0.03; p=0.02). In addition, CCOPs that were cancer centers (β=0.05; p=0.02), research institutions (β=0.02; p=0.04), and had other types of structures (β=0.03; p=0.02) compared to separate non-profit organizations had higher enrollment through IPP and perceptions of climate. Implications of these findings are discussed in detail below.

Policy and Practice Implications

Findings from this dissertation have important policy and clinical practice relevance. The CCOP Network is in the midst of undergoing significant changes. NCI is merging CCOP with components of the NCI Community Cancer Centers Program (NCCCP), to create one comprehensive network for cancer care delivery research, the NCI Community Oncology Research Program (NCORP) (NCI, 2013). The goal of NCORP is to bring advanced cancer prevention, control, treatment, and imaging clinical trials, cancer care delivery research, and disparities studies to individuals within the community (NCI, 2013). Awards for the community sites will occur in 2014. Findings from this dissertation are relevant for current CCOP sites considering repositioning themselves to participate in NCORP. Given the requirement for NCORP sites to enroll a minimum of 80 patients per year, our results could be used to create policies or institute practices aimed at increasing enrollment. For example, in Aims 1 and 3 physicians'

attitudes and values were strong predictors of performance. These findings highlight the importance of recruiting physicians who value participating in clinical trials, find participating in trials important, and feel they are able to do so.

Our results also highlight the importance of a strong perceived implementation climate on physician enrollment of patients in clinical trials. Physicians who felt their organization was supportive, provided rewards, and instituted expectations enrolled more patients in clinical trials than physicians who did not view their organization as having a strong implementation climate. Therefore NCORP or other sites may want to focus their efforts on creating an environment that physicians perceive as supporting implementation. For example, there is no “magic” number regarding the number of support staff needed to help screen or enroll patients, rather physicians need to feel that they are supported and perceive that they get what they need to identify and enroll patients in clinical trials.

Our findings from Aim 3 suggest that organizational IPP influence physician perceptions of their organization even if they do not influence physicians’ attitudes and values as seen in Aim 1. Therefore, administrators should not discount the importance of instituting polices and practices that encourage enrollment. For example, program administrators should consider providing support for physicians’ research activities, such as staff to help consent and enroll patients, incentives for enrollment goals (e.g., small tokens of appreciation, public acknowledgment), and trainings to learn about latest developments in research. Such strategies may not directly change physician attitudes, but evidence from Aims 1 and 3 demonstrate that a supportive organizational context can encourage active physician participation in recruiting patients and

encourage positive physicians' perceptions of how well their organization supports implementation.

Our results extend beyond physician enrollment of patients in cancer clinical trials to other innovations and evidence-based practices in healthcare that are implemented by individual physicians on a voluntary basis. The ACA will require both healthcare organizations and individual physicians to implement complex and innovative strategies to improve the quality, efficiency, and value of healthcare. Some of the ACA directed innovations as well as the use of novel therapies only require implementation by a single physician, not collective, coordinated implementation among multiple individuals in an organization. Our results indicate that managers looking to increase use of an innovation, especially among physicians, should consider instituting expectations for its use. In addition, our results showed that managers should focus on ensuring physicians feel that they are supported and perceive that they get what they need to effectively implement an innovation as perceptions of climate can be more important than having a certain number of staff available or offering trainings in terms of encouraging implementation. Under this new era of reform, healthcare organizations are going to need to continuously implement complex innovations. Unfortunately, however, the failure rates for implementing such complex innovations are high (Alexander & Hearld, 2011). The results from this dissertation indicate that not only do individual characteristics impact innovation implementation, but organizational contextual factors help determine successful and sustained implementation as well.

