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**UNDERSTANDING ELEMENTS INVOLVED IN ACTIVE RACIAL AND ETHNIC
MINORITY RECRUITMENT PRACTICES FOR BIOPHARMACEUTICAL-
SPONSORED CLINICAL TRIALS:
A SOCIO-ECOLOGICAL QUALITATIVE INQUIRY**

BY

Rebecca Rae Johnson

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Deborah DeLuca, M.S., JD

Submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy (PhD) in Health Sciences

Seton Hall University

2020

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SETON HALL UNIVERSITY
School of Health and Medical Sciences

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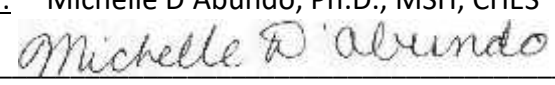
Doctoral Candidate, **Rebecca Rae Johnson**, has successfully defended and made required modifications to the text of the doctoral dissertation for the **Ph.D.** during the **Spring Semester 2020**.

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2020

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ABSTRACT

**UNDERSTANDING ELEMENTS INVOLVED IN ACTIVE RACIAL AND ETHNIC
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SPONSORED CLINICAL TRIALS:
A SOCIO-ECOLOGICAL QUALITATIVE INQUIRY**

by

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Seton Hall University

2020

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Inequitable participation in clinical trials continues to be a problem, and trial populations do not always reflect the demographics of the population that the investigational product will ultimately be treating. Because genetic differences between racial and ethnic groups affect the safety and efficacy of new treatments, it is important that standard of care decisions are made based on a representative population. The purpose of this study is to understand the socio-ecological elements that are involved in the active implementation of racial and ethnic minority recruitment practices for biopharmaceutical-funded trials in the United States. This general qualitative study was both descriptive and exploratory in nature and utilized semi-structured, in-depth interviews for data collection. The socio-ecological model was utilized as the conceptual framework guiding this study (McLeroy, Bibeau, Stecker, & Glanz, 1988). The interview guide was designed to explore the perceptions, practices and experiences of 15 clinical research site professionals related to recruiting racially and ethnically diverse trial participants. Data analysis

utilized a coding process in which data were coded inductively. Codes were classified according to the socio-ecological model. Following data analysis, 20 themes emerged from information pertaining to the actual implementation of minority recruitment practices. These 20 themes represent each level of the socio-ecological model and provide explanations for intrapersonal, interpersonal, organizational, community and policy components. A holistic view that facilitates a comprehensive understanding of effective minority recruitment practices is offered after considering the interaction of the components at all levels of the socio-ecological model. These multi-faceted findings reveal that an ecological perspective offers insight into improving access to clinical trials by focusing on environmental change initiatives, rather than individual change on a patient level. This study's findings offer practical guidance for the implementation of change initiatives in minority recruitment practices at research sites. The results of this study demonstrate that environmental change can provide a premise for improving access to clinical trials among minority populations.

Chapter I

INTRODUCTION

Currently, racial and ethnic minority populations are underrepresented as participants in most clinical trials (CISCRP, 2017; Diehl et al., 2011; Duda et al., 2011; Killien et al., 2000; Martin, Negron, Balbierz, Bickell, & Howell, 2013; Murthy, Krumholz, & Gross, 2004; The Society for Women's Health Research & FDA, 2011). Aggravated by the fact that health disparities also disproportionately affect racial and ethnic minorities (USHHS, Centers for Disease Control and Prevention [CDC], 2011a; USHHS, CDC, 2011b), clinical trial results need to be generalizable to a wider population that includes racial and ethnic minority groups, women, and the elderly. To gain insight into improving health outcomes, it is imperative to have equal representation of all members of the applicable population subgroups represented in clinical trials. Many known barriers to minority recruitment into clinical trials contribute to this problem, yet successful strategies used in biopharmaceutical-sponsored trials to address those barriers are not documented in the literature. Additionally, it is important to understand how research site staff and organizational characteristics may play a role in the successful recruitment of these underrepresented populations. The purpose of this study is to explore the involvement of physical and social environmental elements when investigator sites actively focus on minority recruitment when conducting biopharmaceutical sponsored clinical trials.

Background of the Problem

Researchers conduct clinical trials to improve the standard of care for diseases and survival rates and health outcomes in patients. These trials are designed to evaluate the safety and efficacy of new therapies and to provide scientific evidence in support of decisions health care practitioners must make about the care of all affected patients. This includes how new

therapies may affect women and members of various minority groups differently. Demographic profiles of clinical trial participants need to be representative of the disease prevalence in order for the results to be generalized to demographic subgroups (Diehl et al., 2011; Duda et al., 2011; USHHS, NIH, 2001; USHHS, NHLBI, 2011). In particular, it is important to test the efficacy and safety of potential new therapies across all racial and ethnic groups since genetic differences occur amongst various demographic populations. This leads to variations in drug metabolism and toxicity within different racial and ethnic groups (Hershman et al., 2003; Rotger, Csajaka, & Telenti, 2006). For example, while angiotensin-converting enzyme (ACE) inhibitors have been found to be effective in decreasing blood pressure in both African American and white patients with hypertension, African Americans respond less well than white patients to such treatments (Cohn et al., 2004). The first race-specific drug, BiDil[®] (isosorbide dinitrate and hydralazine hydrochloride), was approved by the Food and Drug Administration (FDA) in 2005 for the treatment of heart failure in African American patients when added to standard therapy. When analyzing data from clinical trials, researchers determined that African American and white patients had a different response to BiDil, with a treatment effect apparent in African American patients only (Brody & Hunt, 2006; Temple & Stockbridge, 2007). Additionally, a clinical trial examining the use of gefitinib in non-small-cell lung cancer was conducted. The investigators found through racial and ethnic molecular profiling that gefitinib works better than the standard of care in the treatment of patients with a specific mutation that occurs more frequently in Asian populations (Chen, Lara, Dang, Paterniti, & Kelly, 2014; Mok et al., 2009; Paez et al., 2004). Therefore, it is imperative that there is adequate participation in clinical trials of patients from racial and ethnic minorities so treatment effects are tested outside of adult white males, who represent the majority of clinical trial participants (CISCRP, 2017; Killien et al., 2000; The

Society for Women's Health Research & FDA, 2011). More diverse representation in clinical trials ensures that study results can be of benefit to a wider population through the use of evidence-based medicine.

