ORGANIZATIONAL DETERMINANTS OF MINORITY PARTICIPATION IN CLINICAL RESEARCH

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ABSTRACT

Charles Micha Belden I: Organizational Determinants of Minority Participation in Clinical Research
(Under the direction of Bryan Weiner)

Poor rates of minority participation in cancer clinical trials, and inequitable distribution of results from clinical research contribute to persistent disparities in cancer care outcomes. Systematic reviews of minority participation in clinical trials reveal extensive research on patient and provider-level barriers to participation; however, there is limited research on the organizational drivers of minority enrollment in treatment trials. The goal of this dissertation is to enhance our understanding of the organizational determinants of minority participation in cancer treatment trials. The objectives of this dissertation are: (1) estimate the impact of organizational characteristics associated with black enrollment in National Cancer Institute (NCI) sponsored treatment trials offered by organizations participating in the NCI Community Clinical Oncology Program; (2) examine the strategies of organizations participating in the NCI Community Clinical Oncology Program resulting in high enrollment of minorities in National Cancer Institute (NCI) sponsored treatment trials; and (3) evaluate disparities in geographic access to organizations offering National Cancer Institute (NCI) sponsored treatment trials for minority populations in the continental United States.

The first study employs a multivariate regression approach to estimate the impact of organizational characteristics on enrollment of blacks in treatment trials. The second study employed a fuzzy-set qualitative comparative analysis to investigate organizational strategies,

comprised of tactics, which achieve high enrollment of minorities in treatment trials as defined by NCI officials. Finally, a network analysis approach was employed using ZIP code tabulation area (ZCTA) data, and geocoded locations of organizations offering NCI-sponsored trials in order to investigate disparities in geographic access to CTOs.

Results from the three studies have theoretical, practical, and policy implications. This dissertation provides empirical support for Ford and colleagues conceptual framework describing barriers and facilitators to underrepresented populations' participation in clinical trials. CTO leaders can use findings from this dissertation to enhance their strategies to enroll minority patients in clinical treatment trials. Additionally, whereas our results demonstrate that overall geographic access to CTOs is excellent, policymakers can use the findings from the network analysis in order to address disparities in geographic access to CTOs for racial and ethnic groups residing far from CTOs.

To my clan, you have my endless gratitude for your support along this journey.

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LIST OF ABBREVIATIONS

ACS	American Community Survey
ACS-COC	American College of Surgeons Commission on Cancer
AHRQ	Agency for Healthcare Research & Quality
ASCO	American Society of Clinical Oncologists
BIC	Bayesian Information Criteria
CCOP	Community Clinical Oncology Program Organization
CTO	Clinical Trial Organization
fsQCA	Fuzzy-set Qualitative Comparative Analysis
MBCCOP	Minority-based Community Clinical Oncology Program Organization
MSA	Metropolitan Statistical Area
NCI	National Cancer Institute
NIH	National Institutes of Health
PBRN	Provider-based research network
US	United States
ZCTA	ZIP Code Tabulation Area
ZINB	Zero-inflated Negative Binomial Regression Model

CHAPTER 1: INTRODUCTION

Clinical treatment trials are considered the gold standard for evaluating the efficacy of cancer therapeutic regimens. Racial and ethnic diversity among clinical trial participants is critical in order to evaluate therapeutic effects, and ensure that the burdens and benefits of cancer clinical research are equitably shared. However, disparities in minority participation in clinical trials have been long-standing and well documented in the US. Estimates suggest that 3-5% of adult cancer patients in the US participate in a clinical trial, but less than less than 3% of minority cancer patients participate in trials despite extensive Federal efforts to promote the development of organizations intended to enhance minority participation in clinical research (NCI Cancer Bulletin, 2010). Moreover, studies have demonstrated an overall decline in minority participation in clinical research in recent years (Murthy, et. al., 2004), which may exacerbate disparities in the receipt of high-quality cancer care (Carpenter, et. al., 2011; Laliberte, et. al., 2005; Johnson, et. al., 1994). In order to improve minority participation in clinical research, and specifically treatment trials, it is essential that we improve our understanding of the organizational determinants of minority participation in clinical treatment trials.

Cancer care organizations provide a wide variety of treatment and prevention services to patients in the United States (US). The majority of cancer patients in the US seek care in community-based cancer care organizations; and for over 30 years, the National Institutes of Health (NIH) has promoted cancer care organizations that enhance overall and minority participation in clinical trials by funding collaborations between academically based researchers and community-based physicians. In 1983, the National Cancer Institute (NCI) initiated the

Community Clinical Oncology Program to foster the development of a provider-based research network (PBRN), comprised of community-based clinical trial organizations (CTOs) located throughout the US. The specific goals of this NIH endeavor have focused on promoting the implementation of CTOs that: (a) advance scientific discoveries in cancer therapies through conducting clinical trials in community-based locations; and (b) accelerate the translation and dissemination of clinical trial results into community-based practice settings. In addition to CTOs funded by the NCI Community Clinical Oncology Program, the American College of Surgeons Commission on Cancer (ACS-COC) has a long history of efforts aimed at improving cancer care, and specifically accredit cancer care organizations that offer clinical trials to patients in both academic and community-based hospital settings. Cancer care organizations accredited by ACS-COC that offer clinical trials to patients are included in the analysis presented in Chapter 4 as CTOs.

CTOs are organizations of specialists, primary care physicians, and other staff linked to NCI Cancer Centers and Research bases where treatment trials are initiated. Indeed, recent research has shown that CTOs have demonstrated their ability to address disparities in cancer care at the local level (Wheeler, et. al., 2012; Vicini, 2011). A physician principal investigator provides overall leadership for the CTOs' physicians and staff members; and CTO staffs vary in their composition, and may include program coordinators, research nurses, clinical research associates, data managers, and regulatory specialists. Staff members coordinate the review and selection of clinical treatment trial, disseminate protocols to participating physicians, and other staff members; and collect and submit study data. CTO physicians refer or enroll patients to clinical trials, and typically include cadres comprise of medical, surgical and radiation oncologists, general surgeons, urologists, gastroenterologists, and primary care physicians.

Through their collaboration with NCI research bases, CTO affiliated physicians may also participate in the development of clinical trials by proposing potential study ideas, providing input on study designs, and serving as a principal investigator or co-principal investigator for trials (Macaulay & Nutting, et. al., 2006). However, CTOs are challenging to implement and sustain. Challenges include obtaining sustainable funding, creating the infrastructure for clinical trial enrollment, locating and opening appropriate clinical trials appropriate for the populations served, managing complex regulatory compliance issues, and sustaining ongoing participation from community-based physicians.

Patient and physician level factors associated with minority participation in clinical research have been studied exhaustively, and included in several recent literature reviews (Rivers, et. al., 2014; Schmotzer, 2012; Ford, et. al., 2008), however, limited research has investigated the organizational characteristics associated with minority enrollment in clinical treatment trials (Lai, et al., 2006). Studies have sought to identify organizational characteristics associated with overall enrollment of patients to clinical trials at CTOs (Carpenter, et. al., 2012; Weiner, et. al., 2012; Jacobs, et. al., 2013), but these studies did not examine minority enrollment. This gap in research limits the ability to effectively develop policies and strategies to address disparities in minority participation in clinical research, and thus, it is critical for further studies to examine the impact of organizational factors associated with minority enrollment in clinical trials. This dissertation seeks to enhance our understanding of the role of organizational characteristics associated with the enrollment of minority populations in NCI-sponsored. The specific research objectives are: (1) examine the organizational characteristics associated with African American participation in NCI-sponsored clinical treatment trials; (2) examine the organizational strategies of CTOs resulting in high enrollment of minority patients in NCI-sponsored clinical treatment

trials; and (3) examine disparities in geographic access to cancer care organizations offering NCI-sponsored clinical trials (CTOs) in the continental United States. The central hypothesis is that organizational factors directly impact the enrollment of minorities in clinical research. This central hypothesis is tested with three research aims:

- **Aim 1: Estimate the impact of organizational characteristics on African American enrollment in NCI-sponsored clinical treatment trials available through PBRNs participating in the Community Clinical Oncology Program.**
- **Aim 2: Identify organizational strategies associated with high enrollment of minorities in NCI-sponsored clinical treatment trials among PBRNs participating in the Community Clinical Oncology Program**.
- **Aim 3**: **Examine disparities in geographic access to CTOs for demographic groups in the continental US.**

Data for this dissertation were drawn from 7 sources: 1) 2010-2012 NCI Annual Community Clinical Oncology Program Progress Reports; 2) 2011 Community Clinical Oncology Program Administrator Survey; 3) 2010-2012 American Community Surveys; 4) Kaiser Family Foundation; 5) National Cancer Institute website; 6) American College of Surgeons Commission (ACSO) on Cancer database; and the 7) Association of American Medical Colleges, Council of Teaching Hospitals database.

Annual counts of black patients enrolled in clinical treatment trials by CTOs participating in the Community Clinical Oncology program were drawn from the NCI Annual Progress Reports and used as the dependent variable for Aim 1. Annual counts of minority patients enrolled in trials drawn from the reports are the outcome of interest for Aim 2. Names and locations for each of the CTO's enrolling sites were also drawn from the Annual Progress

Reports and used in the development of the geographic information system (GIS) for Aims 1 and 3. A survey of CTOs delivered to program administrators, and conducted from 2011-2012, collected detailed organizational characteristics of the CTOs participating in the Community Clinical Oncology Program for Aims 1 and 2. American Community Surveys (ACS) provided data on metropolitan statistical area (MSA) demographic characteristics for black populations in the US for the multivariate regression analysis in Aim 1. Additional data for Aim 1 on CTO environmental context were drawn from the Kaiser Family Foundation website. In addition to the locations of enrolling sites of the Community Clinical Oncology Program for the GIS employed in Aims 1 and 3, the National Cancer Institute's website provided names and addresses for NCI-designated Comprehensive Cancer Centers in the US; the American College of Surgeons database provided names and addresses for accredited Commission on Cancer hospitals enrolling patients in clinical trials; and the Council of Teaching Hospitals provided names and addresses for academic medical centers.

This dissertation employs three distinct analytical approaches in order to examine organizational determinants of minority participation in NCI-funded clinical treatment trials. Aim 1 in this dissertation employs a multivariate regression approach in order to examine the impact of organizational factors on the enrollment of black Americans in clinical treatment trials. Aim 2 employs a fuzzy-set qualitative comparative analysis in order to identify the organizational strategies resulting in high organizational enrollment of minorities to clinical treatment trials. And Aim 3 employs a network geographic analysis in order to estimate median travel times from zip code tabulation area (ZCTA) centroids to he nearest CTO for racial and ethnic groups in the continental US. The geographic information system (GIS) capturing the locations of CTOs in the US underlies the overall study aims; specifically provides a measure of

hospital competition for Aim 1, and was employed as the analytical tool used to investigate disparities in geographic access to clinical trial organizations with estimated travel times for populations in the continental US in Aim 3.

The multivariate regression approach of Aim 1 presented in Chapter 2 focuses on the impact of organizational-level characteristics on black enrollment in clinical treatment trials. Aim 1 follows on Carpenter and colleagues' studies of organizational and market characteristics associated with overall enrollment in treatment trials by CTOs participating in the Community Clinical Oncology Program (2012, 2006). Organizational-level characteristics associated with black enrollment are examined since previous studies have extensively studied patient and provider-level data, and did not employ probabilistic analytical approaches. Moreover, detailed information on race or ethnicity, geographic location, and other socioeconomic characteristics of patients enrolled in clinical trials by specific physicians participating in the Community Clinical Oncology program is not available. Disparities in minority enrollment in clinical trials is the overall issue addressed in this dissertation; however, there is wide variation in the educational attainment, insurance coverage, and unemployment by racial and ethnic minority groups, and by region; thus Black enrollment was selected as the dependent variable of interest in Aim 1 because it specifically allows for the control of potentially endogenous socioeconomic factors (education, insurance, unemployment) using metropolitan statistical area data linked to each CTO. The multivariate regression approach employed in Aim 1 was also selected in order to estimate the net impact (marginal effects) of organizational characteristics on black enrollment in cancer clinical treatment trials. Examining the net impact of organizational characteristics on black enrollment allows us to understand which organizational factors are associated with enrollment, and the effect they have on enrollment while simultaneously controlling for the

effects of other organizational characteristics and potentially endogenous market-level factors (Carpenter, et. al., 2006).

The contribution of Aim 1 is significant because it will improve our understanding of the organizational factors that influence black participation in clinical treatment trials, and therefore enhance efforts to increase black participation. Previous research examining the impact of organizational characteristics of CTOs on overall treatment trial enrollment found that the number of trials available and trial-enrolling physicians were significantly associated with enrollment of patients in clinical treatment trials; and whereas greater hospital competition resulted in lower enrollment, results indicated that managed care penetration was positively associated with enrollment during early stages, and declined in later stages (Carpenter, et. al., 2006). A more recent study by Carpenter and colleagues (2012) reexamining the CTOs found that organizational characteristics remained significant; however, the only significant market-level factor was the proportion of nearby hospitals with medical school affiliations. Unfortunately, these studies did not examine black participation in clinical treatment trials, and it is unknown whether organizational characteristics have the same impact on black enrollment. For example, whereas a greater number of enrolling physicians are positively associated with overall clinical treatment trial enrollment; it is possible that a few physicians located in a densely populated minority region can enroll substantial numbers of black or minority patients in trials. Aim 1 is particularly relevant to the current reorganization of NCI's clinical trials infrastructure, and its mandate to continue addressing disparities in cancer care. A specific policy concern addressed in Aim 1 is the continued funding of CTOs that serve large minority populations. Whereas the NCI has funded community-based organizations focused on enrolling minority populations in clinical research since 1990, more evidence is needed to ensure that funding

minority-based organizations is an effective approach to enhancing minority participation in clinical research. Many of the CTOs examined in this study that serve large minority populations fail to enroll the minimum number of patients per NCI guidelines; however, they typically have fewer resources than CTOs that do not serve large minority populations. Aim 1 demonstrates that holding other organizational characteristics constant, CTOs serving large minority populations enroll significantly more blacks to clinical treatment trials. Additionally, in order to address the substantial number of barriers that black participants face (George, et. al., 2014; Rivers, et. al., 2013), a larger research staff may be necessary to enroll black patients in clinical treatment trials (Ghebre, et. al., 2014; Green, et. al., 2013).

The fuzzy-set qualitative comparative analysis (fsQCA) approach presented in Chapter 3 focuses on organizational strategies resulting in high enrollment of minorities in treatment trials. In this analysis, an organizational strategy consists of multiple tactics, and different combinations of tactics may result in high enrollment of minorities in treatment trials. Aim 2 seeks to improve our understanding of both the individual organizational design features, and combinations of individual design features that result in high enrollment of minorities in clinical treatment trials. The outcome of interest in Aim 2, minority enrollment in treatment trials, differs from Aim 1 due to the strength of the fsQCA case study approach to examine the organizational design features of PBRNs that achieve high minority enrollment without concerns for missing endogenous individual or contextual socioeconomic determinants of enrollment. The fsQCA case study approach differs from the probabilistic approach from Aim 1, and specifically utilizes Boolean logic to investigate the individual organizational design features that are necessary for high enrollment of minorities; and combinations of design features that are sufficient for achieving high minority enrollment.

The contribution of Aim 2 is significant because it provides a limited number of evidence-based organizational strategies that result in high enrollment of minorities in clinical treatment trials that may be employed to enhance overall minority participation in clinical research. Previous research on Community Clinical Oncology Program CTOs suggest that enrollment of patients in clinical trials varies with certain organizational factors (Teal, et. al. 2012; Clauser, et. al., 2009; McKinney, et. al., 2006; Weiner, et. al., 2006; Kaluzny, et. al., 1989). For example, studies examining specific organizational design features resulting in minority enrollment have suggested community-based participatory research approaches, outreach and trainings (Vicini, et. al., 2011), or patient navigation programs (Holmes DR, et. al., 2012). Results from a fuzzy-set analysis of organizational design features associated with high enrollment to clinical trials among CCOP organizations indicated that a strategy of having many available clinical trials in addition to a large number of patients results in high levels of enrollment (Weiner, et. al, 2012). However, the study did not evaluate organizational strategies associated with enrollment of minorities in clinical treatment trials. CTOs vary in the organizational design features they implement, and it is unknown whether there are consistent organizational strategies used by CTOs in order to achieve high enrollment of AA to clinical treatment trials.

The study presented in Chapter 4 focuses on disparities in geographic access to clinical trials organizations for populations in the continental United States. In this study, geographic access is measured as the travel time from the centroid of ZIP Code Tabulating Areas (ZCTAs) in which populations reside, to the nearest clinical trial organizations (CTOs). CTOs include the enrolling sites of organizations participating in the NCI's Community Clinical Oncology Program, and hospitals certified by the American Society of Clinical Oncologists Commission

on Cancer program. Aim 3 follows on Onega and colleagues (2008) study of geographic access to specialized cancer care organizations in the continental US, and employees the geographic network approach used in their study. Whereas our study examines disparities in geographic access to CTOs (NCI Cancer Centers, CCOPs, MBCCOPs, ACS-COC hospitals), Onega and colleagues (2008) study examined disparities in geographic access to specialized cancer care organizations, including NCI Cancer Centers, academic medical centers, and community-based oncology specialists. Overall, Onega and colleagues' study estimated that 92% of the US population has less than one hour of travel time to any oncologist-based specialty care. The study also found that the overall median travel time to NCI Cancer Centers for all demographic groups was 78 minutes (Interquartile range, 27-172); and overall median travel time to academic-based cancer care organizations is 30 minutes (Interquartile range, 13-72). The study found that disparities in geographic access to specialized cancer care organizations for racial and ethnic minorities in the US are most pronounced in the regions with large minority populations and limited cancer care organizations. With regards to minority populations, Onega and colleagues (2008) study found that Asian populations experience the least disparities in geographic access to specialized cancer care organizations, whereas Native Americans experience the greatest disparities. Black populations in the US tend to reside closer to NCI Comprehensive Cancer Centers than white and Hispanic populations; however all ethnic and racial minorities in the South experience issues with geographic access to cancer care organizations (Onega, et. al., 2008). However, Onega and colleagues (2008) study failed to include organizations participating in the NCI's Community Clinical Oncology Program, which may result in the misidentification of regions with disparities in geographic access to CTOs. For example, Onega and colleagues' (2008) study found disparities to geographic access to specialty cancer care in the south; their

study did not include CCOP, MBCCOP, or all ACOS-COC hospital locations, and generalizations about geographic access to CTOs in the south cannot be made.