Research and Theory Implications

This dissertation also has important implications for research and extends the use of

innovation implementation theories in healthcare. First, our research is novel in that it is the first study to examine physician characteristics, physicians' attitudes, values, and perceptions, along with organizational factors to explain the significant individual variation that occurs among physicians enrolling patients in cancer clinical trials. Our research is important as it demonstrates the utility of Klein and Sorra's (1996) theory of innovation implementation in explaining individual level implementation effectiveness. Specifically, Aims 2 and 3 suggest that the model can be adapted to explain individual implementation by including personal characteristics and key constructs (e.g., perceptions of implementation climate, innovation-values fit) assessed at the individual level as opposed to aggregate measures assessed at the organizational level. This will help guide future research, given many innovations and evidence-based practices in healthcare are implemented by individual physicians on a voluntary basis rather than by practices or organizations. Our findings also extend the literature as the models used in these studies focus both on individual and organizational level determinants of implementation effectiveness. Despite several theories that predict innovation implementation or implementation effectiveness among individuals *or* organizations, little research has focused on understanding the cross-level relationship between individual- and organizational-determinants. Our results, however, highlight the importance of organizational context, personal characteristics, and individual attitudes, values, and perceptions in predicting implementation effectiveness at the individual level.

We were also able to extend the current literature by quantitatively testing the theory of innovation implementation (Klein & Sorra, 1996) in a healthcare setting. It is often

difficult to test this theory quantitatively given the large sample of participants and organizations required. Although the model has been discussed within health services before, the studies have been predominately qualitative in nature (Weiner et al., 2011; Weiner, Haynes-Maslow, Campbell, Kahwati, & Kinsinger, 2012; Teal, Bergmire, Johnston, & Weiner, 2012; Weiner, Lewis, & Linnan, 2009; Helfrich et al., 2007). Although important, qualitative studies tend to utilize smaller sample sizes, have limited external generalizability, and present challenges in standardizing the measurement of key constructs. Our analysis, however, tested the framework with greater precision, which allows researchers to compare results across settings, samples, and innovations.

Our studies advance the use of the theory of innovation implementation in healthcare (Klein & Sorra, 1996) as we empirically examined whether innovation-values fit moderates the effect of perceptions of implementation climate on implementation effectiveness**.** Prior research testing the theory has included both concepts in their research, but our study is the first to examine the proposed moderated relationship between innovation-values fit, implementation climate, and implementation effectiveness (Holahan et al., 2004) (Dong et al., 2008) (Klein et al., 2001) (Osei-Bryson et al., 2008). Although including innovation-values fit as a moderator improved model fit and explained 3% of the overall variation in implementation effectiveness, it approaches significance (p=0.06). Explaining 3% of the overall variance, however, is noteworthy as moderator effects are notoriously difficult to detect (Evans, 1985) (Champoux, 1987). This model should be tested in additional settings to ensure its generalizability in other healthcare contexts.

Lastly, our results can be used in conjunction with other innovation theories and frameworks. For example, the Consolidated Framework for Implementation Research (CFIR) offers guidance as to the possible relevant predictors of implementation effectiveness, such as intervention characteristics, factors at the system and organizational levels, and characteristics of the individuals implementing the innovation (Damschroder et al., 2009). The CFIR does not, however, provide rationale as to *why* some of the domains may be more relevant than others and *how* they are related in certain circumstances. Therefore our results could be useful in selecting relevant constructs from the CFIR to examine implementation effectiveness of individually driven innovations in a healthcare setting. For example in Aim 3, as part of the inner setting or organizational level construct, the CFIR includes organizational characteristics, such as size and structure, which we found to be important determinants of organizational IPP. The inner setting also includes policies and practices related to implementation climate, such as organizational incentives and rewards, clearly communicated goals and feedback, available resources, and access to information through trainings, all of which were included in our model as IPP and/or in physicians' perceptions of implementation climate. Lastly, the CFIR also includes characteristics of the individual such as tenure, age, and experience. Our research indicates how these constructs not only relate to one another, but how they also impact implementation effectiveness.