The contribution of Aim 3 is significant because it will enhance the ability of NCI, AHRQ, existing CTOs, and other organizations to address disparities in geographic access to CTOs in the continental US through identification of regions with high travel times to CTOs. Research has demonstrated that travel times to cancer organizations is a substantial barrier to minority participation in clinical research trials (Holmes JA, et. al., 2012; Ford et. al., 2008; UyBico, et. al., 2007); therefore a detailed examination of disparities in minority populations' geographic access to clinical trial organizations is necessary to address overall disparities in in clinical research participation. Aim 3 utilizes the network geographic analysis methods employed by Onega and colleagues (2008) with additional geocoded data on organizations participating in the NCI Community Clinical Oncology Program and the American College of Surgeons Commission on Cancer in order to estimate median travel times from ZCTAs to the nearest location offering clinical treatment trials (CTO).

The following three chapters in this dissertation are manuscripts that align with the three specific aims and are intended for submission for peer-reviewed publication. The first manuscript follows-up on William Carpenter's analysis (2012) of overall enrollment in clinical trials with a focus on black enrollment in clinical treatment trials, and will be submitted to *Medical Care*. The second manuscript is a follow-up to Bryan Weiner's study (2012) of organizational design features of CTOs participating in the Community Clinical Oncology Program that result in high overall enrollment to clinical treatment trials, and will be submitted to *Clinical Trials*. The third manuscript follows-up on a study by investigators at Dartmouth College that examined geographic access to organizations offering specialized cancer care

services in the continental US, and will be submitted to *Cancer*. Chapter 5 concludes the dissertation with a review of the findings from each of the three manuscripts, provides a summary of the implications of study findings for policy, practice, and research, and a discussion of the limitations of this dissertation. Tables and figures for each manuscript are located at the end of each chapter. Finally, additional materials are provided in an Appendix followed by a bibliography at the end.

CHAPTER 2: IMPACT OF ORGANIZATIONAL CHARACTERISTICS ON ENROLLMENT OF BLACK AMERICANS IN CANCER TREATMENT TRIALS

INTRODUCTION

Disparities in minority participation in clinical research have been long-standing and well documented in the US. These disparities are particularly relevant for black Americans[1] who have the highest cancer mortality rates, poorest survival rates, and the lowest enrollment rates in clinical trials, even when compared with other minority groups (Chen, et. al., 2014; Murthy, et. al., 2004). Black Americans comprise over 10% of all new cancer cases in the US (US Centers for Disease Control), however only an estimated 2-3% participate in clinical treatment trials. After more than 20 years since the NIH Revitalization Act mandated the inclusion of minorities in NIH funded research, blacks remain disproportionately affected by cancer, and continue to experience substantial individual and systemic barriers to participating in cancer clinical trials when compared with non-Hispanic whites (Chen, et. al., 2014; Durant, et. al., 2014; Newman, et. al., 2008; Stewart, et. al., 2007; Murthy, et. al., 2004; Sateren, et. al., 2002).

Previous studies have extensively examined individual barriers and facilitators to blacks participation in clinical treatment trials;[2] however, quantitative studies focused on organizational characteristics associated with black enrollment have been limited (Vickers and Fouad, 2014; Ford, et. al., 2008). In a recent systematic review of barriers and facilitators to minority participation in clinical research, George and colleagues (2014) discuss numerous distinct

[1] Black Americans is a heterogeneous racial/ethnic group in the US, but hereafter simplified to 'blacks.'
[2] Focus of this study is on cancer clinical treatment trials, and hereafter is simplified to 'trials.'

individual barriers to black participation in trials including: beliefs regarding conspiracies to harm blacks; knowledge of the Tuskegee Syphilis study; poor experiences with research staff cultural competency; and distrust of health care systems (Murphy and Thompson, 2009; Corbie-Smith, et. al., 2002; Freimuth, et. al., 2001). Rivers and colleagues' (2013) systematic literature review focusing on factors associated with black participation in trials found similar results, and suggested that organizations focusing on targeted enrollment of minorities may be key to addressing disparities in trial participation. However, no study has empirically examined the impact of organizational characteristics on black enrollment in trials. Empirical studies focusing on organizational characteristics associated with black participation in trials have been limited to descriptive studies examining mistrust and reputation of research organizations (Murphy and Thompson, 2009; Gadegbeku, et. al., 2008; Linden, et. al., 2007; BeLue, et. al., 2006); are focused on enrollment to a single trial (Cook, et. al., 2010; Cook, et. al., 2005); or are case studies of a single enrolling organization (Holmes, et. al., 2012; Paskett, et. al, 2011; Vicini, et. al., 2011; Baquet, et. al., 2006). Studies examining participation of black patients in clinical research with multiple organizations did not examine enrollment in trials (Cook et. al., 2010; Cook et. al., 2005); or did not include detailed characteristics of the enrolling organizations (Lara, et. al., 2005; Murthy, et. al., 2004). Results from other studies have suggested that more organizational resources are necessary to establish community support, increase awareness, and alleviate barriers to participation (George, et. al., 2014; Ghebre, et. al., 2014; Green, et. al., 2013; McCaskill-Stevens, et. al., 2005; Kaluzny, et. al., 1993); and organizations with culturally competent members are more likely to enroll blacks and minorities to trials (Durant, et. al., 2014; Ejiogu, et. al., 2011; Baquet, et. al., 2006). However, the qualitative approaches and lack of empirical studies on modifiable organizational characteristics limits the generalizability of results.

The lack of empirical studies of organizational characteristics associated with black enrollment in trials limits our ability to develop, implement, and evaluate organizational strategies that enhance black participation in trials and address disparities in the receipt of innovative cancer therapies. Due to the broad range of barriers to black participation in trials, and with the current restructuring of NCI's clinical trials infrastructure, it is critical that we improve our understanding of the organizational characteristics associated with black participation in trials in order to address disparities in clinical research participation (Ford, et. al., 2008). The objectives of this study are to estimate and evaluate the impact of organizational characteristics on enrollment of blacks in NCI-funded trials. To our knowledge, this is the first study that empirically estimates the impact of organizational characteristics on enrollment of blacks in trials.

CONCEPTUAL FRAMEWORK

This study is informed by the conceptual framework proposed by Ford and colleagues' (2008) systematic review describing barriers and facilitators to minority enrollment in clinical research (see Figure 1). Based on their systematic review of the literature framework, enrollment of black populations requires awareness of and the opportunity to participate in trials; however, barriers and facilitators to acceptance or refusal to enrollment in trials are also particularly relevant for the enrollment of black and minority populations. Ford's model was originally proposed to explain individual-level barriers and facilitators to enrolling minority populations in trials; however, it strongly suggests pathways in which psychosocial (e.g. culture) and physical characteristics (e.g. resources) of an organization can promote awareness of trials, opportunities to participate in trials, and facilitate acceptance of an offer to participate in a trial for black populations.

Organizational characteristics were selected for this study based on their potential impact on black populations' awareness of trials, opportunities to participate in a trial, and acceptance of an offer to enroll in a trial. Lack of education about clinical research is the most commonly cited barrier to awareness of trials (Ford, et. al., 2008), and previous studies have demonstrated the association between education and awareness (Lara, et. al., 2005; Advani, et. al., 2003; Lara, et. al, 2001). Formal education regarding clinical research is not commonly provided to populations in the US; therefore, implementation of annual CCOP or MBCCOP disparities themed training events may be a key organizational characteristic that improves awareness of trials amongst black populations. The targeted dissemination of trial information was also cited as a key factor in awareness for minority populations; and may be limited by the number of organizations or physicians offering trials in regions with specific racial or ethnic backgrounds (Ford, et. al., 2008). Indeed, studies have identified the impact of the number of enrolling physicians on overall enrollment in trials (Carpenter, et. al., 2012), and demonstrated the key role of physicians as resources in offering trials to patients (Schmotzer, 2012; Klabunde, et. al., 2011). Therefore, we would expect that organizational efforts to increase the number of training events, enrolling sites, and enrolling physicians to enhance awareness and result in greater enrollment of blacks in trials.

Organizational characteristics commonly associated with enhanced opportunities to participate in trials for black populations include the implementation of policies and procedures supporting enrollment and having a large menu of trials for which black patients are eligible. Ford and colleagues' review (2008) found provider attitudes towards trials and the availability of appropriate trials for minority populations were frequently reported as key opportunity barriers. Organizations may implement supportive policies in order to improve physician attitudes

towards enrolling patients in trials such as an expectation for enrolling patients, or providing recognition for physicians who enroll patients in trials. Jacobs and colleagues' (2014) study examining the impact of supportive policies on physician enrollment in trials suggests that a minimum enrollment expectation and recognition are both positively associated with overall enrollment. Whereas the study did not examine black enrollment specifically, we expect supportive policies to have the same positive impact on opportunities for black participation.

With regards to acceptance, the model posits that mistrust in health care systems and costs of participation are the most commonly cited barriers to accepting enrollment in a trial. Mistrust in health care systems and costs to the patients are commonly cited as barriers to acceptance of an offer to participate in literature reviews and supported by qualitative studies (Durant, et. al., 2014; Advani, et. al., 2003; Corbie-Smith, et. al., 2002). Therefore, it is expected that organizations which serve large minority populations and have tailored strategies for enrolling minorities, may be associated with enhanced trust and overall higher enrollment of blacks in trials (McCaskill-Stevens, et. al, 2005). Furthermore, additional organizational resources such as research staff may be made available to address patient issues with trust; or the costs of participating in a trial, and increase the likelihood that black patients will accept an offer to participate in a trial (Vickers and Fouad, 2014; Rivers, et. al., 2013).

The Ford model posits that socioeconomic factors mediate and moderate the impact of efforts to enhance awareness and opportunities and to address barriers to accepting participation in a trial, and therefore should be included as control variables in quantitative studies of enrollment. Studies have found mixed results with regards to the impact of income on enrollment in trials (Linden, et. al., 2007; Lara, et. al., 2005; Ford, et. al., 2004; Advani, et. al., 2003); however, education, employment, and insurance are key socioeconomic factors associated with

black or minority enrollment (Brown and Moyer, 2010; Langford, et. al., 2010; Baquet, et. al., 2006; Lara, et. al., 2005; Trauth, et. al., 2005; Simon, et. al., 2004; Advani, et. al., 2003; Sateren, et. al., 2002). Studies have investigated the impact of competition, managed care, and state-level clinical trial insurance mandates on overall enrollment in trials (Carpenter, et. al., 2012; Carpenter, et. al., 2006); however, were unable to locate any empirical studies examining the impact of competition, managed care penetration, or state insurance coverage mandates on black enrollment specifically.

METHODS

Setting and Sample Selection

Since 1983, the NCI Community Clinical Oncology Program has successfully demonstrated the ability to implement over 60 provider-based research network organizations (PBRNs) in the US including Hawaii and Puerto Rico (Minasian, et. al., 2010; McCaskill-Stevens, et. al., 2005) (See **Map 1**). The Community Clinical Oncology Program is comprised of: (1) NCI's Division of Cancer Prevention providing overall direction and funding, (2) Clinical Research Group Bases and NCI Cancer Centers designing and developing trials, and (3) the PBRN organizations. PBRNs are local networks of community-based oncologists and hospitals with the primary goals of: engaging patients in clinical research, disseminating clinical research findings into community practice, and enrolling patients in NCI-sponsored clinical trials.

PBRN organizations in this study are hereafter referred to as "CCOPs;" whereas CCOPs that achieve minority-based institutional status based on demonstrated access to a patient population comprised of 30% minorities are hereafter referred to as "MBCCOPs." As of 2014, 47 CCOPs represent over 300 hospitals and over 3,000 physicians, and 17 MBCCOPs represent 55 hospitals and approximately 500 physicians. MBCCOPs were implemented beginning in 1990

in order to expand the NCI's efforts to increase minority participation in clinical research. MBCCOPs tend to be smaller than CCOPs in terms of enrolling sites, enrolling physicians, number of available trials, and number of research staff. Whereas CCOPs may not be lead by a university hospital, MBCCOPs tend to be located at universities, or academic medical centers; and are in more urban regions (Jacobs, et. al., 2013). The primary tactics MBCCOPs employed to enhance minority participation in clinical trials were physician education, and tailored community outreach efforts (McCaskill-Stevens, et. al., 2005). Early efforts of the MBCCOPs were hindered by the lack of clinically relevant trial protocols, institutional support, and community-specific factors (Kaluzny, et. al., 1993). However, the Community Clinical Oncology Program has been very successful, resulting in one-third of all patients, and one-fifth of minority patients enrolled in NCI-sponsored clinical treatment trials (Minasian, et. al., 2010).

CCOPs and MBCCOPs actively enrolling patients in trials from 2010-2012 in the continental US were included in this study. Each CCOP and MBCCOP was matched to a metropolitan statistical area (MSA) and state based on the geographic location of enrolling sites per Carpenter and colleagues (2006) in order to allow for the inclusion of independent variables that account for differences in demographic characteristics of patient populations. The analysis was restricted to CCOPs and MBCCOPs actively enrolling patients in trials in the continental US from 2010-2012 in order to reflect recent trends in clinical research. MBCCOPs located in Puerto Rico and Hawaii were excluded from the analysis due to substantially different organizational characteristics based on their geographic context (Carpenter, et. al., 2006). The final sample includes 45 CCOPs actively enrolling patients from 2010-12, and 13 MBCCOPs in 2010, increasing to 15 MBCCOPs in 2012; resulting in 177 PBRN-year observations.

Descriptive statistics are included for the dependent variable and independent variables in **Table 1**. CCOPs and MBCCOPs vary widely in their organizational characteristics and the environments in which they operate. CCOPs are typically larger research organizations than MBCCOPs, and have larger numbers of enrolling physicians, research staff, available trials, and enrolling sites. Moreover, MBCCOPs typically operate in resource-constrained environments, with wide variation in organizational characteristics depending on their organizational structure (Kaluzny, et. al., 1993).

Data Sources

Data for this study were derived from seven sources. NCI Community Clinical Oncology Program annual progress reports provided annual organizational data on CCOP and MBCCOP black enrollment to trials and the addresses of CCOP and MBCCOP enrolling locations. A survey distributed to CCOP and MBCCOP administrators from 2011-12 as part of another NCI-funded study (5R01CA124402) supplied additional data on CCOP and MBCCOP organizational characteristics in operating year 2011 (annual training events; number of enrolling sites and enrolling physicians; enrollment expectation and recognition; number of trials available; and number of research staff). The survey from CCOP and MBCCOP administrators did not collect data on CCOP organizational characteristics in 2010 and 2012; however, a 100% response rate was achieved, and the organizational characteristics collected typically do not vary from year to year (Weiner, et. al., 2012). The American Community Survey provided metropolitan statistical area (MSA) demographic data matched to each CCOP and MBCCOP. Kaiser Family Foundation (http://kff.org/) supplied state-level data on unemployment, managed care penetration, and policies regarding insurance coverage mandates matched to the state where the CCOP/MBCCOP headquarters is located. The National Cancer Institute website provided names and addresses of

NCI Comprehensive Cancer Centers in the US. The American College of Surgeons (ACoS) website provided names and addresses of Commission on Cancer certified hospitals with research nurses offering access to clinical trials. Names and addresses of academic medical centers in the US were drawn from the Association of American Medical Colleges data on Council of Teaching Hospitals members.

Dependent variable

The dependent variable of interest in this study is the annual count of black patients enrolled in NCI-sponsored trials offered by the sample CCOPs and MBCCOPs. Enrollment in trials is the primary measure of performance used by the NCI to evaluate CCOP/MBCCOPs PBRNs (Klabunde, et. al., 1994). CCOPs and MBCCOPs have minimum enrollment requirements for trials, but do not have specific requirements for the minimum number of black patients enrolled. Black enrollment was selected for this analysis rather than minority enrollment due to the consistent availability of annual MSA-level community data to control for confounding demographic effects. The dependent variable in this study remained in the natural count form rather than conversion to a logged form based on the results of Wooldridge tests of functional form (Wooldridge, 1994).

Independent variables of interest

The independent variables of interest in this study are organizational characteristics of the CCOP and MBCCOPs participating in the Community Clinical Oncology Program. These variables are intended to capture characteristics that improve awareness of trials, enhance opportunities to participate in trials, and promote acceptance of an offer to participate in a trial. Organizational characteristics theorized to have a positive impact on awareness include: a dichotomous measure for whether the CCOP or MBCCOP organizes annual disparities themed

training events; and count measures for the number of sites where patients can enroll in trials and the number of physicians enrolling patients for each CCOP or MBCCOP. Organizational characteristics theorized to enhance opportunities to participate include a dichotomous variable designating an expectation for the physicians to annually enroll a minimum number of patients, and a dichotomous designation for CCOP or MBCCOP recognition of physicians' enrollment in trials. Having a large menu of available trials for black populations to be eligible for is also expected to improve opportunities for participation in a treatment trial, and is included as the count of trials available at each CCOP or MBCCOP. Organizational characteristics expected to improve acceptance of an offer to participate include a dichotomous measure for MBCCOP status (serving a large minority population), and having a larger number of research staff available to help patients navigate the difficulties of participating in a trial.

Control Variables

Independent control variables include demographic, and CCOP or MBCCOP market characteristics associated with enrollment in trials. Metropolitan statistical area (MSA) total black population (in thousands), MSA black uninsured rate, and MSA black unemployment rate were included to account for potential demographic confounders in the model (Advani, et. al., 2003; Sateren, et. al., 2002). State managed care penetration, and a dichotomous measure indicating CCOP or MBCCOP situated in states mandating coverage for costs of clinical trials (Ellis, et. al., 2012; Gross, et. al., 2005; Gross, et. al., 2004) were included as independent variables describing the state environments in which the CCOP and MBCCOPs operate to control for endogenous socioeconomic and market factors which may be associated with enrollment in trials that have been suggested by previous studies of the Community Clinical Oncology Program (Carpenter, et. al., 2012; Carpenter, et. al., 2006). In order to measure

competition for trial enrollment, CCOP/MBCCOP organizations, NCI Comprehensive Cancer Centers, academic medical centers, and hospitals recognized by American College of Surgeons (ACoS) Commission on Cancer that offer NCI trials were identified and geocoded in ArcGIS 12.1. Fifty-mile buffers were placed on each CCOP/MBCCOP organization, and the number of other cancer care organizations unaffiliated with the CCOP/MBCCOP that fell within these buffers were identified and tallied in order to generate the measure. Non-affiliated CCOP or MBCCOP enrolling locations in the fifty-mile buffers were also included as potential sources of competition. An interaction term between minority-based institutional status and MSA black population was included in the model to account for MBCCOPs in regions with particularly large black populations.

Analytic Model

The analysis examined black enrollment in trials using longitudinal, multivariate negative binomial count models with standard errors adjusted for clustering at the organizational level. Annual CCOP or MBCCOP enrollment of blacks was regressed on the independent variables. Skewness and kurtosis tests were used in order to evaluate normality of the error term. A common failure of count models is overdispersion, or the assumption that variance is equal to the mean (Long and Freese, 2006). Likelihood-ratio tests with a Poisson count model indicated overdispersion, and thus a negative binomial count model was selected for final analyses. Estimates of marginal and differential effects were analyzed with bootstrapped standard errors using 2000 iterations in order to evaluate the impact of organizational characteristics on a CCOP or MBCCOP's annual black enrollment in trials. Analyses were conducted in Stata 12 (StataCorp. 2009. College Station, TX: StataCorp LP).

RESULTS

Bivariate analyses did not reveal problems with multicollinearity among the selected variables (Results available in Appendix). Marginal effects with bootstrapped standard errors for the models examining black enrollment in trials are presented in Table 2. Overall, CCOPs and MBCCOPs experienced declining enrollment of blacks in trials during the 2010-2012 study years. Results suggest that CCOPs and MBCCOPs in the South are associated with greater enrollment of blacks when compared with CCOPs and MBCCOPs in the Midwest; whereas CCOPs and MBCCOPs in the Northeast and West appear to have lower enrollment compared to CCOPs and MBCCOPs in the Midwest.

Results suggest organizational characteristics vary in their net impact on black enrollment. When examining organizational characteristics theorized to promote awareness of trials, a CCOP or MBCCOP's implementation of annual training or education events appears to have a positive and significant impact on enrollment. Additionally, the number of enrolling physicians and enrolling sites appear to have a positive, but insignificant impact on enrollment. With regards to the impact of organizational characteristics on barriers to opportunity to participate in clinical trials, an enrollment expectation has a negative and significant impact on black participation in trials; whereas recognition for enrolling patients in trials is associated with a positive and significant impact on enrollment of blacks for both CCOPs and MBCCOPs. There is a positive and insignificant impact of the number of available treatment trials on black enrollment for CCOPs and MBCCOPs. Organizational characteristics appear to be associated with a positive impact on black Americans' acceptance of an offer to participate in a clinical trial. Minority-based institutional status, and the number of research staff both appear to have a positive and significant impact on black enrollment in trials.

Annual black enrollment ranged from 0 to 63 in the sample (mean = 8.2, standard deviation = 10.3), and very few CCOPs and MBCCOPs enrolled more than 12 - 15 blacks to a treatment trial. The magnitude of the organizational characteristics on black enrollment also varies. The net impact of a training event, or an additional enrolling site or physician is between zero and one additional black participating in a treatment trial. An organizational expectation that physicians enroll a minimum number of patients appears to have a large negative impact on black enrollment. Organizations with enrollment expectations appear to enroll approximately 6 fewer blacks to treatment trials. Increasing the number of trials each CCOP or MBCCOP has available appears to have a negligible impact; however, efforts to provide recognition for physician enrollment appears to promote opportunities to participate, and may result in three or more black patients enrolling in a treatment trial. Finally, increasing the number of research staff may result in reducing barriers to acceptance of offers to clinical trials, but it appears that organizations with tailored strategies to serving large minority populations have the largest impact on enrollment with 12 additional blacks enrolled by MBCCOPs.

With regards to the control variables, results indicate that a CCOP or MBCCOPs' proximity to a large black population is associated with a positive and significant impact on black enrollment, although the magnitude of the effect is small. Results also indicate that an increase in the surrounding region's proportion of uninsured blacks is associated with a positive and significant impact on enrollment. The proportion of blacks attaining a high school diploma, and proportion of unemployed blacks also each appear to have a positive impact on enrollment, but these results were not significant. Hospital competition has a positive and significant impact on enrollment. State managed care penetration has a positive and significant impact; and a state insurance coverage mandate to cover the costs of trials also appears to have a positive and

significant impact on enrollment. The interaction terms between MBCCOP status and MSA black population is statistically significant; and the parameter coefficients included in Table 2 include the partial effect of the interaction since we sought to estimate marginal effects, and therefore analyzed the net impact of each organizational characteristic on black enrollment.

Sensitivity Analyses

In order to evaluate model fit and omitted variable bias, we conducted two sensitivity analyses. First, our analytical dataset included 24 (13.6%) observations with zero enrollments of blacks to trials. Zero-inflated negative binomial (ZINB) models are often used to account for excessive zeros in the dependent variable (Long and Freese, 2006). A ZINB model utilizes maximum likelihood estimates that are approximately normal in large samples, with standard errors and confidence intervals constructed to account for possible processes that result in a zero dependent variable (Cameron and Trivedi, 2010). The *a priori* assumption underlying the ZINB model lies in the probability that observations with a zero count are fundamentally different from other observations. Specifically, there is a 100% probability of always having a zero count for some of the observations. This requires the use of a separate modeling process predicting an outcome with a zero count. This study utilized the proportion of blacks in the MSA to explain observations that would have 100% probability of having zero enrollments of blacks. Standard and bias-corrected Vuong tests were used to compare negative binomial and zero-inflated negative binomial models, and results from each test indicated a better fit with the negative binomial model (Desmarais and Harden, 2013).

Our model included MSA-level measures of black high school attainment and uninsured rates; and state-level unemployment due to lack of full unemployment data at the MSA level to account for confounding effects of socioeconomic conditions on black enrollment. A direct

measure of black wealth was not included in the original analysis due to the correlations between income, education, insurance, and unemployment. Moreover, a parsimonious selection of variables was included due to the small sample size of CCOPs and MBCCOPs. Since it is unclear if wealth is an endogenous factor in our model (Rivers, et. al., 2013; Baquet, et. al., 2006; Sateren, et. al., 2002), we collected data on median family wealth from U.S. Census American Community Survey 3-year estimates and added this variable to a post-hoc regression analyses to investigate potential omitted variable bias. Whereas MSA median black family income has very little impact on enrollment, and is not statistically significant, its inclusion in the model results in changes to other parameters, indicating model instability. The Bayesian Information Criteria (BIC) goodness-of-fit measure for the model including MSA black family wealth is slightly higher than the model that does not include it, and the difference between the pseudo R^2 for the models is very small. Overall, the impact of the potential model instability on the organizational characteristics is negligible, but including family wealth appears to have a substantial impact on the environmental variables. Based on preliminary analyses using black enrollment data from 2000-2008, this model instability may be due to a failure to include key interactions between organizational or environmental variables. For example, preliminary analyses indicated a statistically significant interaction between MSA black education and unemployment. These measures are likely highly correlated at the individual level; however bivariate analyses do not indicate a high degree of correlation between these two MSA-level variables, and were not included as an interaction term in the final model for lack of theory guiding the interaction, and parsimony.

DISCUSSION

This study focused on the impact of organizational characteristics on enrollment of blacks in clinical treatment trials sponsored by PBRNs participating in the NCI Community Clinical Oncology Program from 2010-2012. Overall, our analysis provides support for Ford's conceptual framework, and demonstrates that organizational characteristics do have an impact on the enrollment of black patients in trials. This is the first study to find empirical support for the implementation of organizations with tailored strategies for serving minority populations on enrolling black patients using a multivariate statistical approach and detailed longitudinal data on organizations. On average, MBCCOPs enroll approximately 13 more blacks to trials than CCOPs. This may not appear a large number; however, this is no small number for an organization to enroll when considering the complexities of opening trials, and the multitude of individual-level barriers to black participation in clinical research (Chun & Park, 2012; Adams-Campbell, et. al., 2004). Therefore, our study suggests that policies further supporting the implementation of minority-focused clinical trials organizations may be critical to improve black participation in clinical research.

Whereas organizational characteristics appear to have an impact on black enrollment, it is important to note that few of the key modifiable organizational characteristics in our study appear to have large net substantial impact on black enrollment. For example, implementing an annual training event; or increasing the number of enrolling sites or physicians in order to increase awareness of clinical trials appear to result in small average gains in black enrollment (i.e. less than one). This is consistent with findings from Lara and colleagues (2005) study of cancer patients that strongly suggested the importance of awareness improvement activities alongside other activities to improve participation of blacks in clinical research. However, it

appears that organizational characteristics theorized to address opportunity barriers to enrollment have a larger net impact. For example, providing tokens of recognition to physicians for enrolling patients may result in three or more black patients participating in trials annually. Implementing an enrollment expectation among physician appears to have a negative impact on black enrollment in trials. This was an interesting finding in light of recent research demonstrating the impact of an expectation on individual-enrollment in clinical trials for all populations (Jacobs, et. al., 2014). We expect this is due to a subset of CTOs that have adopted strategies aimed at efficiently enrolling large number of patients. These "efficiency-oriented" CTOs typically do not open trials that are clinically relevant for minority populations; and more importantly, also implement an enrollment expectation as an approach to efficiently recruiting large numbers of overall patients to treatment trials. Considering findings from Jacobs and colleagues' (2014) study, additional analyses may be necessary to understand the impact of expectations on overall trial enrollment versus minority trial enrollment. For example, a certain type of CCOP may enroll large numbers of blacks in trials with an enrollment expectation in combination with other organizational characteristics.

Despite the overall low net impact of many organizational characteristics, post-hoc analyses suggest that combinations of organizational characteristics are associated with enhanced participation of blacks in trials, regardless of the size or characteristics of the black population served. For example, estimates suggest that a CCOP in a state that mandates insurance coverage of trial costs, in a region with approximately 400,000 blacks, which implements an enrollment expectation and annual disparities training events, and also recognizes physician enrollment will result in an average annual enrollment of 20 black patients. That is a substantial number of blacks enrolled when compared with the average impact of minority-based institutional status of

a PBRN; and is particularly relevant for organizations located in regions with sizable black or minority populations. This suggests that while MBCCOPs may have an edge in enrollment of black patients, non-minority focused organizations can employ strategies capable of enrolling blacks in clinical treatment trials. For example, in addition to promoting the development of MBCCOPs, promoting the development of focused research staff at CCOPs that are dedicated to enhancing minority participation may be an effective overall strategy for addressing barriers (Rivers, et. al., 2013; Vicini, et, al., 2011; Ford, et. al., 2008).

The positive and significant impact on enrollment of the number of other cancer care organizations in a CCOP or MBCCOP's region suggests that nearby hospitals do not compete for black enrollment. Results from our study differ from previous studies on competition, which found that CCOPs had lower overall trial enrollment in communities with a larger presence of hospitals affiliated with a medical school (Carpenter, et. al., 2011). MBCCOPs are typically housed in, or closely affiliated with, an academic medical center. Thus, our findings may reflect the predominance of minority enrollment in academic organizations in regions with overall larger number of hospitals. Combined, these factors suggest that in order to enroll greater numbers of blacks to treatment trials, it may be appropriate to have both an MBCCOP and CCOP; or a CCOP with specific physicians and staff dedicated to enhancing minority participation located in regions with large minority populations.

Whereas our analysis demonstrates that organizational characteristics can have an impact on enrollment of blacks to trials, it appears that environmental factors are still important. We found that state policies mandating insurance coverage of clinical trial costs are associated with a positive and significant impact on black enrollment. This supports previous studies indicating that black patients may be particularly sensitive to the costs of participation in trials (Ford, et. al.,

2008), however, differs from a previous study on the impact of state insurance coverage mandates on minority trial participation (Chun & Park, 2012). However, the previous study examined enrollment of minorities from 2001-2007, which may have not have been enough time for policies regarding insurance coverage to have an impact on minority enrollment. Moreover, our study examined enrollment from 2010-2012, and our results may reflect the long-term impact of policies mandating coverage of clinical trials costs for minority populations.

Our study demonstrates that the environment in which CTOs operate are important for enrollment; however, we compared the pseudo R^2 and BIC scores from our final model, and a model excluding organizational characteristics in post-hoc analyses. Estimates suggest that a model with only environmental variables explains approximately 9% of the variation in black enrollment in treatment trials (Appendix), whereas the model that includes organizational characteristics explains approximately 16% of the variation. Additionally, the BIC score for the model without organizational characteristics is greater than the BIC for the model with organizational characteristics, indicating superior goodness-of-fit. However, based on results from post-hoc analyses, we urge caution in considering the net impact of an organizational characteristic on black enrollment in trials when it is possible that multifaceted strategies, comprised of combinations of tactics employed in specific environments, are responsible for high organizational enrollment of blacks to trials.

There are several limitations to this study. The relatively small sample of CCOPs and MBCCOPs is a limitation to the generalizability of our results to other clinical trials organizations. However, we are unaware of a larger sample of organizations enrolling blacks in clinical trials, and the organizations in this study vary substantially in their organizational characteristics. Furthermore, this study is strengthened by its longitudinal design, inclusion of

regional demographic data, and detailed organizational characteristics. Additionally, there is a potential limitation in using spatially aggregated MSA variables in this analysis, including the potential for ecological fallacy if CCOPs and MBCCOPs operating environments are not accurately characterized by the MSAs in which they are located (Portnov, et. al., 2007; Openshaw, 1984). For example, hospital referral region data may reflect more accurately the demographics and market characteristics of each PBRN; however, those data were not available for the years of this study.

CONCLUSION

It is unclear how the reorganization of NCI's infrastructure, and changes in health care markets as a result of states implementing health reforms will impact CCOPs and MBCCOPs. Findings from this study demonstrate that minority-based PBRNs make sense. Our study also suggests that strategic combinations of characteristics may be implemented by minority-based and non-minority based organizations in order to address barriers to awareness, opportunity, and acceptance of clinical trials and enhance black participation in clinical research. Recent research has demonstrated the importance of specific combinations of organizational characteristics resulting in high performing clinical trials organizations. However, those studies failed to examine strategies resulting in minority participation in treatment trials; therefore, additional research is necessary to examine the organizational strategies that CCOPs and MBCCOPs implement in order to enroll blacks and other minorities in trials.

Figure 1. Aim 1 Conceptual Framework (Ford, et. al., 2008)

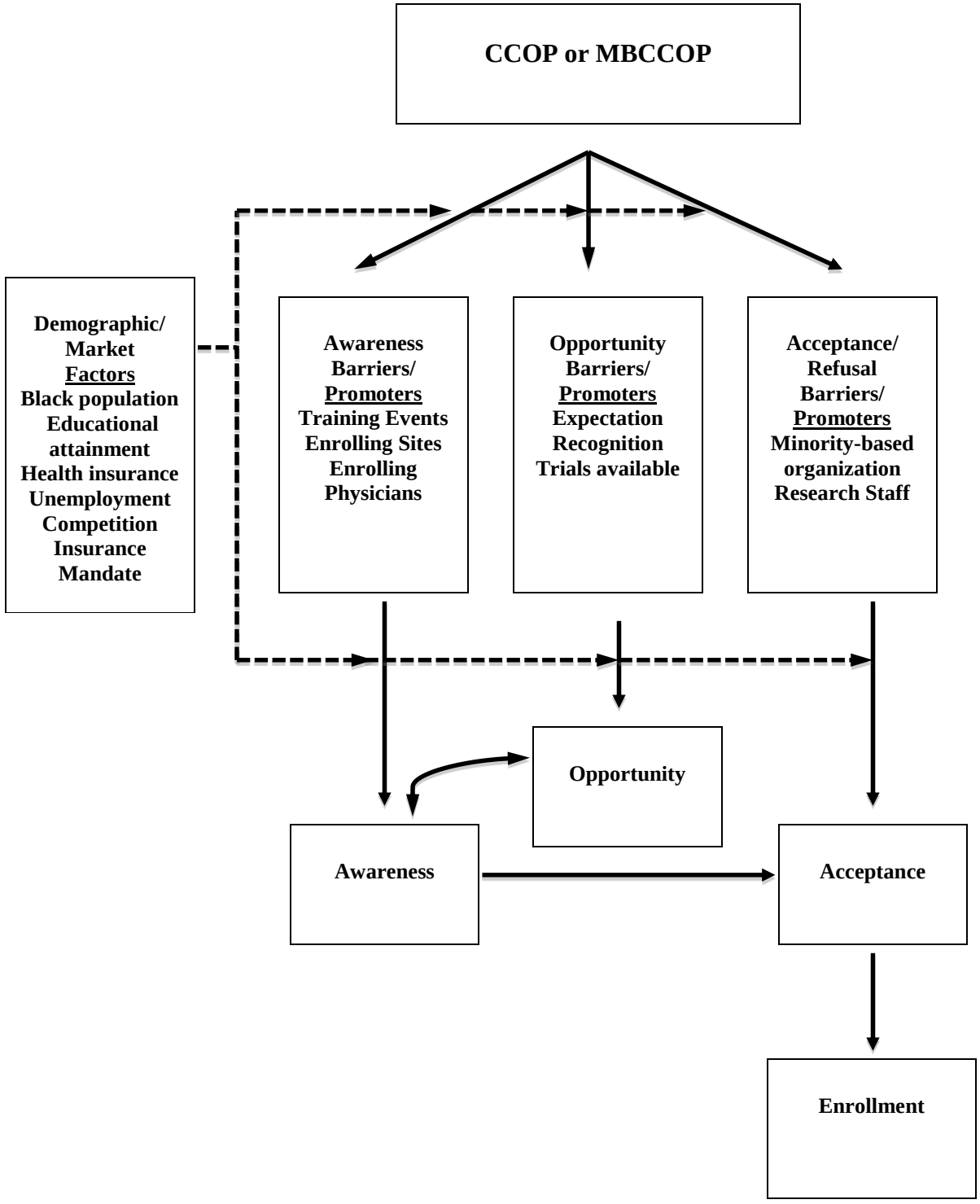


Table 1. Descriptive Statistics of Analytical Sample

Variables	Mean	Min/Max	Standard Deviation
Dependent Variables			
African American enrollment	8.51	0/63	10.32
Independent Variables			
Minority-based Institutional Status	24.3%		
No. of Enrolling Physicians	40.08	3/209	34.44
No. of Research Staff	14.58	2/77.7	12.35
No. of Treatment Trials Available	32.88	3/79	16.37
No. of Enrolling Sites	7.70	1/28	5.72
Enrollment Expectation	32.2%		
Recognition	47.5%		
No. Training Events	1.83	0/13	3.51
Black MSA population	401,909	655/2,613,412	681,989
Proportion MSA Black High School Grad			
Proportion MSA Black Uninsured	0.178	0.063/0.312	0.040
Proportion MSA Black Unemployment	0.160	0.006/0.247	0.038
Hospital Competition	27.88	0/94	25.96
State HMO Penetration	0.184	0.025/0.435	0.093
State Insurance Coverage Mandate	62.1%		
Census Region Northeast	15.0%		
Census Region South	26.7%		
Census Region Midwest	45.0%		
Census Region West	13.3%		
Year 2010	32.8%		
Year 2011	33.9%		
Year 2012	33.3%		