Limitations

There were several limitations associated with these studies. First, we only included physicians who participated in CCOP and completed the 2011 CCOP Physician Survey. Therefore, our findings suggest the organizational factors and

individual physician characteristics that are most relevant to encourage *active* participation in CCOP or other volunteer research programs. It is important to note, however, that many organizational strategies (e.g., recognition of high achievers, expectations for enrollment) could be implemented by diverse organizations to increase physician participation in clinical research or increase physician adoption of voluntary based innovations. Second, our study is cross-sectional and represents a single point in time. Future studies should consider examining implementation climate over the course of implementation to better understand how climate may vary over time or among different groups within a single organization. We also lacked the data to incorporate patient characteristics in the analyses. Ultimately patients are the final decision makers regarding their participation in a cancer clinical trial. We were unable to distinguish physicians failing to offer a cancer clinical trial from patients' refusal to enroll. However, given that 75% of patients agree to enroll if offered (Albrecht et al., 2008) we do not believe this to be a significant limitation. Lastly, we were also limited in the data available to examine individual physician enrollment within each of the models. Given we were only able to explain 21%, 38%, and 24% of the variance in enrollment in Aims 1, 2, and 3 respectively, there are clearly other relevant factors of implementation effectiveness that we were not able to capture in this analysis. Also given data constraints we were not able to examine some of the other model constructs proposed by Klein and Sorra (1996) (e.g., innovation effectiveness, strategic accuracy of innovation adoption) to understand their role in explaining implementation effectiveness.

Future Directions

This dissertation provides the foundation for several future studies. In this

dissertation we were interested in explaining variation in enrollment among individual physicians (i.e., implementation effectiveness), thus we tested the models at the individual level. The models are proposed, however, at the organizational level and should also be tested with the intended unit of analysis. Although the intraclass correlations are modest, due to low between group variance, the relatively high interrater agreement statistics indicate that there is likely enough within group agreement to aggregate many of the variables to the CCOP level (Table 3). Therefore the models tested in Aims 2 and 3 should be examined at the organizational level within a health services setting. We could explore this further using a cross-level moderation test in multilevel modeling.

In addition, these studies should also be replicated in other health services settings implementing other innovations. In Aim 1, we found that physicians' attitudes and values was not a significant mediator between organizational context and enrollment. Similarly in Aim 2, we found that innovation-values fit was not a significant moderator between physicians' perceptions of implementation climate and enrollment. Future work should explore these proposed relationships further given that attitudes may be a significant mediator or innovation-values fit a significant moderator in contexts where innovation implementation is mandatory and there is more variation in attitudes and in the perceptions regarding innovation-values fit or implementation climate. For example, if physicians are forced to adopt an innovation, those that feel that the innovation aligns with their values may be more likely to adopt and use the innovation, regardless of climate. A strong sense of innovation-values fit would also likely strengthen their perceptions of their organization's implementation climate as they are