Figure 2. NCI Cancer Centers, CCOPs/MBCCOPs, Commission on Cancer Hospitals, Academic Medical Centers

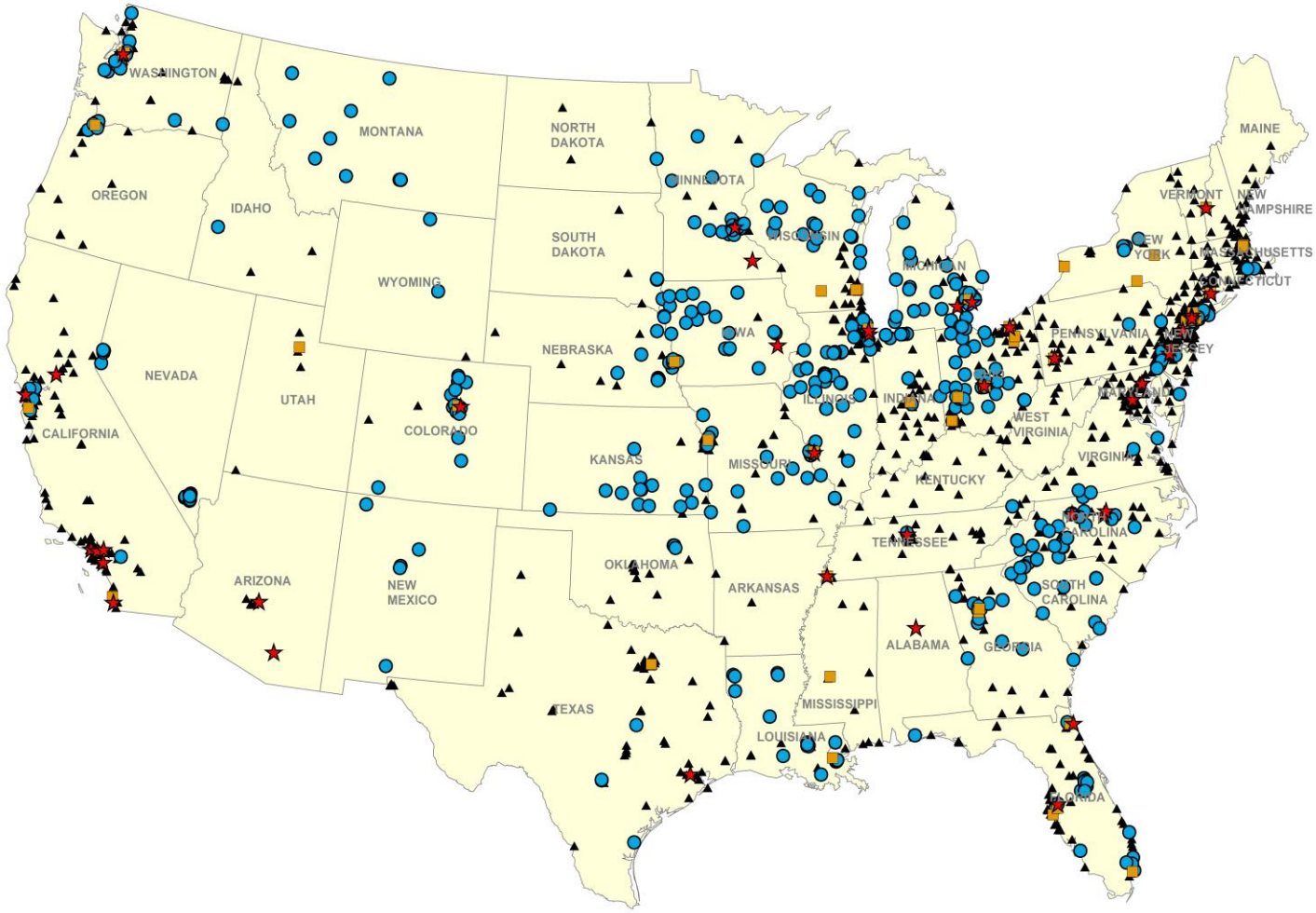


Table 2. Regression Results: Impact of Organizational Factors on Enrollment of Blacks in Cancer Clinical Treatment Trials

Variable	Marginal Effects	Standard Error♯	*P*-value	95% Confidence Interval	
Number of Training Events	0.496***	0.194	0.011	0.116	0.876
Number of Enrolling Sites	0.159	0.191	0.403	-0.214	0.533
Number of Enrolling Physicians	0.035	0.030	0.253	-0.025	0.094
Enrollment Expectation	-6.623***	2.022	0.001	-10.585	-2.661
Enrollment Recognition	2.319	1.689	0.170	-0.992	5.631
Number of Treatment Trials Available	0.073	0.093	0.429	-0.108	0.255
MBCCOP	11.323**	5.165	0.028	1.199	21.466
CCOP	-	-	-	-	-
Number of Research Staff	0.260**	0.113	0.022	0.038	0.483
MSA Black Population (1000s)	0.004**	0.002	0.012	0.001	0.008
MSA Proportion Black High School Graduates	18.209	23.974	0.448	-28.780	65.197
MSA Proportion Black Uninsured	68.679**	34.633	0.047	0.799	136.558
MSA Proportion Black Unemployed	-1.697	31.980	0.958	-64.376	60.982
Hospital Competition	0.219***	0.055	0.000	0.111	0.328
State Managed Care Penetration	17.454	14.094	0.216	-0.181	45.078
State Insurance Coverage Mandate	3.335*	1.793	0.063	-0.181	6.850
Northeast	-2.775	2.999	0.355	-8.654	3.105
South	7.799***	2.845	0.006	2.222	13.377
West	-4.756***	1.769	0.007	-8.223	-1.289
Midwest	-	-	-	-	-
2010	-	-	-	-	-
2011	-1.167	1.213	0.336	-3.543	1.209
2012	-2.193	1.331	0.100	-4.802	0.417

n = 172

Pseudo R2 = 0.1556; BIC = 1059.52

* $p < 0.10$; ** $p < 0.05$; *** $p < 0.01$

Bootstrapped Standard Errors (2000 replications)

Table 3. ZINB Regression Results: Impact of Organizational Factors on Enrollment of Blacks in Cancer Clinical Treatment Trials

Variable	Marginal Effects	Standard Error♯	*P*-value	95% Confidence Interval	
Number of Training Events	0.397	0.301	0.188	-0.193	0.986
Number of Enrolling Sites	0.307**	0.140	0.028	0.033	0.580
Number of Enrolling Physicians	0.019	0.021	0.383	-0.024	0.062
Enrollment Expectation	-3.768	1.950	0.053	-7.589	0.054
Enrollment Recognition	1.812	2.289	0.428	-2.673	6.298
Number of Treatment Trials Available	0.083	0.058	0.153	-0.031	0.196
MBCCOP	8.606*	5.145	0.094	-1.479	18.690
CCOP	-	-	-	-	-
Number of Research Staff	0.165**	0.078	0.036	0.010	0.318
MSA Black Population (1000s)	0.026**	0.009	0.003	0.009	0.042
MSA Proportion Black High School Graduates	8.776	22.887	0.701	-36.081	53.633
MSA Proportion Black Uninsured	58.928	42.460	0.165	-24.291	142.148
MSA Proportion Black Unemployed	-7.961	37.631	0.832	-81.717	65.795
Hospital Competition	0.166***	0.047	0.000	0.747	0.257
State Managed Care Penetration	21.518	14.121	0.128	-6.160	49.195
State Insurance Coverage Mandate	1.987	2.089	0.341	-2.107	6.081
Northeast	-2.259	3.425	0.510	-8.972	4.454
South	4.424	3.022	0.143	-1.498	10.347
West	-5.242***	3.022	0.004	-8.799	-1.685
Midwest	-	-	-	-	-
2010	-	-	-	-	-
2011	-0.851	0.832	0.307	-2.482	0.780
2012	-1.931***	0.936	0.039	-3.766	-0.097

n = 172

Pseudo R2 = 0.1220; BIC = 1055.52

* $p < 0.10$; ** $p < 0.05$; *** $p < 0.01$

Bootstrapped Standard Errors (2000 replications)

Table 4. Regression Results: Impact of Organizational Factors on Enrollment of Blacks in Cancer Clinical Treatment Trials (Add MSA Median Black Family Income)

Variable	Marginal Effects	Standard Error♯	*P*-value	95% Confidence Interval	
Number of Training Events	0.617***	0.202	0.002	0.221	1.013
Number of Enrolling Sites	0.226	0.171	0.187	-0.11	0.562
Number of Enrolling Physicians	0.039	0.028	0.164	-0.016	0.093
Enrollment Expectation	-6.295***	1.899	0.001	-10.016	-2.573
Enrollment Recognition	2.815*	1.699	0.097	-0.514	6.145
Number of Treatment Trials Available	0.065	0.082	0.427	-0.095	0.225
MBCCOP	10.293**	5.061	0.042	0.373	20.213
CCOP	-	-	-	-	-
Number of Research Staff	0.231**	0.097	0.017	0.041	0.421
MSA Black Population (1000s)	0.005**	0.002	0.031	0	0.01
MSA Proportion Black High School Graduates	19.76	29.105	0.497	-37.285	76.805
MSA Proportion Black Uninsured	77.209**	34.555	0.025	9.482	144.935
MSA Proportion Black Unemployed	2.645	37.841	0.944	-71.523	76.813
MSA Median Black Family Income	-0.0001	0	0.654	-0.001	0
Hospital Competition	0.139***	0.047	0.003	0.046	0.232
State Managed Care Penetration	27.377*	14.911	0.066	-1.849	56.603
State Insurance Coverage Mandate	2.097	1.698	0.217	-1.231	5.425
Northeast	-4.384	2.841	0.123	-9.953	1.184
South	4.768**	2.345	0.042	0.173	9.364
West	-5.0899***	1.558	0.001	-8.144	-2.036
Midwest	-	-	-	-	-
2010	-	-	-	-	-
2011	-0.813	1.16	0.483	-3.086	1.46
2012	-2.063	1.231	0.094	-4.476	0.35

n = 172

Pseudo R2 = 0.1573; BIC = 1065.76

* $p < 0.10$; ** $p < 0.05$; *** $p < 0.01$

Bootstrapped Standard Errors (2000 replications)

CHAPTER 3: A FUZZY-SET ANALYSIS OF ORGANIZATIONAL STRATEGIES PROMOTING MINORITY PARTICIPATION IN CANCER TREATMENT TRIALS

INTRODUCTION

More than 20 years since the NIH Revitalization Act mandated the inclusion of minorities in NIH funded research, minorities remain disproportionately affected by cancer, and continue to be underrepresented in cancer clinical trials when compared with non-Hispanic whites (Chen, et. al., 2014; Durant, et. al., 2014; Newman, et. al., 2008; Stewart, et. al., 2007; Murthy, et. al., 2004; Sateren, et. al., 2002). Overall, less than 3% of adult cancer patients participate in trials, and minority populations represent less than 0.3% of participants (Vickers and Fouad, 2014; Stewart, et. al., 2007). Moreover, research has also found an overall decline in the proportion of minorities participating in clinical trials (Heller, et. al., 2014; Kwiatkowsky, et. al., 2013; Newman, et. al., 2008).

For more than 30 years, the National Cancer Institute's Clinical Oncology Program has enrolled patients in clinical trials through the implementation of provider-based research network (PBRN) organizations in community-based settings. These PBRN organizations are hereafter referred to as "CCOPs," or "MBCCOPs" for minority-based CCOPs, which specialize in serving minority populations. CCOPs and MBCCOPs are collaborations between academic-based physicians and oncology physicians in community-based hospitals and private practices. CCOPs and MBCCOPs have been very successful, resulting in one-third of all patients, and one-fifth of minority patients enrolled in NCI-sponsored clinical treatment trials (Minasian, et. al., 2010). Systematic reviews of minority participation in clinical research reveal extensive research on

patient and provider-level barriers to participation in clinical trials; however, studies focusing on organizational strategies to enroll minority populations in clinical treatment trials are limited. (George, et. al.2014; Schmotzer, 2012; Ford et. al., 2008; Howerton, et. al., 2007). Barriers to participation include lack of provider awareness of locally available trials, unfavorable provider attitudes, patient mistrust and limited geographic access (George, et. al., 2014; Schmotzer, 2012; Ford, et. al. 2008; Lara, et. al., 2001). Unfortunately, empirical studies focusing on strategies associated with minority participation in clinical trials have been limited to descriptive studies examining organizational staffing and resource barriers (McCaskill-Stevens, et. al., 2006; Adams-Campbell, et. al., 2004); and single site case studies of minority outreach or patient navigator programs (Holmes, et. al., 2012; Paskett, et. al, 2011; Vicini, et. al., 2011). Specific studies on CCOPs and MBCCOPs suggest that enrollment of patients in clinical trials varies with certain organizational strategies, comprised of tactics (Weiner, et. al. 2012; Teal, et. al. 2012; Clauser, et. al., 2009; McKinney, et. al., 2006; Weiner, et. al., 2006; Kaluzny, et. al., 1989). In this study, tactics are the organizational characteristics implemented by CTOs such as training events, or a large research staff. For example, studies examining specific tactics resulting in high minority enrollment have suggested community-based participatory research approaches, outreach, and trainings (Vicini, et. al., 2011), or patient navigation programs (Holmes DR, et. al., 2012) are associated with greater enrollment of minorities in treatment trials. Results from a fuzzy-set analysis of strategies associated with high levels of overall enrollment in clinical treatment trials among CCOP organizations indicated that the number of new patients, the number of available treatment trials, and the number of enrolling sites are key tactics in achieving high levels of enrollment (Weiner, et. al, 2012). However, the study did not examine

strategies or tactics consistently associated with high enrollment of minorities in clinical treatment trials.

This gap in the research limits our ability to develop, implement, and evaluate strategies in order to improve minority participation in clinical treatment trials. The aim of this study is to examine the organizational strategies and tactics implemented by CCOPs and MBCCOPs that result in high organizational enrollment of minority populations in NCI-sponsored clinical treatment trials. In order to accomplish this aim, we collected detailed organizational data on CCOPs and MBCCOPs actively enrolling patients in clinical trials from 2010-2012; and employed a novel method, fuzzy-set qualitative comparative analysis to investigate the tactics, and combinations of tactics that lead to high organizational enrollment of minorities to treatment trials. Fuzzy-set qualitative comparative analysis (fsQCA) is used for this study based on results from a multivariate analysis of organizational characteristics suggesting that CCOPs and MBCCOPs may achieve high enrollment of minorities in trials based on the impact of combinations of organizational characteristics (Belden, et. al., dissertation chapter 2 – manuscript 1). Moreover, fsQCA is particularly appropriate when an outcome of interest (high organizational enrollment of minorities to treatment trials) may be the result of varying strategies, which are themselves combinations of different tactics. To our knowledge, this is the first study to empirically examine the tactics that CCOP and MBCCOP organizations implement in order to enroll high numbers of minorities to clinical treatment trials.

METHODS

Study Setting

This study focuses on provider-based research network (PBRN) organizations participating in the National Cancer Institute Community Clinical Oncology Program. PBRNs

are local networks comprised of community-based oncologists and hospitals. The primary goals of CCOPs and MBCCOPs are: engaging physicians in clinical research, disseminating clinical research findings into community practice, and enrolling patients in NCI-sponsored clinical trials. Since 1983, the NCI Community Clinical Oncology Program has successfully demonstrated the ability to effectively implement over 60 PBRNs in communities across the US (Minasian, et. al., 2010). The Community Clinical Oncology Program is comprised of: (1) NCI's Division of Cancer Prevention which provide overall direction and funding, (2) Clinical Research Group Bases and NCI Cancer Centers which design and develop clinical trials, and (3) the PBRN organizations which enroll patients. As of June 2013, 47 CCOPs represent 340 hospitals and nearly 3,000 physicians; and 16 MBCCOPs represent 55 hospitals and nearly 500 physicians.

Data Measures and Sources

The outcome of interest for this study, high organizational enrollment of minorities in trials, is based on the total annual count of non-white patients CCOPs and MBCCOPs enrolled in clinical treatment trials from 2010-2012. Enrollment in treatment trials is the primary measure of performance for CCOPs and MBCCOPs. MBCCOPs are required to serve a population comprised of a minimum of 40% minorities (McCaskill-Stevens, et. al., 2005); but do not have a minimum requirement for minority enrollment. Both CCOPs and MBCCOPs however do have minimum requirements for overall enrollment in treatment trials. Annual data on the number of minority patients enrolled in clinical treatment trials by CCOP and MBCCOP organizations were drawn from the NCI Community Clinical Oncology Program annual program reports. NCI Division of Cancer Prevention officials established the threshold for high minority enrollment in treatment trials as described below.

CCOP and MBCCOP tactics were drawn from a survey of CCOP and MBCCOP program administrators conducted from 2011-2012. The CCOP Administrator Survey aimed to examine how CCOPs and MBCCOPs operate. Data were gathered from 100% of active CCOPs and MBCCOPs. The survey gathered detailed information on tactics including: MBCCOP status, the number of enrolling physicians, number of research staff, number of available treatment trials, number of enrolling sites, number of enrolling sites with screening and/or staff assistance with enrollment, enrollment expectation, recognition for enrollment, and annual training events.

Study Design and Data Analysis

Fuzzy-set qualitative comparative analysis (fsQCA) was used to examine the strategies, comprised of multiple tactics implemented by CCOPs and MBCCOPs, that consistently achieve high organizational enrollment of minority patients in clinical treatment trials. FsQCA is a case study approach used to investigate logical relationships between causal conditions (e.g. tactics), and an outcome of interest using set theory. Statistical approaches can be used to estimate the net impact of a causal condition on an outcome of interest; however, the assumptions required for unbiased estimates with statistical approaches may not hold with small sample sizes. For example, omitted variables may introduce substantial bias in statistical approaches. The strength of the fsQCA approach is the examination of causal conditions (e.g. tactics) that are individually necessary or sufficient for an outcome of interest (e.g. high minority enrollment); and to investigate the combinations of causal conditions (e.g. strategies) that are sufficient for the outcome of interest (e.g. high minority enrollment) in small samples (Kane, et. al., 2014; Longest and Thoits, 2012; Ragin, 2000; Ragin, 2008). Moreover, the fsQCA approach allows an examination of the organizational tactics (i.e. characteristics) implemented by CTOs that enroll large numbers of minorities to clinical trials without meeting the strict assumptions necessary for

statistical approaches. This is particularly appropriate in this analysis with 62 CCOPs and MBCCOPs under study.

The fsQCA approach examines set, subset, and superset relationships between causal conditions (e.g. organizational tactics) and the outcome of interest (high minority enrollment). Causal conditions, or combinations of causal conditions, that are always required for an outcome of interest demonstrate a superset relationship with the outcome set, and are considered necessary for the outcome of interest. Causal conditions, or combinations of causal conditions, that frequently result in the outcome of interest and demonstrate subset relationships with an outcome set, are considered sufficient to achieve the outcome. A set-theoretical underpinning of fsQCA is *equifinality*, which proposes that multiple combinations of causal conditions (e.g. tactics) can lead to the same outcome of interest (e.g. membership in the set of CCOPs or MBCCOPs with high organizational enrollment of minorities in treatment trials). (Goertz and Mahoney, 2005; Ragin, 2000; Ragin, 2008). Furthermore, set theory allows us to logically assume that strategies resulting in high minority enrollment may contain different combinations of tactics. For example, set theory allows for the explanation that one strategy resulting in high minority enrollment includes a large number of physicians with a large menu of trials, and many enrolling sites with screening assistance; whereas another strategy resulting in high minority enrollment includes a small number of physicians who receive assistance with enrollment at many sites, and an annual training event.

FsQCA has been previously used to identify organizational strategies resulting in overall high enrollment of patients to treatment trials (Weiner, et. al., 2012). This fsQCA examined the necessary tactics, and sufficient strategies resulting in high minority enrollment. The analysis was completed in 7 steps: 1) Calibrate crisp and fuzzy membership scores; 2) Construct a truth

table, a matrix containing the fuzzy and crisp membership scores in the outcome and condition sets; 3) Examine necessity of tactics with consistency scores; 4) Logical minimization of redundant cases with Quine-McCluskey algorithm; 5) Assess sufficiency of organizational strategies with consistency scores, and inclusiveness; 6) Examine the empirical relevance of organizational strategies with coverage scores; 7) Counterfactual analysis of organizational strategies.

A key step in the fsQCA approach is calibration, or the decision rules for establishing membership scores in causal condition and outcome sets. Membership scores in fsQCA vary from 0.0 to 1.0, and are categorized as *crisp* or *fuzzy*. Membership in a crisp set is similar to a dichotomous variable: a case has full membership in the causal condition, or has full non-membership in the causal condition. For example, if an organization meets the criteria outlined by the NCI as a minority-based institution, it would receive a membership score of '1' in the set of MBCCOPs; if the organization does not meet the criteria, it is not an MBCCOP and would receive a crisp membership score of '0,' and thus have full non-membership in the set of MBCCOPs. Fuzzy membership scores range from 0.0 to 1.0 in order to allow for finer gradients of membership in a set. The use of external standards such as expert judgment, theoretical knowledge, and prior research findings is the preferred approach for developing decision rules for anchor points for full membership in a set, full non-membership in a set, and a cross-over point indicating maximum ambiguity of membership in a set (Ragin, 2008; Ragin, 2000). For example, an MBCCOP may have a fuzzy membership score that indicates it is fully in the outcome set of organizations achieving high minority enrollment; the MBCCOP may have a fuzzy membership score indicating it is not in the set of organizations achieving high minority

enrollment; or the MBCCOP has a fuzzy membership score indicating it is ambiguous as to whether it is fully in or out of the set of organizations achieving high minority enrollment.

To prepare fuzzy set membership scores, expert opinion was sought from NCI Division of Cancer Prevention officials to establish anchor points indicating full membership, full non-membership, and a cross-over point of maximum ambiguity for the following study measures: minority-enrollment, number of enrolling locations, number of physicians enrolling, number of trials available, and the number of research staff at each CCOP and MBCCOP. Based on substantive knowledge, and discussions with NCI officials, different anchor points were developed to account for differences in the actual sizes of CCOP and MBCCOP organizations. The anchor points established by NCI Division of Cancer Prevention officials were also used in order to transform the measures for number of screening sites, and the number of sites with enrollment assistance, into fuzzy set membership scores. Fuzzy membership scores for sites with screening and sites with enrollment assistance were standardized for each CCOP and MBCCOP using the total number of enrolling locations, and then re-scaled using the anchor points suggested by NCI officials. Anchor points for CCOP and MBCCOP tactics are listed in Table 6. Additional study measures were dichotomous, and included in the fsQCA analysis as crisp membership scores. A crisp membership score is either one or zero, with one indicating full membership in the set of interest (e.g. PBRNs serving a large minority population and categorized as MBCCOPs), and zero indicating full non-membership in the set of interest (e.g. PBRNs that do not serve large minority populations, and are categorized as CCOPs). The following study measures are crisp: MBCCOP, enrollment expectation, enrollment recognition, feedback on overall organizational enrollment, feedback on individual physician enrollment, and whether the CCOP or MBCCOP implemented annual training events.

After fuzzy-set membership scores were calibrated, a data matrix was created each of the CCOP and MBCCOP case strategies. The data was then reduced by eliminating strategies that do not consistently result in high minority enrollment by removing rows with a fuzzy membership score greater than 0.5 in the set of PBRNS with high minority enrollment in treatment trials. Further minimization of the remaining cases in the truth table was based on three criteria: (1) the minimum number of cases for *inclusiveness*; (2) the minimum *consistency* of a strategy; and 3) the Quine-McCluskey algorithm derived from Boolean Algebra was used in order to eliminate redundant organizational strategies. *Inclusiveness* is selected as the minimum number of cases required in order to identify a set of conditions that lead to the outcome of interest. Due to the moderately small number of organizations in the study (N=63), the minimum number of cases will be set equal to one as proposed by Ragin (2008). Thus, strategies that did not exhibit an empirical case were used in the counterfactual analysis. Consistency is used to evaluate the frequency with which cases result in the outcome of interest. Consistency is measured as $(X_i \leq Y_i) = \sum[\min(X_i, Y_i]/ \sum(X_i)$, where X is the fuzzy-set membership score in a set for an organizational strategy and Y is the fuzzy-set membership score in the set for high minority enrollment. As suggested by Ragin (2008) and Weiner's (2012) analyses, the minimum acceptable consistency threshold is set at 0.80 (Ragin, 2008). Final minimization of the data matrix into a truth table used Boolean algebra and the Quine-McCluskey algorithm to logically minimize organizational strategies that are sufficient for achieving high minority enrollment (Ragin, et. al. 2008). The truth table contains 2^k rows, where k is the number of tactics included in the analysis, and includes the score in the outcome set of interest (Ragin, 2008).

The final truth table was used to examine the empirical relevance of each of the logical organizational strategies that consistently result in high enrollment of minorities in treatment

trials with coverage scores. Coverage is a proportional measure describing the degree of overlap among two or more combinations of tactics (Ragin, 2008). Coverage evaluates the frequency with which a strategy results in the outcome of interest, and is measured as $(X_i \leq Y_i) = \sum[\min(X_i, Y_i]/ \sum(Y_i)$, where X is the fuzzy-set membership score in a set representing a strategy, and Y is the fuzzy-set membership score in the set for high minority enrollment. Raw coverage

A counterfactual analysis was used to examine the strategies that lead to high minority enrollment that lack empirical cases. This approach specifically allows for investigation of strategies that are theoretically or empirically suggested to result in high minority enrollment; and may lead to further reduction of organizational strategies that require further study (Ragin, 2008; Weiner, et. al., 2012). The counterfactual analysis focused on easy counterfactuals where a redundant tactic is added to a strategy that results in high minority enrollment (Weiner, et. al., 2012; Ragin, 2008). For example, previous studies have indicated that having a large number of enrollment sites is associated with high minority enrollment. Starting with the assumption that CCOPs with a large physician cadre and research staff, a large trial menu, and strong policies and practices would also be a key tactic resulting in high minority enrollment regardless of the number enrollment sites, the truth table can be examined to evaluate if there are logical and empirical cases of that strategies that do and do not have membership in the set of CCOPs with a large number of enrolling sites. The counterfactual analysis will be unable to produce logically simpler strategies resulting in high minority enrollment and "simplifies" the causal conditions for that organizational strategy to large physician cadre and research staff, a large trial menu, and strong policies and practices.

RESULTS

Descriptive statistics for CCOPs and MBCCOPs are listed in Table 7 and Table 8. Enrollment of minority patients in NCI-sponsored treatment trials varied between CCOP and MBCCOPs. In the study period, CCOPs enrolled 0-66 minority patients; and MBCCOPs enrolled 0-138 minority patients in treatment trials. The 22 logically possible strategies resulting in high levels of enrollment of minority patients in clinical treatment trials are described in Table 9. Our study did not find a single tactic that was necessary for achieving high minority enrollment in treatment trials. Our results suggest that a single CCOP strategy consistently results in high organizational enrollment of minority patients, whereas MBCCOPs may employ 3 distinct strategies in order to achieve high organizational enrollment of minorities in trials.

The CCOP strategy resulting in high organizational enrollment of minorities appears to be a variation of the "size matters" theme proposed by Weiner and colleagues (2012). The CCOP strategy resulting in high minority enrollment had a large cadre of enrolling physicians, with a large staff providing screening and assistance with enrollment at a large number of community sites. This CCOP strategy also had supportive policies and practices, with the implementation of annual training events; and an expectation that physicians enroll a minimum number of patients, and recognition for enrollment of patients in trials.

The first MBCCOP strategy that consistently results in high minority enrollment simply has a large staff that holds at least one annual training event, and physicians enrolling patients in treatment trials are not necessarily required to enroll a minimum number of patients. The second MBCCOP strategy employs a large research staff that does not provide screening and enrollment assistance in a large number of sites; and physicians are not required to enroll a minimum number of patients enrolled in treatment trials. The third MBCCOP strategy resulting in high

minority enrollment has a small cadre of physicians enrolling patients, with screening and assistance for enrollment occurring at a large number of sites. This strategy also includes a large menu of available treatment trials and implementation of at least one annual training event, however, did not have strong supportive policies or practices. Notably, this strategy also required that the MBCCOP does not have the expectation that physicians annually enroll a minimum number of patients.

Consistency scores for each of the strategies were greater than 90% indicating that nearly all of the cases with those strategies achieved high enrollment of minorities to treatment trials. Counterfactual analysis for the CCOPs did not result in further strategies, or further logical reduction of strategies. Coverage scores for overall and individual strategies were low, which is not uncommon with high consistency scores (Ragin, 2008). The coverage score for the CCOP strategy was 0.16; and the coverage scores for each of the MBCCOP strategies are 0.05, 0.06, and 0.01, respectively. Coverage scores indicate the variation in each strategy's ability to explain the outcome of interest. A high coverage score for a strategy indicates that the outcome set is highly explained by this particular strategy; however, the low coverage scores in our results indicate low empirical relevance for the resulting MBCCOP strategies.

In order to assess the sensitivity of our analysis, the anchor points for each of tactics recommended by NCI officials were increased and decreased by 5%, and two additional fsQCA models were run using the revised anchor points to calibrate the study measures. Lowering the anchor points resulted in one additional MBCCOP strategy resulting in high minority enrollment. This potential MBCCOP strategy had a small cadre of enrolling physicians, and a small research staff that does not provide screening and assistance at many enrolling sites. This strategy also had a large trial menu, and strong policies and practices to support minority enrollment; but did

not meet our inclusiveness criteria of having one empirical case. Raising the anchor points by 5% resulted in another CCOP strategy; however it also did not have an empirical case. Sensitivity testing appeared to indicate that the fsQCA model was robust to uncertainties in substantive knowledge of CCOP and MBCCOP tactics.

DISCUSSION

This study focused on identifying the strategies and tactics used by CCOPs and MBCCOPs in order to achieve high enrollment of minorities in clinical treatment trials. Four strategies were identified, including a single strategy for clinical trial organizations that do not provide cancer care for large minority populations; and three strategies for organizations serving large minority populations. Our study did not find any tactics that are logically necessary for high minority enrollment for CCOPs or MBCCOPs. However, it appears that it may be important for CCOPs and MBCCOPs to implement annual training events since the CCOP strategy achieving high minority enrollment includes an annual training event; and two out of the three MBCCOP strategies include an annual training event. Additionally, not implementing an expectation for enrollment may also be a key tactic associated with enhanced participation of minority patients since the CCOP strategy, and each of the MBCCOP strategies do not include an expectation that physicians enroll a minimum number of patients per year. As previously mentioned, this may be due to the various types of organizations that comprise a CCOP or MBCCOP. For example, large research institutions may be more likely to implement an enrollment expectation, and experience greater distrust from minority populations, and therefore not achieve high enrollment of minority patients to treatment trials.

It is not surprising that a CCOP with a substantial amount of resources and strong supportive policies is capable of enrolling high numbers of minority patients to treatment trials.

This offers support for the claim that enrollment of minorities in clinical trials may require more resources to address barriers to participation, but this appears to be the case for organizations that do not serve large minority populations. With regards to specific modifiable supportive policies and practices, our results indicate that it may important for CCOPs to implement annual training events, and an expectation for enrollment among physicians in order to enhance enrollment of minority populations; however, CCOPs may not need to implement a system for recognizing physician enrollment. Our results provide support for results from a survey of CCOP and MBCCOP physicians demonstrating the impact of supportive policies on physician-level enrollment in clinical trials (Jacobs, et. al., 2014); but our results did not find that enrollment recognition is a key tactic for enhancing enrollment of minorities for CCOPs. This difference may be due to predisposed attitudes that CCOP physicians have towards enrollment of patients in clinical trials. For example, CCOP physicians receive intrinsic rewards for enrolling patients in trials, and small tokens of recognition simply may not have a substantial impact on their attitudes towards enrolling minority patients. Additional research focused on tactics that impact CCOP physician attitudes towards minority enrollment might be critical in order to enhance minority participation in trials at organizations that do not serve large minority populations.

Our findings support the claim that MBCCOPs implement a variety of strategies in order to achieve high levels of minority enrollment in treatment trials (McCaskill-Stevens, et. al., 2005), and provide support for ongoing NCI policies that promote the development and funding of MBCCOPs and other research organizations that serve large minority populations. Our findings demonstrate that in order to consistently achieve high levels of minority enrollment, MBCCOPs may particularly benefit from having annual training events, or a large research staff.

These findings support results of a multivariate analysis of organizational characteristics associated with enrollment of blacks to treatment trials that demonstrate a positive net impact of implementing an annual training event, or increasing the number of research staff (Belden, et. al., dissertation chapter 2). In addition to annual training events as a key CCOP tactic for enrolling minorities in treatment trials; two of the MBCCOP strategies resulting in high minority enrollment also included training events suggesting that efforts to improve awareness of clinical trials is an important aspect of enhancing minority participation in treatment trials for both CCOPs and MBCCOPs. Unfortunately, the low empirical relevance of the MBCCOP strategies compels us to caution against a strict interpretation that seeking to increase the number of research staff or annual training events, for example, will result in greater enrollment of minorities in clinical trials. Post-hoc analyses of the empirical cases revealed that having a large research staff resulted in high enrollment for a small, academic-based MBCCOP (3 enrolling sites), located in a region with nearly a 30% minority population. This strategy appears to differ for MBCCOPs in regions with a smaller proportion of minorities (<18%), with two cases demonstrating comparable resources; however, achieving high minority enrollment by remaining focused on a single enrolling location, or serving 6 enrolling sites. Post-hoc analysis of high enrolling CCOP empirical cases suggests that CTOs with substantial resources in regions with minority populations ranging from 15-20% are capable of enrolling large numbers of minority patients in clinical trials (Table 10). For example, four out of the 6 empirical CCOP strategies resulting in high minority enrollment are located in MSAs with less than a 20% minority population. Empirically, it appears that the continued funding of CCOPs in regions with minority populations of approximately 20% may be an equally effective strategy for enhancing minority participation in clinical research as funding “minority-based“ clinical trial organizations.

A further examination of cases was conducted in order to identify examples of CCOP and MBCCOP strategies resulting in high enrollment of minorities in clinical treatment trials (20+ minorities enrolled annually), and are presented in Table 11. The selection of CCOPs and MBCCOPs presented in Table 11 is based on the proportion of minorities enrolled annually to total enrollment in treatment trials using historical data on enrollment extending back to 2005. CCOPs A and B are empirical cases of the "size matters" approach to enrollment, and have large numbers of enrolling physicians, large research staff, large trial menu, and supportive policies and practices. CCOPs C and D achieved high enrollment of minorities with fewer physicians, fewer staff, and small trial menus; but did exhibit strong supportive policies and practices. In the fsQCA analysis, these strategies resulted in high minority enrollment, but did not meet the threshold for consistency (80%). This suggests that these strategies may result in high enrollment of minorities, but do not consistently achieve that outcome. Additional examination of the tactics of CCOPs and MBCCOPs may highlight additional strategies that can be employed to enhance minority enrollment in treatment trials. The MBCCOP strategies presented in Table 11 illustrate the variation in how organizations serving large minority populations enroll high levels of minority patients in treatment trials. For example, MBCCOP A has a large number of enrolling sites with screening and enrollment assistance, and does not have a large trial menu. MBCCOP B has a large research staff, does not have a large trial menu, and is focused on providing screening and enrollment assistance at a small number of enrolling locations. MBCCOP C and D have large physician cadres, with large trial menus, however MBCCOP C has a large number of enrolling sites and a small research staff compared to not many enrolling sites and a large staff for MBCCOP D. Future qualitative research is necessary to understand how the tactics identified in this study, and other tactics may result in high minority enrollment.