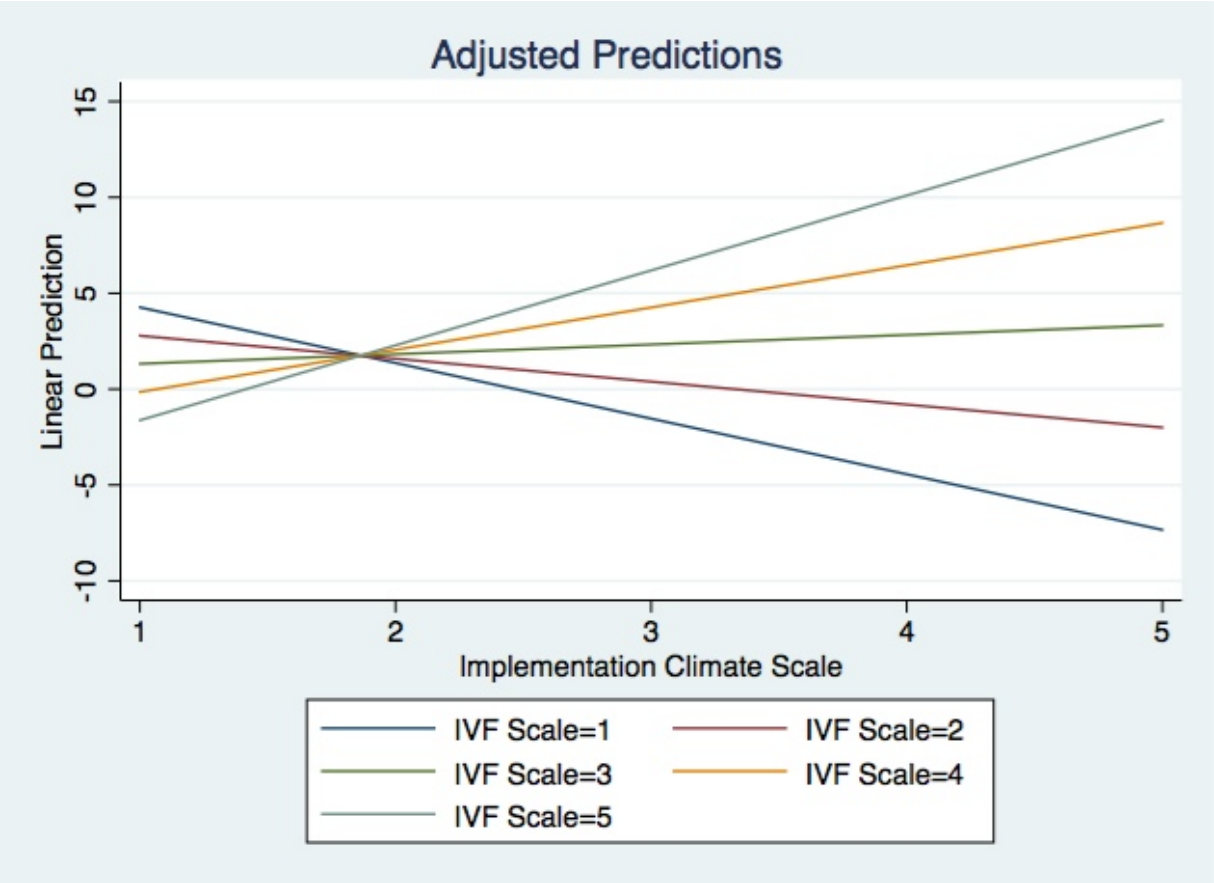
enthusiastic about the innovation and are committed to using it. If innovation-values fit is weak and users are forced to implement an innovation, they are likely unenthusiastic and unwilling to implement regardless of the organization offering incentives to adopt.

Conclusion

The goal of this dissertation was to examine the individual characteristics and organizational contextual factors that determine patient enrollment in cancer clinical trials among CCOP physicians. This was accomplished through three aims that explored the ways organizational context can be incorporated into research. The first aim used objective assessments of organizational context, the second aim used physicians' perceptions of context, and the third aim included both objective assessments of organizational context and physicians' perceptions. Overall, we found that physician characteristics, such as status as the CCOP PI and age, physicians' attitudes, values, and perceptions regarding climate, and organizational policies and practices determined enrollment. Our results can not only be used in the formation of new NCORP policies and in clinical practice to increase physician participation in voluntary based innovations, but they can also be used in research as we extended the boundaries in which innovation implementation frameworks can be used. We demonstrated the utility of these models to explain individual innovation implementation in a health services setting.

APPENDIX

Aim 2: : Interaction Between Implementation Climate and Innovation-Values Fit using Linear Regression



REFERENCES

Ajzen I. (1991). The theory of planned behavior. *Organizational Behavior and Human Decision Processes 50*: 179-211.

Albrecht T.L., Eggly S.S., Gleason M.E.J., et al. (2008). Influence of Clinical Communication on Patients' Decision Making on Participation in Clinical Trial. *Journal of Clinical Oncology 26*(16): 2666-2673.