A limitation of this study is the possibility that the survey failed to capture tactics with the greatest impact on minority enrollment. For example, this study examined the impact of the number of research staff at each CCOP or MBCCOP on minority enrollment, but research has demonstrated that patient navigators are particularly important in addressing the barriers of minority patients (Ghebre, et. al., 2014; Holmes, et. al. 2012; Paskett, et. al., 2011). Further research is necessary to examine the impact of patient navigators on minority enrollment at institutions that do not serve large minority populations.

Table 5. Fuzzy-set Anchor Points			
	Full Non-membership (CCOP/MBCCOP)	**Crossover (CCOP/MBCCOP)**	**Full Membership (CCOP/MBCCOP)**
Minority enrollment	10/10	16/16	20/20
No. of enrolling physicians	25/12	51/18	100/25
No. of research staff	12/4	16/12	25/15
No. of enrolling sites	4/2	12/4	15/8
No. of screening sites	4/2	12/4	15/8
No. of sites with assistance	4/2	12/4	15/8
No. of available treatment trials	20/10	31/15	50/25

Table 6. CCOP Descriptive Statistics				
	Mean	**SD**	**Minimum**	**Maximum**
Minority enrollment	10	12	0	66
No. of enrolling physicians	45	36	9	209
No. of research staff	16	13	2	80
No. of enrolling sites	14	16	2	87
No. of screening sites	10	14	0	71
No. of sites with assistance	11	14	0	69
No. of available treatment trials	36	16	11	78
Enrollment expectation	34%	-	0	1
Enrollment recognition	60%	-	0	1
Training Events	36%	-	0	1

Table 7. MBCCOP Descriptive Statistics				
	Mean	**SD**	**Minimum**	**Maximum**
Minority enrollment	17	16	0	138
No. of enrolling physicians	20	13	3	62
No. of research staff	10	6	3	30
No. of enrolling sites	5	4	1	16
No. of screening sites	5	4	1	16
No. of sites with assistance	5	4	1	16
No. of available treatment trials	18	10	6	37
Enrollment expectation	27%	-	0	1
Enrollment recognition	20%	-	0	1
Training Events	53%	-	0	1

Table 8. Summary Truth Table for Strategies Resulting in High Minority Enrollment					
Strategy Solution	**Number of CCOPs and MBCCOPs**	**Consistency Value**	**Consistency Threshold**	**F-test**	***P***
mPFSATXE	2	0.937	0.8	7.69	0.007
MpfSATxE	1	0.973	0.8	24.48	0
MpFsatxe	1	0.998	0.8	4353.97	0
MpFsatxE	0	0.975	0.8	34.6	0
MpFsaTxe	0	0.982	0.8	59.05	0
MpFsaTxE	0	0.964	0.8	13.1	0.001
MpFsAtxe	0	0.954	0.8	7.17	0.01
MpFsAtxE	0	0.975	0.8	34.6	0
MpFsATxe	0	0.954	0.8	7.01	0.01
MpFsATxE	0	0.964	0.8	13.1	0.001
MpFSatxe	0	0.954	0.8	7.17	0.01
MpFSatxE	0	0.975	0.8	34.6	0
MpFSaTxe	0	0.954	0.8	7.01	0.01
MpFSaTxE	0	0.964	0.8	13.1	0.001
MpFSAtxe	0	0.954	0.8	7.17	0.01
MpFSAtxE	0	0.996	0.8	1142.84	0
MpFSATxe	0	0.954	0.8	7.01	0.01
MpFSATxE	0	0.996	0.8	981.46	0
MPFsatxe	0	0.977	0.8	31.87	0
MPFsatxE	0	0.972	0.8	26.96	0
MPFsaTxe	0	0.976	0.8	31.54	0
MPFsaTxE	0	0.964	0.8	13.1	0.001
MPFsAtxe	0	0.954	0.8	7.17	0.01
MPFsAtxE	0	0.972	0.8	26.96	0
MPFsATxe	0	0.954	0.8	7.01	0.01
MPFsATxE	0	0.964	0.8	13.1	0.001
MPFSatxe	0	0.954	0.8	7.17	0.01
MPFSatxE	0	0.972	0.8	26.96	0
MPFSaTxe	0	0.954	0.8	7.01	0.01
MPFSaTxE	0	0.964	0.8	13.1	0.001
MPFSAtxe	0	0.954	0.8	7.17	0.01
MPFSAtxE	0	0.996	0.8	1089.68	0
MPFSATxe	0	0.954	0.8	7.01	0.01
MPFSATxE	0	0.996	0.8	981.46	0

NOTE: M = MBCCOP; P = No. Physicians Enrolling; F = No. Research Staff; S = No. Sites with Screening; A = No. Sites with Enrollment Assistance; T = No. Trials Available; X = Enrollment Expectation; E = Training Events.

Table 9. Simplified Strategies for Achieving High Minority Enrollment				
	Strategy			
Tactics	**1**	**2**	**3**	**4**
MBCCOP		X	X	X
Many Physicians Enrolling	X	x		
Large Research Staff	X		X	
Many Screening Sites	X	X	x	
Many Sites with Enrollment Assistance	X	X	x	
Many Trials Available	X			
Enrollment Expectation	X	x	x	x
Enrollment Recognition	X			
Annual Training Event	X	X		X

NOTE: Upper-case X indicates causal condition (tactic) present; lower-case x indicates causal condition absent.
Abbreviation: MBCCOP, Minority-based Community Clinical Oncology organization.

Table 10. Empirical Strategies for Achieving High Minority Enrollment									
	Empirical Strategy								
Tactics	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
MBCCOP	x	x	x	x	x	x	X	X	X
Many Physicians Enrolling	x	X	x	X	X	x	x	x	x
Large Research Staff	x	x	X	X	X	x	X	x	x
Many Screening Sites	x	x	x	X	X	x	x	x	x
Many Sites with Enrollment Assistance	x	x	x	X	X	x	x	x	x
Many Trials Available	x	x	X	X	X	X	x	x	x
Enrollment Expectation	x	X	X	X	X	X	x	x	x
Enrollment Recognition	x	x	X	X	X	x	X	x	x
Annual Training Event	x	x	X	X	X	X	x	X	X
MSA Proportion Minority Population	33%	17%	20%	25%	15%	16%	29%	16%	17%

TABLE 11. Detailed Organizational Characteristics of CCOP/MBCCOPs Achieving High Minority Enrollment in Treatment Trials								
	MBCCOP A	**MBCCOP B**	**MBCCOP C**	**MBCCOP D**	**CCOP A**	**CCOP B**	**CCOP C**	**CCOP D**
Funded	2007	2001	1994	1990	1994	1988	1983	1983
1. Organizational Structure	Research institute, department, or center	Separate, non-profit organization	Hospital Cancer Center	Hospital Cancer Center	Hospital Cancer Center	Separate, non-profit organization	Hospital Cancer Center	Research institute, department, or center
2. Enrollment Minimum	No	No	No	No	Yes	Yes	Yes	No
3. Feedback on Personal Enrollment	No	No	Monthly, Quarterly	Monthly	Annual	Quarterly	No	Monthly
4. Feedback on CCOP Enrollment	Monthly	Monthly	Monthly, Quarterly	Monthly	Quarterly	Quarterly	Monthly	Monthly
5. Recognition for Enrolling Physicians	No	No	No	No	Yes	Yes	No	No
6. Education and Training Events	1	1	0	0	1	1	0	0
7. Disparities Education and Training Events	1	0	0	0	0	0	0	0
8. CCOP PI Input for Opening Clinical Trials	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
9. No. Physicians Enrolling	11	13	47	30	100	193	66	28
10. No. Physicians for whom Charts are Screened	10	13	21	30	100	155	25	14
11. No of Physicians who Receive Routine Assistance with Enrollment	10	10	13	30	100	161	25	14
12. No. of Enrolling Sites	6	1	9	3	56	87	40	4
13. Sites Where Patient Charts are Screened	4	1	6	3	56	71	7	4
14. Sites Where Staff Assist with Enrollment	4	1	6	3	56	69	7	4
15. CCOP Staff Members	5	10	5	30	42	78	8	11
16. No. CCOP Registered Nurses	0	0	3	10	26	42	6	5
17. No. Non-Nurse Clinical Research Associates	4	7	1	9	16	28	1	5
18. No. Staff Members Focused on Control Trials	1	1	0	4	3	14	8	1
19. No. Regulatory Staff Members	1	2	2	4	3	16	1	1
20. No. of Available Treatment Trials	10	6	29	23	61	70	24	28

CHAPTER 4: GEOGRAPHIC ACCESS TO CLINICAL TRIAL ORGANIZATIONS IN THE US

INTRODUCTION

Twenty years since the NIH mandated the inclusion of minorities in NIH funded research, minorities remain disproportionately affected by cancer, and continue to experience substantial barriers to participating in cancer clinical trials when compared with non-Hispanic whites (Chen, et. al., 2014; Durant, et. al., 2014; Newman, et. al., 2008; Stewart, et. al., 2007; Murthy, et. al., 2004; Sateren, et. al., 2002). Systematic reviews of minority participation in clinical research reveal extensive research on patient-level barriers to participation in clinical trials, and research has demonstrated that travel time is a key barrier to minority participation in clinical trials (Durant, et. al., 2014; Holmes JA, et. al., 2012; Ford et. al., 2008; UyBico, et. al., 2007). Improving minority participation in clinical trials suggests the need for clinical trial organizations that are located in close proximity to areas with sizable minority populations (Joseph and Dohan, 2009); however, the associations between travel time to clinical trial organizations (CTOs) and detailed population demographic characteristics (e.g. race/ethnicity, race/ethnicity by urban versus rural areas, and race/ethnicity by region) are currently unknown.

Previous studies have examined geographic disparities in access to specialized cancer care using estimated travel times from Zip Code Tabulation Areas (ZCTAs) to NCI Cancer Centers, academic medical centers, and community-based oncology specialists (Onega, et. al., 2008; Onega, et. al., 2009; Onega, et. al., 2010). These studies specifically examined place accessibility, a measure of spatial separation, versus individual accessibility, which measures

variation in geographic access based on individual characteristics (Shi, et. al., 2012; Kwan, 1998). Results suggested that 69.4% of the US population has less than one hour of travel time to an academic-based cancer care organization, and found the overall median travel time to academic-based cancer care was 30 minutes (Interquartile range, 13-72). In addition to a wide range of travel times, the study also found wide variation by race, regions, and demographic characteristics. Overall, results suggested that rural areas experience substantial disparities in geographic access to CTOs. Black populations had shorter median travel time than whites or Hispanics in urban ZCTAs, but blacks in rural areas experienced greater travel times. The study also found disparities in geographic access to specialized cancer care organizations for Native Americans, and other minority populations residing in rural ZCTAs. Additional research by Onega and colleagues (2010) found that whereas African Americans in urban settings have comparable travel times to cancer care organizations as Caucasians, rural African Americans experience significant disparities in travel time to NCI Cancer Centers, particularly in the South. The majority of specialized cancer care in the US is provided in a community-based setting, and a key limitation of Onega and colleague's analyses was the failure to capture the locations of CCOPs and MBCCOPs, and other organizations offering NCI-sponsored treatment trials, which may lead to erroneous conclusions regarding disparities in geographic access to organizations offering NCI-sponsored clinical trials. Therefore a detailed examination of disparities in geographic access to clinical trial organizations is necessary to address disparities in minority participation in clinical research.

This study employed the network geographic analysis approach employed by Onega and colleagues (2008) with data on organizations participating in the NCI Community Clinical Oncology Program and the American College of Surgeons Commission on Cancer approved

cancer centers in order to estimate median travel times from ZCTAs to the nearest location offering NCI-sponsored clinical treatment trials, and investigate disparities in geographic access to clinical trial organizations (CTOs) for racial and ethnic groups in the continental US. To our knowledge, this is the first study to estimate travel times to organizations offering NCI-sponsored clinical trials for demographic groups in the US.

CLINICAL TRIAL ORGANIZATIONS

NCI Community Clinical Oncology Program (CCOPs and MBCCOPs)

Since 1983, the NCI Community Clinical Oncology Program has implemented over 60 networks of clinical trial organizations in community-based settings across the US (Minasian, et. al., 2010). The Community Clinical Oncology Program is comprised of: (1) NCI's Division of Cancer Prevention providing overall direction and funding, (2) Clinical Research Group Bases and NCI Cancer Centers providing design and development of clinical trials, and (3) the clinical trials organizations enrolling patients. The clinical organizations,' hereafter referred to as "CCOPs" or "MBCCOPs" for CCOPs which specialize in providing cancer care to minority populations, are collaborations between physicians and oncology physicians in academic medical centers, community-based hospitals and private practices. In 2014, 47 CCOPs represent more than 300 hospitals, and more than 3,000 physicians. Additionally, a total of 17 MBCCOPs represent 55 hospitals and approximately 500 physicians. The primary goals of CCOPs and MBCCOPs are engaging physicians in clinical research, disseminating clinical research findings into community practice, and enrolling patients in NCI-sponsored clinical trials. CTOs participating Community Clinical Oncology Program have been very successful, resulting in one-fifth of minority patients enrolled in NCI-sponsored clinical treatment trials (Minasian, et. al., 2010). We included all active hospitals and enrolling sites affiliated with the Community

Clinical Oncology Program located in the continental US in this analysis. We excluded CCOPs and MBCCOPs in Alaska, Hawaii, and Puerto Rico due to the different commuting patterns in those states per Onega and colleagues (2008).

Commission on Cancer Accredited Hospitals (CoC)

Over 70% of newly diagnosed cancer patients are treated annually at more than 1500 Commission on Cancer accredited hospitals in the US. The American College of Surgeons Commission on Cancer grants different categories of accreditation to hospitals in the US. These include Comprehensive Community Cancer Programs, Community Cancer Programs, Academic Comprehensive Cancer Programs, Integrated Network Cancer Programs, Hospital Associate Cancer Programs, Free Standing Cancer Center Programs, and NCI-designated Comprehensive Cancer Centers (NCI Cancer Centers). Hospitals categorized as Comprehensive Community Cancer Programs provide services to 500 or more newly diagnosed cancer patients and offer a range of cancer care services, and enroll or refer patients to clinical trials. Hospitals categorized as Community Cancer Programs annually serve between 100 and 500 newly diagnosed cancer patients with diagnostic and treatment services, and directly enroll or refer patients to clinical trials. Hospitals categorized as Academic Comprehensive Cancer Programs provide medical education, diagnostics and treatment, and enroll or refer patients to clinical trials. Integrated Network Cancer Programs do not have minimum cancer caseloads, but either directly enroll patients to clinical trials, or refer patients to clinical trials at other organizations. Hospital Associate Cancer Programs serve 100 or fewer newly diagnosed cancer patients annually, provide a limited range of cancer care services, and have the option to participate in offering or referring patients to clinical trials. The Free Standing Cancer Center Program includes organizations that are not hospitals, but provide a range of diagnostic and treatment services,

with on-site clinical trials and referrals to other organizations offering clinical trials. NCI-designated Comprehensive Cancer Centers receive peer-reviewed funding, offer a full range of diagnostic and treatment services, and directly enroll patients in clinical trials.

METHODS

Data Sources

Data for this study were obtained from: the US Census, American Community Survey, The US Department of Agriculture Economic Research Service, the American College of Surgeons, the National Cancer Institute website, and NCI Community Clinical Oncology Program Progress Reports. ZCTA shapefiles and geographic data for 2010 were obtained from the US Census. American Community Survey 2008-2012 5-year estimates of racial and ethnic population totals were abstracted and matched to the ZCTAs. Rural Urban Commuting Area Codes data were used to determine the status of each ZCTA as follows: Urban, Suburban, Small Rural Town, Rural and isolated areas. In this analysis, we included all NCI-designated Comprehensive Cancer Centers, and all other CoC organizations with research nurses. Finally, hospitals participating in the Community Clinical Oncology Program were identified from Annual NCI Progress Reports and included in the analysis if operating in 2012.

Data Analysis

Geographic locations for NCI-designated Cancer Centers, hospitals and physician practices participating in the NCI Community Clinical Oncology Program, and Commission on Cancer hospitals in the continental US were converted to latitude/longitude and mapped using BusinessMAP 4.0 software (Environmental Systems Research Institute). These locations were then individually assessed using Google Maps for accuracy. Longitudes and latitudes of population centroids for each zip code tabulation area (ZCTA) were mapped in ArcGIS 10.1

software (Environmental Systems Research Institute) and matched to the demographic characteristics data from the American Community Survey. Per Onega and colleagues (2008), travel times were estimated in ArcView GIS Network Analyst using the closest facility algorithm that establishes unique origin-destination pairs and evaluates the one-way travel time between the origin and the destination (ESRI). This study estimated travel time from each ZCTA in the continental United States to the nearest clinical trial organization based on a major and minor road network that accounted for travel burden with speed limits assigned to road segments. Briefly, this method classified roads into segments and assigned each segment an average travel speed adjusted for rural versus urban status. Per Onega and colleague's study (2008), travel times were calculated for each region with a 250-mile road network buffer. A 250-mile road network buffer is used to estimate ZCTAs with more than four hours of travel time to the nearest CTO. A 4-hour travel time was selected as the threshold at which attendance at a CTO is achievable in 1 day of travel (Onega et. al., 2008). Travel time categories were analyzed at: <30 minutes, 30 minutes to <1 hour, 1 hour to <2 hours, 2 hours to <3 hours, 3 hours to <4 hours, and greater than 4 hours. In order to evaluate demographic characteristics of the US population proximate to CTOs, ACS data was matched to each ZCTA. Finally, Rural-Urban Classification Area data (3.0) was matched to ZCTAs to evaluate urban versus rural travel times to CTOs.

RESULTS

The analysis included 32,961 ZIP codes in the continental US, and a total population of 307,049,317. Our analysis found 429 ZIP codes contained a CCOP or MBCCOP (n = 497, 1.3%). American College of Surgeons Commission on Cancer accredited hospitals are located in 1199 ZIP codes (n =12833, 4.0%). A total of 1509 ZIP codes contained at least one CCOP, MBCCOP, or CoC organization (4.6%). For the total population, geographic access to CTOs appears to be

excellent, and there are few ZCTAs in the continental US where geographic access to any CTO is poor. Overall, results suggest that nearly 95% of the US population resides within one hour of any CTO. Moreover, our analysis did not find a ZCTA centroid more than 4 hours away from any CTO, and less than 1% of the total US population was located more than 3 or more hours from any CTO (Table 11). Median travel times to CTOs for all races and ethnic groups in the study are presented in Table 12. The median travel time to any CTO for the total population is 28 minutes (IQR = 11-40 minutes), 28 minutes for white populations (IQR = 13-41 minutes), 28 minutes for African American population (IQR = 16-37 minutes), 30 minutes for Hispanic populations (IQR = 16-34 minutes), 26 minutes for Asian populations (14-36 minutes), and 27 minutes for Native American population (IQR = 16-30 minutes).