Alexander, J.A., Hearld, L.R. (2011). The Science of Quality Improvement Implementation: Developing Capacity to Make a Difference. *Medical Care, 49,* S6-S20.

Alexander, J.A., Weiner, B.J., Shortell, S.M., Baker, L.C., Becker, M.P. (2006). The role of organizational infrastructure in implementation of hospitals' quality improvement. *Hospital Topics, 84,* 11-20.

Berlowitz, D.R., Young, G.J., Hickey, E.C., Saliba, D., Mittman, B.S., et al. (2003). Quality Improvement Implementation in the Nursing Home. *Health Services Research, 38*, 65-83.

Carpenter W.R., Fortune-Greeley A.K., Zullig L.L., et al. (2012). Sustainability and performance of the National Cancer Institute's Community Clinical Oncology Program. *Contemporary Clinical Trials 33*: 46-55.

Carpenter W.R., Weiner B.J., Kaluzny A.D., et al. (2006). The Effects of Managed Care and Competition on Community-Based Clinical Research. *Medical Care 44:* 671-679.

Champoux J.E., Peters W.S. (1987). Form, effect size, and power in moderated regression analysis. *Journal of Occupational Psychology*, *60*: 243-255.

Chaplin W.F. (1991). The Next Generation of Moderator Research in Personality Research. *Journal of Personality*, *59*: 143-178.

Choi J.N. (2004). Individual and contextual dynamics of innovation-use behavior in organizations. *Human Performance 17*(4): 397-414.

Comis R.L., Miller J. D., Aldigé, C.R., et al. (2003). Public Attitudes Toward Participation in Cancer Clinical Trials. *Journal of Clinical Oncology 21*(5): 830-835.

Comis R. L., Miller J. D., Colaizzi D.D., et al. (2009). Physician-related factors involved in patient decisions to enroll onto cancer clinical trials. *Journal of Oncology Practice 5*(2): 50-56.

Damschroder LJ., Aron D.C., Keith R.E., Kirsh S.R., Alexander J.A., Lowery J.C. (2009). Fostering implementation of health services research findings into practice: a

consolidated framework for advancing implementation science. Implementation Science, *4*:50.

Davies, P., Walker, A.E., Grimshaw, J.M. (2010). A systematic review of the use of theory in the design of guideline dissemination and implementation strategies and interpretation of the results of rigorous evaluations. *Implementation Science 5*:14.

Davis F. D. (1989). Perceived usefulness, perceived ease of use, and user acceptance of information technology. *MIS Quarterly 13*(3): 319-339.

Davis F.D., Bagozzi, R.P., Warshaw, P.R. (1989). User Acceptance of Computer Technology: A Comparison of Two Theoretical Models. *Management Science 35*(8): 982-1003.

Dong L,. Neufeld D.J., Higgins C. (2008). Testing Klein and Sorra's innovation implementation model: An empirical examination. *Journal of Engineering and Technology Management*, *25*(4): 237–255.

Ellis P.M. (2000). Attitudes towards and participation in randomised clinical trials in oncology: A review of the literature. *Annals of Oncology 11:* 939-945.

Evans M.G.(1985). A Monte Carlo study of the effects of correlated method variance in moderated multiple regression analysis. *Organizational Behavior and Human Decision Processing*, *36*: 305-323.

Fisher, W.B., Cohen, S.J., Hammond, M.K., et al. (1991). Clinical Trials in Cancer Therapy: Efforts to Improve Patient Enrollment Among Community Oncologists. *Medical and Pediatric Oncology 19*: 165-168.

Frambach R.T., Schilewaert N. (2002). Organizational innovation adoption a multi-level framework of determinants and opportunities for future research. *Journal of Business Research 55:* 163-176.