Median travel times by race and RUCA codes are presented in Table 13. Urban populations in the US experience the lowest travel times to any CTO (20.8 minutes), with increasing travel times for suburban populations (34.0 minutes), populations in small rural towns (38.2 minutes), and populations in isolated rural areas (38.8 minutes). Travel times to any CTO for white populations mirror the travel times for the total population in urban (20.8 minutes), suburban (34.0 minutes), rural towns (38.2 minutes), and isolated or rural regions (38.8 minutes). Urban black populations experience greater travel times to any CTO than the total population (23.0 minutes), and similar travel times in suburban regions (33.6 minutes); however, black populations experience lower travel times to any CTO than the total population in rural towns (33.9 minutes) and isolated rural areas (36.6 minutes). Hispanic populations experience the greatest travel time to any CTO in urban areas (25.3 minutes). However, Hispanic populations experience similar travel times as the total population in suburban areas (33.5 minutes), and lower travel times than the total population to any CTO in rural towns (33.6 minutes) and

isolated rural areas (33.6 minutes). Asian populations experience greater travel time to any CTO than the total population in urban areas (24.0 minutes) and suburban areas (35.5 minutes), however, they experience lower travel times in rural towns (35.5 minutes) and isolated rural areas (35.5 minutes). Native American populations experience greater travel times to any CTO than the total population in urban areas (24.0 minutes); but travel times for Native American populations are lower than the total population in suburban (30.1 minutes), rural towns (30.1 minutes), and isolated rural areas (30.1 minutes).

Travel times to any CTO by race and region are presented in Table 14. Travel time for the total population to any CTO is lowest in the Northeast region (22.8 minutes). The median travel time for the total population to any CTO is greater in the South (27.1 minutes), West (29.0 minutes), and Midwest (29.3 minutes). Travel times for white populations mirror the total population in the Northeast region (22.8 minutes), South region (27.1 minutes), West region (29.0 minutes), and Midwest region (29.3 minutes). Black populations experience greater travel time than the total population in the Northeast region (26.7 minutes) and Midwest region (31.3 minutes), similar travel time to the total population in the West region (28.8 minutes); however travel times to any CTO for Black populations are lower in the South than the total population (23.1 minutes). Hispanic populations experience the greatest travel times in the Northeast region (29.5 minutes). However, Hispanic populations experience similar travel times as the total population in the South region (27.5 minutes), lower travel times in the West region (25.7 minutes), and greater travel times in the Midwest region (31.6 minutes). Asian populations experience greater travel times than the total population in the Northeast region (27.3 minutes), South region (29.2 minutes), and Midwest region (33.2 minutes); however, Asian populations experience lower travel times than the total population in the West (25.8 minutes). Native

American populations experience greater travel times to any CTO than the total population in the Northeast (29.3 minutes), lower travel times in the South region (24.5 minutes) and West region (21.6 minutes), and similar travel times to the total population in the Midwest (30.0 minutes).

DISCUSSION

The goal of this study was to examine disparities in geographic access to CTOs offering NCI-sponsored clinical trials for racial/ethnic groups in the continental US. There is currently no standard for travel time to a CTO; however, Congress has set a goal that US populations should live within 200 miles of an NCI Cancer Center (NCI Cancer Bulletin, 2002). Onega and colleagues' study (2008) demonstrated that geographic access to NCI Cancer Centers is adequate for most racial/ethnic populations in the US, and this study demonstrates that overall geographic access to CTOs is excellent for racial/ethnic groups in the US. The median travel time from ZCTA centroids to any CTO for the total US population was 28 minutes, ranging from 11-40 minutes. This compares favorably to Onega and colleagues (2008) study, which found the median travel time from ZCTA centroids to any academic-based cancer care organization was 30 minutes, ranging from 13-72 minutes.

With regards to overall racial/ethnic disparities in geographic access to organizations offering NCI-sponsored treatment trials, this study demonstrates that most ethnic/racial populations in the US reside within 30 minutes or less to the nearest CTO. Overall, our study demonstrates that African American populations in the US experience a similar median travel time to any CTO as the total population (28 minutes). These results differ from Onega and colleagues' study (2008), which demonstrated that the median travel time for all populations to an academic-based cancer care organization is 30 minutes, whereas the median travel time for African Americans to an academic-based cancer care organization is 15 minutes. It is unclear

whether this difference is due to the proximity of academic medical centers to inner city populations as proposed in previous studies (Kahn, et. al., 1994); or findings from Onega and colleagues' study (2010) that a greater proportion of African Americans than Whites live within 30 minutes of academic medical centers (66% vs. 45%). However, data on academic medical centers offering clinical treatment trials were unavailable, and future studies examining geographic access to CTOs using locations of academic medical centers may reveal that African Americans have lower travel times to CTOs than the total population. This study demonstrates that Hispanic populations in the US generally experience the greatest travel time to any CTO. These results differ from Onega and colleague's (2008) study that suggested Native Americans experience the most substantial disparities in geographic access to cancer care organizations; however, this may be due to the lack of CTOs in the Southwestern region of the US, and the extensive reach of CCOP and MBCCOP sites in remote regions in the Midwest where Native American populations are concentrated. Our results suggest that policies are needed to address disparities in geographic access to CTOs for Hispanic populations, particularly in the Southwest regions of the US where Hispanic populations are concentrated, and there are few CTOs. Our analysis supports previous results from Onega and colleagues' study demonstrating that Asian populations experience the least disparities in geographic access, which is likely due to the concentration of Asian populations residing in urban areas (Onega, et. al., 2008).

Onega and colleagues (2008) study demonstrated the importance of urban versus rural place of residence and disparities in geographic access to specialized cancer care organizations. For example, their study found the median travel time to an academic-based care organization for populations dwelling in isolated rural areas was 105 minutes, with an interquartile range from 76-153 minutes. Previous research has demonstrated disparities in geographic access to clinical

trials for urban and rural populations (Baquet, et. al., 2006). However, our study has demonstrated that the efforts of the Community Clinical Oncology Program and the ASCO Commission on Cancer to extend clinical research into community-based settings appears to ameliorate rural versus urban disparities in access to CTOs when compared to geographic access to academic-based cancer care organizations. For example, our study found that all racial/ethnic groups in rural regions appear to reside within a maximum of 50 minutes to a CTO. Unfortunately, whereas our results demonstrate that disparities in place accessibility for rural populations may be less than previously considered, disparities in individual accessibility may be the key factors limiting geographic access to clinical treatment trials for rural dwelling populations.

This study identifies specific regions with disparities in geographic access to CTOs for racial/ethnic groups in the continental US. Our results provide mixed support for Onega and colleagues (2008) contention that disparities in geographic access to cancer care organizations are most prominent in the South. Their analysis included the NCI Cancer Center located at the University of Alabama at Birmingham, but failed to include the locations of CTOs participating in the Southeast Cancer Control Consortium CCOP, the Upstate Carolina CCOP, Greenville CCOP, Atlanta Regional CCOP, Georgia Regents MBCCOP, and the Virginia Commonwealth University MBCCOP. Post-hoc analysis examining point locations of CCOPs, MBCCOPs, and CoC hospitals in the South clearly show a substantial number of CTOs in North Carolina, South Carolina, Georgia, and Louisiana, and the overall lack of cancer care organizations in Alabama and Mississippi. Moreover, examination of all CTOs with 50-mile buffers in the US further highlights small regions with disparities in geographic access in Alabama and Mississippi (Figure 4). These particular areas may be in the greatest need of enhanced, and tailored

organizational efforts to make trials more geographically accessible to all racial and ethnic populations that dwell in the Black Belt and Mississippi Delta regions of the US.

A limitation in using the network geographic methods proposed by Onega and colleagues (2008) is that origin-destination pairs do not always match up perfectly to road networks, which could potentially lead to inaccurate local travel burden and travel times. In those cases (<2%), we used estimates of travel time from Google Maps API. Additionally, there can be substantial variation in different approaches to estimating travel times; and previous research has suggested that predicted travel times might be longer than observed travel times for urban and suburban ZIP codes, and shorter for rural ZIP codes (Bliss, et. al., 2012). However, models evaluating distance between ZCTA centroids and hospitals have been found to be adequate in accurately measuring geographic access (Bliss, et. al., 2012). The strength of this study is that it highlights an approach that can be used in order to examine disparities in geographic access to organizations that provide high-quality, or perhaps even NCI-quality cancer care. Further Research by Onega and colleagues (2010) has demonstrated that African Americans and Caucasians who seek cancer care at National Cancer Institute (NCI) Cancer Centers have no differences in adjusted 1-year mortalities, 3-year all-cause mortalities, and cancer-specific mortalities (Onega, et. al., 2010b). Moreover, previous studies have shown that travel time is a significant predictor of attendance at NCI Cancer Centers; and suggested that wide variations in travel time by race and place of residence contribute to disparities in access and utilization of the most specialized cancer care (Onega, et. al., 2010; Onega, et. al., 2009a; Onega, et. al., 2008). Future studies on disparities in geographic access to high-quality cancer care should consider a network geographic approach using locations of organizations providing high-quality cancer care.

In 2014, the Community Clinical Oncology Program was reorganized into the newly funded NCI Community Research Program (NCORP); however, the goals of offering clinical trials in community settings and reducing disparities remain the same. Unfortunately, the reorganization resulted in the overall reduction of NCI-sponsored CTOs, particularly in the South and Southwestern regions of the US. As previously noted, these regions already experience disparities in geographic access to CTOs, and a reduction in CTOs may exacerbate existing disparities in geographic access to CTOs in the South and Southwest for all racial/ethnic populations residing in those regions. A post-hoc analysis of travel times to the nearest CTOs that excluded MBCCOP enrolling sites demonstrates the impact of MBCCOPs on travel times for racial/ethnic groups in the continental US. MBCCOPs appear to reduce travel times to the nearest CTO for all racial/ethnic groups, and removal of the MBCCOP sites resulted in increased travel times for all racial/ethnic groups in urban, suburban, large towns, and isolated rural areas. Increasing rurality yielded proportionally larger increases in travel times for each racial/ethnic group. In this analysis, Hispanic populations are projected to experience the greatest increases in travel times without MBCCOP enrolling locations. However, the increase in median travel times across urban and rural geographies did not exceed ten minutes; and increases in interquartile ranges did not exceed 15 minutes for any racial/ethnic group.

Results are similar with regards to the impact of excluding MBCCOP enrolling sites on travel times to CTOs for racial/ethnic groups by region. Median travel times increase for ZCTAs in the Northeast, South, West, and Midwest for all racial/ethnic groups, particularly Hispanic populations. However, increases in travel times do not exceed 8 minutes, and interquartile range increases do not exceed 10 minutes. In light of the recent restructuring of NCI's clinical trials infrastructure, additional analyses using geocoded data on recent grantees of NCORP are crucial

in order to ensure that there is no disruption in the previous efforts of NCI's to ameliorate disparities in access to clinical treatment trials. Moreover, additional research focused on investigating disparities in geographic access in small-area regions in the South and Southwest may be more productive for health care systems and regional authorities to improve dissemination of results from cancer research to community-based settings where minority populations seek care.

Figure 3: Travel Times to Clinical Trial Organization from ZCTAs for Racial/Ethnic Groups

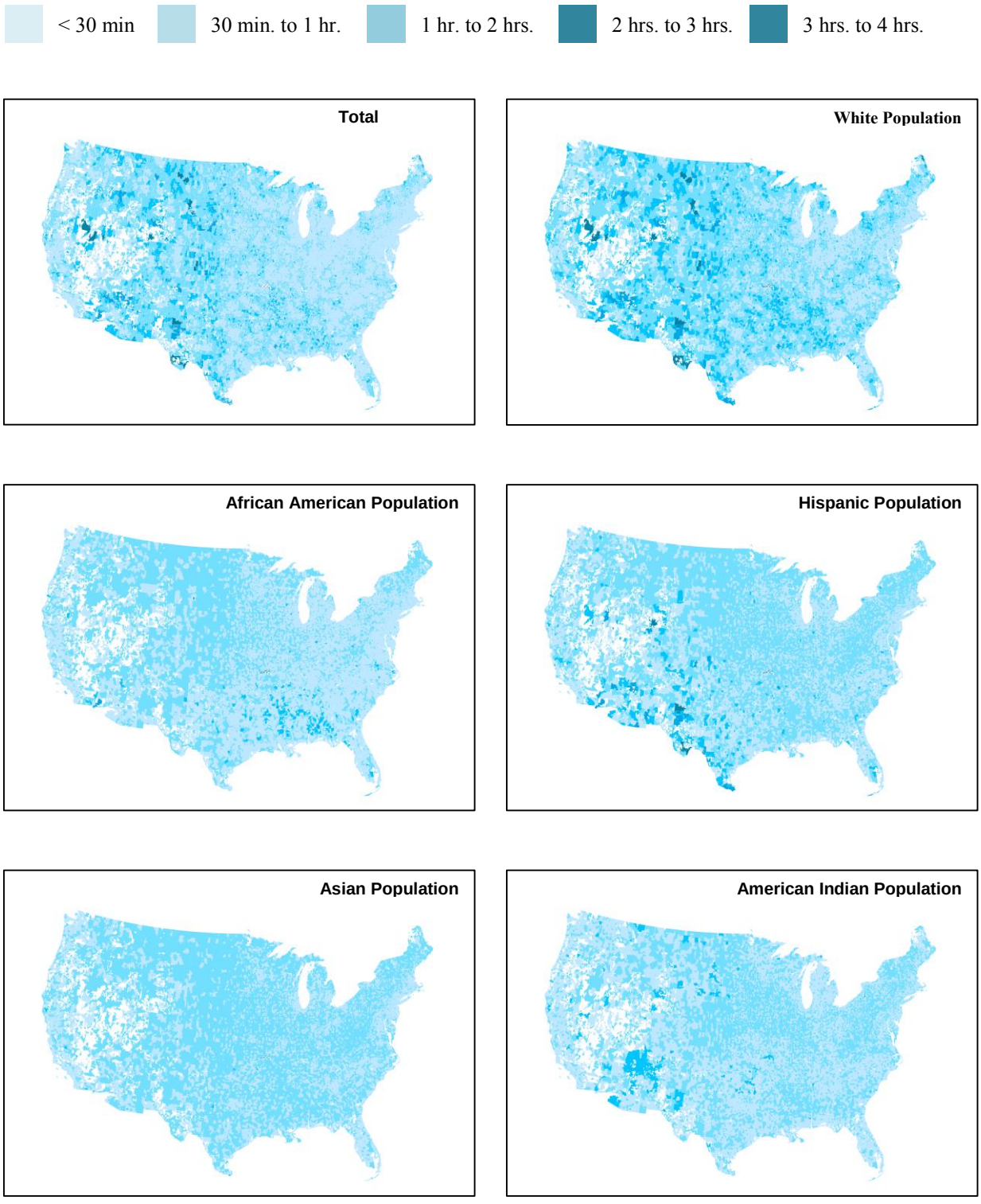


Table 12. Proportion of US Population Across Categories of Travel Time to Nearest CT Organization

	Travel times to clinical trial organization % Population (n=307,049,317)					
	<30 mins	**30-60 mins**	**1-2 hours**	**2-3 hours**	**3-4 hours**	**>4 hours**
CCOP/MBCCOP Hospitals	43.8	15.3	21.8	10.6	4.8	3.8
Commission on Cancer Hospitals*	82.4	10.5	5.1	1.7	0.3	0.0
All Clinical Trial Orgs	84.0	10.3	4.6	0.9	0.2	0.0

* Commission on Cancer hospitals includes CCOPs and MBCCOPs that are also categorized as CoC hospitals.

Table 13. Median Travel Times to Clinical Trial Organizations for the US Population in the Continental US

	Population in Millions (%)	**CCOP/ MBCCOP (IQR)**	**CoC Hospital (IQR)**	**Any CTO (IQR)**
Total Population*	307.04 (100)	71 (43-100)	31 (13-45)	28 (11-40)
White	235.20 (76)	72 (44-99)	30 (15-45)	28 (13-41)
African American	41.86 (14)	72 (56-82)	30 (17-40)	28 (16-37)
Hispanic	50.37 (16)	70 (55-83)	33 (17-36)	30 (16-34)
Asian	16.45 (5)	74 (57-81)	34 (14-39)	26 (14-36)
Native American	4.88 (2)	67 (56-76)	31 (17-32)	27 (16-30)
Urban core	263.01 (85)	50 (50-88)	16 (16-51)	16 (16-51)
Suburban areas	28.05 (9)	50 (50-87)	24 (24-37)	22 (22-32)
Large town areas	9.15 (4)	62 (62-84)	23 (23-51)	21 (21-47)
Isolated/rural areas	6.81 (2)	78 (58-78)	29 (19-55)	29 (19-55)
Northeast	54.89 (18)	63 (63-71)	29 (14-29)	26 (14-26)
Midwest	71.17 (23)	84 (38-84)	23 (23-29)	23 (23-24)
South	110 (36)	62 (62-71)	25 (25-26)	23 (23-25)
West	69.67 (23)	60 (60-84)	25 (25-31)	23 (23-29)

* Total population in racial/ethnic categories exceeds 100% because “Hispanic” is not an exclusive category. Commission on Cancer hospitals includes CCOPs and MBCCOPs that are also categorized as CoC hospitals. Any CTO includes NCI Cancer Centers, CCOPs/MBCCOPs, Academic Medical Centers, and CoC Hospitals.

Table 14. Median Travel Times (IQR) to Any CTO for Racial/Ethnic Groups and RUCA Codes

	Urban	**Suburban**	**Large Town**	**Rural/Isolated**
Total Population	21 (9-35)	34 (24-46)	38 (29-49)	39 (30-49)
White	21 (9-35)	34 (24-46)	39 (29-50)	39 (30-49)
Black	23 (11-34)	27 (20-34)	27 (22-34)	30 (25-35)
Hispanic	25 (11-34)	34 (27-34)	34 (28-34)	34 (30-34)
Asian	24 (9-36)	27 (18-32)	28 (22-32)	32 (28-34)
Native American	24 (13-30)	26 (18-31)	26 (18-31)	30 (24-34)

Table 15. Median Travel Times (IQR) to Any CTO for Racial/Ethnic Groups and RUCA Codes Without MBCCOP Enrolling Locations

	Urban	Suburban	Large Town	Rural/Isolated
Total Population	25 (10-43)	43 (30-57)	48 (36-62)	49 (38-62)
White	25 (10-43)	43 (30-57)	48 (36-62)	49 (38-62)
Black	24 (11-34)	34 (25-41)	33 (27-40)	37 (31-42)
Hispanic	31 (13-42)	42 (34-42)	42 (34-42)	42 (37-42)
Asian	24 (10-37)	33 (23-40)	34 (27-40)	39 (34-41)
Native American	24 (13-34)	33 (22-39)	32 (23-39)	37 (29-41)

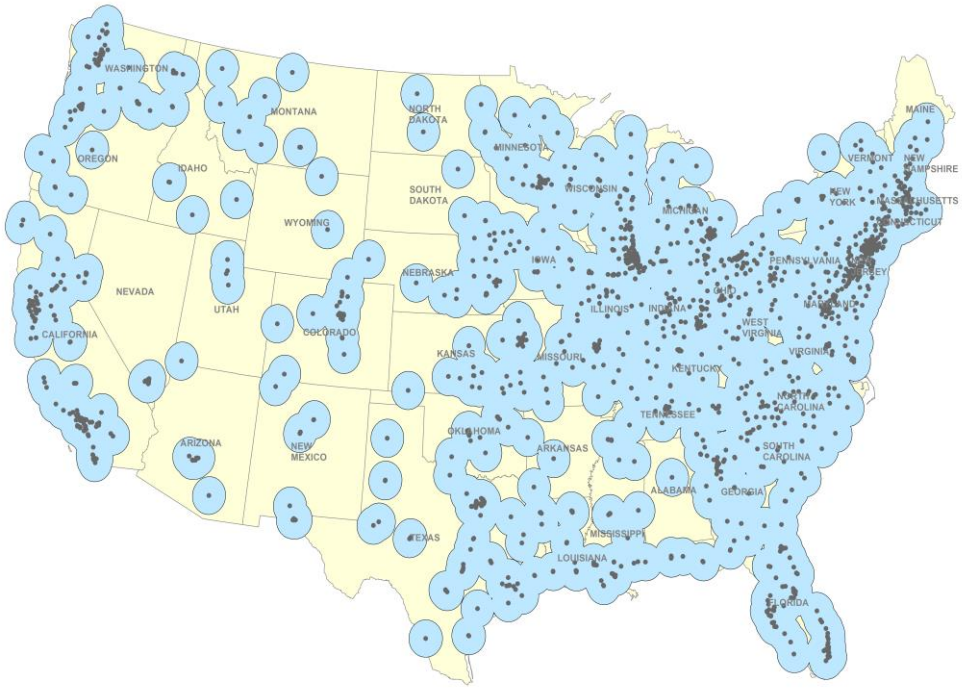
Table 16. Median Travel Times (IQR) to Any CTO for Racial/Ethnic Groups and Regions

	Northeast	South	West	Midwest
Total Population	23 (9-36)	27 (14-41)	29 (11-44)	29 (17-41)
White	23 (9-36)	27 (14-41)	29 (11-44)	29 (17-41)
Black	22 (11-29)	23 (10-28)	21 (10-29)	26 (15-32)
Hispanic	30 (14-34)	27 (14-34)	25 (10-34)	32 (23-34)
Asian	16 (7-28)	18 (9-28)	13 (6-26)	25 (12-32)
Native American	24 (15-30)	20 (11-27)	16 (9-27)	30 (16-31)

Table 17. Median Travel Times (IQR) to Any CTO for Racial/Ethnic Groups and Regions WITHOUT MBCCOP enrolling locations

	Northeast	South	West	Midwest
Total Population	29 (11-45)	34 (16-50)	36 (13-54)	37 (21-51)
White	29 (11-45)	34 (17-50)	37 (13-55)	36 (21-51)
Black	27 (14-36)	25 (13-35)	26 (12-35)	32 (19-39)
Hispanic	36 (18-42)	27 (14-34)	32 (12-42)	39 (29-42)
Asian	20 (8-35)	23 (11-35)	16 (8-33)	31 (15-40)
Native American	30 (19-37)	25 (14-34)	21 (11-34)	31 (19-38)

Figure 4. CTOs in the Continental US with 50-mile Buffers



CHAPTER 5: SUMMARY OF FINDINGS AND IMPLICATIONS FOR POLICY, PRACTICE AND RESEARCH

The National Cancer Institute is currently undergoing a reorganization of its organizational infrastructure. In 2014, the Community Clinical Oncology Program and the Community Cancer Centers program were integrated into the newly funded NCI Community Oncology Research Program (NCORP). The goal of this dissertation was to investigate organizational determinants of minority participation in clinical treatment trials, and findings from the three studies have implications on policy, practice, and research. Results from the multivariate regression analysis in Aim 1 demonstrate that cancer care organizations that serve large minority populations are critical components of the overall strategy of the NCI to reduce disparities in cancer care, and enroll minority populations in clinical treatment trials. Holding other factors fixed, organizations that serve large black populations will enroll an average of 13 blacks to clinical treatment trials ($p < 0.05$). To put this in context, NCI Division of Cancer Prevention officials established that a CCOP or MBCCOP that enrolls twenty minority patients in treatment trials has achieved high enrollment of minorities. Therefore, research organizations that serve large minority populations have the potential to enroll nearly two-thirds of that performance goal, regardless of other organizational characteristics that may promote enrollment in treatment trials.

Aim 1 was the first study to empirically examine the impact of the organizational structure of CCOPs and MBCCOPs on enrollment of blacks to clinical treatment trials. Whereas previous studies of overall enrollment of patients to clinical trials by CCOPs found mixed results

regarding the impact of the number enrolling physicians, available treatment trials, and enrolling sites (Carpenter, et. al., 2012; Carpenter, et. al., 2006), these studies did not include a measure of the number of research staff. Our analysis in Aim 1 included data on the number of research staff, and found by adding that key resource as a variable, the impacts of physicians, trials, and staff were reduced from previous estimates. This finding suggests that previous analyses examining overall enrollment in treatment trials need to be replicated with the inclusion of measures of research staff to enhance our understanding of their impact on overall treatment trial enrollment. Aim 1 also included three additional novel measures of PBRN supportive policies and practices, and found that implementing an enrollment expectation may result in reduced enrollment of blacks in treatment trials ($p < 0.05$). Conversely, recognition for enrollment ($p < 0.10$) and annual training events ($p < 0.05$) are associated with positive and moderate impacts on black enrollment. Finally, Aim 1 also found that managed care penetration has a large and significant impact ($p < 0.01$); a state mandate to cover clinical trials has a moderate and significant impact ($p < 0.05$); and local hospital competition does not appear to be competition at all with a small, yet positive, impact on black enrollment in treatment trials. These findings indicate that whereas organizational characteristics may inhibit or promote enrollment of minorities in treatment trials, environmental characteristics of CCOPs and MBCCOPs are still important factors associated with minority enrollment.

The results from Aim 1 have implications for policy, practice, and research. First, it appears that continued funding of clinical trial organizations dedicated to serving minority populations may make logical sense. Moreover, based on the impact of "hospital competition," NCI officials should consider funding both a CCOP and an MBCCOP in regions where minority populations are concentrated. With regards to practice, it is unfortunate that only three

modifiable organizational characteristics (training events, enrollment recognition, research staff) appear to have a significant impact on black patient enrollment. CCOPs and MBCCOPs should consider organizing annual training events and implementing efforts to recognize physicians for enrolling patients in treatment trials if they are not already doing so. Additionally, MBCCOPs, in particular, need to carefully consider whether a requirement on physicians to enroll patients in treatment trials is necessary and desirable. In practice, it appears that the number of physicians may be less important than the size of the research staff for enrollment of minorities, which suggests that for many research organizations, a small number of physicians may be responsible for enrolling minorities in treatment trials. Moreover, substantially increasing the size of a CCOPs or MBCCOPs may not be feasible due to funding restrictions; therefore, it may be important to consider dedicating specific staff members as patient navigators or peer supporters who are responsible for helping patients overcome burdens to trial participation. Unfortunately, data was unavailable on the existence of patient navigators at CCOPs and MBCCOPs, and it may be that either large, or dedicated, research staff is necessary to enhance minority enrollment. Further research is necessary to elucidate the impact of specific roles research support staff play in making patients aware of clinical trials, giving them the opportunity to participate in trials, and gaining their acceptance when offered participation in a treatment trial.

Results from Aim 2 also have implications for policy, practice, and research. First, results demonstrate that there are multiple logical organizational strategies that result in high enrollment of minorities in treatment trials, and those strategies are comprised of varied organizational design features. Indeed, a key finding for practice and policy from the fuzzy-set qualitative comparative analysis is that a number of CCOP strategies may consistently result in high enrollment of minorities in treatment trials. Not surprisingly, the “size matters” strategies have

substantial resources at their disposal in the conduct of clinical research. However, a large physician cadre may not be sufficient to enroll minorities in trials, whereas supportive policies and practices may be necessary in order for CCOPs to reach their full potential with regards to enrollment of minorities. Policymakers at the NCI that determine funding for CCOPs and MBCCOPs may need to consider the ramifications of locating and funding research organizations with substantial research support. Conversely, the results from the fuzzy-set analysis demonstrate that MBCCOPs may not need as much in the way of resources – except for possibly a large trial menu or supportive policies and practices in order to enroll minorities in clinical treatment trials.

With regards to research implications, Aim 2 has demonstrated that a fuzzy-set qualitative comparative analysis examining 7 organizational tactics with longitudinal data is a feasible approach to investigating complex causality with organizational-level data. This appears to be the case despite a small, or moderate number of observations - in this case, approximately 60 observations each year for three years. Preliminary analyses for Aim 2 included six organizational design features, and four organizational context features; however, none of the strategies in the preliminary analysis met the threshold for consistency (0.80). Future research should continue employing fuzzy-set qualitative comparative analysis, or other set-theoretic methods, in order to evaluate additional organizational strategies with novel organizational context features. Furthermore, after strategies have been logically minimized via Boolean Algebra (e.g. Quine-McCluskey algorithm) and evaluated with set-theoretic parameters-of-fit (e.g. inclusiveness, consistency, and coverage), case study methods can be employed in order to re-examine empirical cases for additional policy and practical needs.

Finally, Aim 3 also has policy, practice, and research implications. The key finding from Aim 3 is the demonstrated overall lack of disparities in geographic access to clinical trials organizations. The finding that the regions with the most concentrated disparities in geographic access to clinical trial organizations are the US Southwest, Mississippi Delta, and Black Belt is not particularly surprising. These regions have large rural areas, and high concentrations of minority populations. Additionally, spatial analysis of the maps of ZIP code tabulation areas and travel times to clinical trial organizations by race reveals that the most widespread disparities in geographic access to clinical trials organizations are for white and Hispanic populations. The policy implications of these findings are straightforward. In order to reduce or eliminate disparities in geographic access to clinical trial organizations, a targeted approach may be preferred over a blanket call from NCI for proposals for implementing clinical trial organizations in regions where minorities reside. In addition to the targeted approach, additional geospatial research can focus on identifying the regions where white and Hispanic populations reside with long travel times. In lieu of creating a new clinical trial organization, that information may be used by existing clinical trial organizations to seek partner physicians and organizations to address the disparities.

Future Directions

Our results indicate that funding CTOs serving large minority populations can be an effective approach to enhancing the participation of minorities in clinical research. However, over half of the MBCCOPs in our sample failed to meet overall enrollment targets. Findings demonstrate that CTOs that do not serve large minority populations can also enhance minority participation in clinical trials. NCORP may wish to consider an approach of implementing CTOs located in regions with moderate or large minority populations, with

particular attention to hiring research staff dedicated to enhancing minority participation, and opening treatment trials appropriate for minority populations. Indeed, only five MBCCOPs attained the anchor point of 20 minorities enrolled to treatment trials proposed by officials at the NCI Division of Cancer Prevention, whereas nine CCOPs enrolled 20 twenty or more minorities to treatment trials from 2010-2012. CTOs may implement training or outreach events, recognize the efforts of physicians to enroll patients, and increase their number of research staff in order to enhance minority enrollment in treatment trials, regardless of whether it serves a large minority population. For example, the Delaware/Christiana CCOP in Newark, Delaware, implements monthly training events, provides recognition for enrolling physicians, and has a large research staff consistently enrolling more than 20 minority patients to trials annually. Notably, the Delaware/Christiana CCOP provides multiple forms of recognition for physician enrollment, including: authorship on publications, plaques, and gift certificates, which is a substantial amount of recognition compared with other CCOPs. Other organizational strategies employed by CTOs may also be effective in enhancing minority participation in trials, and future research is necessary to understand additional strategies that can be implemented to improve minority participation in treatment trials.

The research contained in this dissertation provides the backdrop for further studies in organizational determinants of minority participation in clinical trials. First, results from Aims 1 and 2 of this dissertation lay the groundwork for further empirical investigations of organizational strategies resulting in enhanced participation of minorities in clinical treatment trials. Additional organizational design features can be drawn from the 2011 CCOP Administrators Survey, and novel geographic measures will be developed from further spatial analysis of each CCOP or MBCCOP and employed in future fuzzy-set qualitative comparative

analyses. Second, results from Aim 3 suggest that there are few regions in the continental US with disparities in geographic access to clinical trial organizations. Future spatial analyses will focus on disparities in geographic access to clinical trials organizations in smaller, detailed regions – such as the Deep South or the Southwestern portion of the US. Finally, the geographic information system developed in this dissertation provides a foundation for further studies on disparities in geographic access to high-quality cancer care in the continental US. In order to accomplish this, a refined approach to evaluating which cancer care organizations in the US offer high-quality cancer care services must be harnessed. The American Society of Clinical Oncology developed the Quality Oncology Practice Initiative to assess the quality of oncology practices in the US, which may be adapted to evaluate geographic disparities in access to high-quality cancer care organizations.

APPENDIX

Table 18. Chapter 2: Bivariate Relationships Between Variables

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)
(1) Black enrollment	1.00																		
(2) No. Training events	0.14	1.00																	
(3) No. Enrolling sites	0.21	0.08	1.00																
(4) No. Enrolling physicians	0.49	0.14	0.52	1.00															
(5) Enrollment expectation	0.21	0.13	0.15	0.19	1.00														
(6) Enrollment recognition	0.00	0.04	0.17	0.14	0.05	1.00													
(7) No. Trials available	0.23	0.23	0.53	0.46	0.28	0.44	1.00												
(8) MBCCOP	0.12	-0.06	-0.31	-0.32	-0.10	-0.43	-0.47	1.00											
(9) No. Research staff	0.58	0.23	0.48	0.69	0.29	0.27	0.64	-0.22	1.00										
(10) MSA Black population	0.25	0.05	-0.24	-0.06	0.00	-0.32	-0.38	0.37	-0.21	1.00									
(11) MSA Black HS graduates	-0.01	-0.04	0.10	0.26	0.05	0.08	0.07	-0.05	0.01	-0.02	1.00								
(12) MSA Black uninsured	0.01	0.06	0.13	0.05	0.15	0.06	0.06	0.19	0.00	0.17	-0.11	1.00							
(13) MSA Black unemployed	-0.07	0.25	-0.13	-0.07	0.17	-0.01	0.19	-0.32	0.11	-0.08	0.18	-0.10	1.00						
(14) MSA Black family income	0.12	-0.04	0.12	0.06	0.01	0.12	0.25	0.41	-0.13	0.48	-0.50	0.11	-0.57	1.00					
(15) Hospital competition	-0.34	0.10	-0.11	-0.04	0.12	-0.11	0.14	-0.20	0.02	-0.74	0.02	-0.23	0.03	-0.32	1.00				
(16) State HMO penetration	0.08	0.00	0.16	0.05	0.01	0.06	0.16	0.10	0.17	0.33	-0.01	0.58	0.06	-0.31	-0.27	1.00			
(17) Insurance mandate	0.13	0.15	-0.05	0.23	0.07	0.07	0.20	-0.02	0.17	0.35	-0.08	0.06	0.11	-0.18	-0.34	0.04	1.00		
(18) MSA Black population X MBCCOP	-0.11	0.00	-0.25	-0.26	-0.21	-0.31	-0.38	0.62	-0.18	0.76	-0.01	-0.20	-0.12	-0.37	-0.59	-0.23	-0.35	1.00	
(19) MSA Black education X MSA Black unemployment	-0.06	0.26	-0.15	-0.13	-0.19	-0.01	-0.17	-0.32	-0.11	-0.06	-0.04	-0.07	-0.97	-0.46	-0.01	-0.06	-0.09	-0.12	1.00

Table 19. Regression Results: Impact of Environmental Factors on Enrollment of Blacks in Cancer Clinical Treatment Trials
(MODEL WITHOUT ORG FACTORS)

Variable	Marginal Effects	Standard Error♯	*P*-value	95% Confidence Interval	
MSA Black Population (1000s)	0.001	0.001	0.603	-0.002	0.003
MSA Proportion Black High School Graduates	26.056	21.871	0.234	-16.811	68.923
MSA Proportion Black Uninsured	-7.025	28.699	0.807	-63.273	49.224
MSA Proportion Black Unemployed	41.137	25.921	0.113	-9.668	91.942
Hospital Competition	0.206***	0.039	0.000	0.130	0.282
State Managed Care Penetration	-4.785	11.391	0.674	-27.111	17.540
State Insurance Coverage Mandate	5.709***	1.297	0.000	3.167	8.251
Northeast	-0.583	2.344	0.803	-5.178	4.011
South	8.965***	2.523	0.000	4.019	13.910
West	-2.964*	1.611	0.066	-6.121	0.193
Midwest	-	-	-	-	-
2010	-	-	-	-	-
2011	-1.022	1.023	0.318	-3.028	0.983
2012	-1.233	1.129	0.275	-3.447	0.980

n = 172

Pseudo R2 = 0.0895; BIC = 1094.49

* $p < 0.10$; ** $p < 0.05$; *** $p < 0.01$

Bootstrapped Standard Errors (2000 replications)

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