Grunfeld E., Zitzelsberger L., Coristine M., et al. (2002). Barriers and Facilitators to Enrollment in Cancer Clinical Trials. *Cancer 95*(7): 1577-1583.

Helfrich, C.D., Weiner, B.J., McKinney, M.M., Minasian, L. (2007). Determinants of Implementation Effectiveness: Adapting a Framework for Complex Innovations. *Medicare Care Research and Review 64(3):* 279-303.

Hofmann D.A., Morgeson F.P., Gerras S.J. (2003). Climate as a Moderator of the Relationship Between Leader-Member Exchange and Content Specific Citizenship: Safety Climate as an Exemplar. *Journal of Applied Psychology*, *88*: 170-178.

Hofmann D.A., Stetzer A (1996). A Cross-level Investigation of Factors Influencing Unsafe Behaviors and Accidents. *Personnel Psychology*, *49*: 307-339.

Holahan P.J., Aronson Z.H., Jurkat M.P., Schoorman F.D. (2004). Implementing computer technology: a multi-organizational test of Klein and Sorra's model. *Journal of Engineering and Technology Management, 21*(1): 31–50.

Hox J.J., Bechger T.M. (2007). An Introduction to Structural Equation Modeling. *Family Science Review 11*: 354-373.

Jacobs S.R., Weiner B.J., Minasian L.M., Good M.J. (2013). Achieving high cancer control trial enrollment in the community setting: An analysis of the Community Clinical Oncology Program. *Contemporary Clinical Trials 34*(2): 320-325.

Jacobs S.R., Weiner B.J., Reeve B.B., Weinberger M., Good M.J., Minasian L.M. (2014). Organizational and Physician Factors Associated with Patient Enrollment in Cancer Clinical Trials**.** Doctoral Dissertation.

James L. R., Jones A. P. (1974). Organizational climate: A review of theory and research. *Psychological Bulletin 81*: 1096-1112.

Kaluzny A.D., Lacey L.M., Warnecke R., et al. (1994). Accrual of patients to randomized clinical
trials. Factors affecting cancer prevention and control research. *International Journal of Technology Assessment in Health Care 10*(3): 506-516.

Kaluzny A.D., Lacey L.M., Warnecke R., et al. (1995). Predicting the Performance of a Strategic Alliance: An Analysis of the Community Clinical Oncology Program. *Health Services Research 28*(2): 159-182.

Kellerman S.E., Herold J. (2001). Physician Response to Surveys A Review of the Literature. *American Journal of Preventative Medicine 20*(1): 61-67.

Klabunde C.L., Keating N.L., Potosky A.L., et al. (2011). A Population-Based Assessment of Specialty Physician Involvement in Cancer Clinical Trials. *Journal of the National Cancer Institute 103*(5): 384-397.

Klein A., Moosbrugger A. (2000). Maximum likelihood estimation of latent interaction effects with the LMS method. *Psychometrika*, *65*:457-474.

Klein K.J., Conn A.B., Sorra J.S. (2001). Implementing Computerized Technology: An Organizational Analysis. *Journal of Applied Psychology*, *86*(5): 811-824.

Klein K.J., Kozlowski S.W.J. (2000). From Micro to Meso: Critical Steps in Conceptualizing and Conducting Multilevel Research. *Organizational Research Methods*, *3*(3): 211-236.

Klein K.J., Sorra J.S. (1996).The challenge of innovation implementation. *Academy of Management Review 21*(4): 1055-1080.

Kozlowski S.W.J., Farr J.L. (1988). An Integrative Model of Updating and Performance. *Human Performance 1*(1): 5-29.

Kozlowski S. W. J., Klein K. J. (2000). A multilevel approach to theory and research in organizations: Contextual, temporal, and emergent processes. In K. J. Klein & S. W. J. Kozlowski (eds.), *Multilevel theory, research and methods in organizations: Foundations, extensions, and new directions*. San Francisco, CA: Jossey-Bass.

Lance C.E., Butts M.M., Michels L.C. (2006). The sources of four commonly reported cutoff criteria - What did they really say? *Organizational Research Methods*, *9*:202-220.

Lara P.N., Higdon R., Lim N. (2001). Prospective Evaluation of Cancer Clinical Trial Accrual Patterns: Identifying Potential Barriers to Enrollment. *Journal of Clinical Oncology 19:* 1728-1733.

MacCallum R.C., Browne M.W., Sugawara HM (1996). Power analysis and determination of sample size for covariance structure modeling. *Psychological Methods 1*(2): 130-149.

MacKinnon, D.P. (2008). *Introduction to Statistical Mediation Analysis.* New York: Lawrence Erlbaum Associations.

Mansour E.M. (1994). Barriers to Clinical Trials Part III: Knowledge and Attitudes of Health Care Providers. *Cancer 74*: 2672-2675.

Meropol N.J., Buzaglo J.S., Millard J., et al. (2007). Barriers to Clinical Trial Participation as Perceived by Oncologists and Patients. *Journal of the National Comprehensive Cancer Network 5*: 753-762.

Mills E.J., Seely D., Rachlis B., et al. (2006). Barriers to participation in clinical trials of cancer: a meta-analysis and systematic review of patient-reported factors. *Lancet Oncology 7:* 141-148.

Minasian L.M., Carpenter W.R., Weiner B.J., et al. (2010) Translating research into evidence-based practice: the National Cancer Institute Community Clinical Oncology Program. *Cancer*
116(9): 4440-4449.

Mooijaart A., Satorra A. (2009). On insensitivity of the chi-square model test to non-linear misspecification in structural equation models. *Psychometrika*, *74*: 443-455.

Murthy V.H, Krumholz H.M., Gross C. P. (2004). Participation in cancer clinical trials: Race-, sex-, and age-based disparities. *JAMA 291*(22): 2720-2726.

Muthén B. (2012). Modeling Interactions Between Latent and Observed Continuous Variables Using Maximum-Likelihood Estimation In Mplus. *Mplus Web Notes* Updated 2012.

National Cancer Institute. (2002). Cancer Clinical Trials The Basic Workbook. Available from: http://www.cancer.gov/clinicaltrials/resources/basicworkbook/.

National Cancer Institute. (2010).Cancer Clinical Trials Fact Sheet. Available from: http://www.cancer.gov/cancertopics/factsheet/Information/clinical-trials.

National Cancer Institute. (2010). Special Issue: Clinical Trials Enrollment. *NCI Cancer Bulletin 7*(10). Available from: http://www.cancer.gov/ncicancerbulletin/051810/page6.

National Cancer Institute. (2011). Community Clinical Oncology Program & Minority Based-Community Clinical Oncology Program Accomplishments in Cancer Clinical Trials. Available from: http://ccop.cancer.gov/shareditems/files/ccop-accomplishments.pdf.

National Cancer Institute. (2013).NCI Community Oncology Research Program Approved. Available from: http://ccop.cancer.gov/news-events/news/20130625.

Naveh, E., Marcus, A.A. (2004). When does the ISO 9000 quality assurance standard lead to performance improvement? Assimilation and going beyond. *IEEE Transactions on Engineering Management 51*, 352–363.

Nembhard, I.M., Alexander, J.A., Hoff, T.J., Ramanujam R. (2009). Why Does the Quality of Health Care Continue to Lag? Insights from Management Research. *Academy of Management Perspectives, 23,* 24-42.

Norman G.R., Streiner D.L. (eds). (2003). Chapter 17: Path Analysis and Structural Equation Modeling. *PDQ Statistics Third Edition*. London: BC Decker Inc.

O'Brien R. (1994). Identification of Simple Measurement Models with Multiple Latent Variables and Correlated Errors. *Sociological Methodology*. Oxford: Blackwell

Osei-Bryson K.M., Dong L.Y., Ngwenyama O. (2008). Exploring managerial factors affecting ERP implementation: an investigation of the Klein-Sorra model using regression splines. *Information Systems Journal 18*:499-527.

Patient Protection and Affordable Care Act, 42 U.S.C. § 18001 (2010).

Rivera, D.A. (1999). Paving the Road to Hell: Why Change Programs Ultimately Fail. *The Physician Executive, 25,* 26-31.

Rogers E.M. (1983). The innovation-decision process. *Diffusion of innovations*. London: Collier Macmillan Publishers.

Rousseau D.M. (1985). Issues of Level in Organizational Research: Multi-Level and Cross-Level Perspectives. *Research in Organizational Behavior 7*: 1-37.

Sawang S., Unsworth K.L. (2011). A Model of Organizational Innovation Implementation Effectiveness in Small to Medium Firms. *International Journal of Innovation Management*, *15*, 989-1011.

Schreiber J.B., Stage F.K., King J. (2006). Reporting Structural Equation Modeling and Confirmatory Factor Analysis Results: A Review. *Journal of Educational Research 99*(6): 323-337.

Shea S., Bigger J.T., Campion J., et al. (1992). Enrollment in Clinical Trials: Institutional Factors Affecting Enrollment in the CAST. *Controlled Clinical Trials 13*:466-486.

Shortell S. M., Bennett, C. L., & Byck, G. R. (1998). Assessing the impact of continuous quality improvement on clinical practice: What it will take to accelerate progress. *The Milbank Quarterly, 76*, 593-624.

Sorbye H., Pfeiffer P., Cavalli-Bjorkman N., et al. (2009). Clinical trial enrollment, patient characteristics, and survival differences in prospectively registered metastatic colorectal cancer patients. *Cancer 115*(20): 4679-4687.

Sur D. (2006). The Basics of Structural Equation Modeling. Tutorial. http://www.lexjansen.com/wuss/2006/tutorials/tut-suhr.pdf. Accessed 5 March 2014

Teal R., Bergmire D.M., Johnston M., Weiner B.J. (2012). Implementing community-based provider participation in research: an empirical study. *Implementation Science*, *7*: 41.

VA Health Services Research & Development (2009). *Implementation Research Theoretical Frameworks CyberSeminar Series.*

Venkatesh V., Morris M.G., Davis G.B., et al. (2003). User Acceptance of Information Technology: Toward a Unified View. *MIS Quarterly 27*(3): 425–478

Weiner B.J., Belden C.M., Bergmire D.M., Johnston M. (2011). The meaning and measurement of implementation climate. *Implementation Science*, *6*:78.

Weiner B.J., Haynes-Maslow L., Campbell M.K., Kahwati L.C., Kinsinger L.S. (2012). Implementing the MOVE! Weight-Management Program in the Veterans Health Administration, 2007-2010: A Qualitative Study. *Preventing Chronic Disease*, *9*: E16.

Weiner B.J., Jacobs S.R., Minasian L.M., et al. (2012). Organizational Designs for Achieving High Treatment Trial Enrollment: A Fuzzy-Set Analysis of the Community Clinical Oncology Program. *Journal of Oncology Practice 8*(5): 287-291.

Weiner B.J., Lewis M.A., Linnan L.A. (2009). Using organization theory to understand the determinants of effective implementation of worksite health promotion programs. *Health Education Research*, *24*:292-305.

Werner C., Schermelleh-Engel K. (2009). Structural Equation Modeling: Advantages, Challenges, and Problems. *Introduction to Structural Equation Modeling with LISREL Version May 2009.*

Whitman C.V. (2009). Framing Theories and Implementation Research. In *Case Studies in Global School Health Promotion: From Research to Practice.* Edited by Whitman C.V., Aldinger C.E. New York: Springer.

Winn R.J. (1994). Obstacles to the accrual of patients to clinical trials in the community setting. *Seminars in Oncology 21*(4 Suppl 7): 112-117.