Contributing to the problem.

Drug development process. Several factors contribute to the lack of diversity in clinical trial participation. One probable contributor is the lengthy drug development process and the cost of bringing a drug to market (USHHS, OIG, 2000). The drug development process takes approximately 10 to 15 years from discovery through development (PhRMA, 2016, April). The average cost for each successful drug that goes to market is approximately \$2.6 billion dollars (DiMasi, Grabowski, & Hansen, 2016). The drug development process is highly regulated. It begins with a discovery process where scientists choose a molecule to target a disease, find a drug candidate and conduct extensive laboratory tests and studies on animals to determine if the potential drug is safe to test in humans. This discovery process typically takes between 3 and 6 years. If during the discovery process the researchers deem the drug safe and effective for testing in humans, the drug manufacturer must file an Investigational New Drug (IND) application with the FDA and submit their proposed clinical trial to the Institutional Review Board (IRB). Once approval is received, the manufacturer can then begin testing the safety and efficacy of the drug on humans through clinical trials (PhRMA, 2016, April). The drug must be tested in three phases of clinical trials before the manufacturer is able to submit a New Drug Application (NDA) to the FDA requesting approval to market the drug. During the Phase I clinical trial, researchers determine the safety, pharmacokinetics and pharmacodynamics of the drug in a small group (typically less than 100) of healthy volunteers. If researchers deem the drug safe for humans, they then conduct a Phase II trial. Researchers administer the drug to a group of 100 to 500

patients with the disease or condition for which the drug is being developed and gather additional safety data, examine side effects, determine the dosing strength, as well as determine if the drug is working by the expected mechanism of action. If the administration of the drug results in improvements in the condition or disease, the drug is then tested with a larger group of people with the disease (1,000 to 5,000 patients) to obtain statistically significant data about the safety, efficacy, and benefit versus risk of use of the drug. The three phases of clinical trials generally take 6 to 7 years for completion. Once the trials are complete and the drug is determined safe and effective for use in humans, the manufacturer submits an NDA to the FDA. The FDA takes between 6 months and 2 years to review the preclinical and clinical findings, proposed labeling, and manufacturing plans before they approve the drug for use in patients. Oftentimes, the FDA requires manufacturers to conduct Phase IV studies to evaluate long-term safety or to determine how the drug affects a certain subgroup of patients (PhRMA, 2016, April; USHHS, NIH, 2013a).

Clinical trials play a key role in bringing new drugs to market (USHHS, OIG, 2000). Several trends in the biopharmaceutical industry are contributing to the need for completing clinical trials in the shortest time possible. There's been an increase in pharmaceutical manufacturer's research and development (R&D) activities. Combined with the lengthy and costly drug development process, biopharmaceutical manufacturers need to get their drugs to market quickly. Delays in clinical trial completion result in delays in getting the product to market. Every day that a drug is delayed in getting to market results in more than \$1.4 million dollars of potential loss in future sales (assuming projected annual sales of \$500 million). Further, clinical trial delays increase the cost of clinical development (IMS Health, 2012; Kermani & Bonacossa, 2003; USHHS, OIG, 2000). One of the critical factors in delaying clinical trials is not being able to recruit the necessary number of appropriate participants within

the study timeframe. As a result, 80% of trials are delayed due to difficulties in enrollment (Clinical Trial Arena, 2012; IOM, 2012). For example, recruitment goals were not met in time for the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), resulting in the need to double the amount of investigator sites and extend the recruitment period 1½ years and the follow-up period by an additional year in order to achieve sufficient power (Pressel et al., 2001). Furthermore, half of all research sites under-perform and only enroll between 0 and 1 patients: 20% fail to enroll a single patient and another 30% fewer patients than expected. Overall, the majority of patients (70%) are enrolled by only 30% of research sites (Clinical Trials Arena; 2012; IOM, 2012; PhRMA, 2015 March). As a result, sponsors are looking for rapid recruitment and gauge a site's recruitment ability during the site-selection process to find investigator sites that are high performers and will recruit patients quickly (USHHS, OIG, 2000). This results in a focus on rapid enrollment and not the prioritization of enrolling study participants in proportion with the disease prevalence being studied.

Policy and regulation on clinical trial enrollment. Another factor contributing to the problem of underrepresentation of minorities in clinical trials is related to policy. In an effort to address this challenge, the National Institutes of Health (NIH), the largest government funding body for clinical trials, instituted the Revitalization Act of 1993, which mandates the inclusion of women and minority participants in clinical trials supported or funded by the NIH. As part of this policy, the NIH is obligated to conduct or support outreach programs to recruit women and members of minority groups as participants in clinical research (USHHS, NIH, 2001). The NIH's National Heart, Lung, and Blood Institute (NHLBI) further requires investigators to recruit minorities in the study population in the same proportions as in the U.S. population having the

disease entity being studied. When the prevalence of the disease being studied is unknown, the NHLBI mandates that minority groups be represented in proportions equal to their representation in the total U.S. population. However, the NHLBI does allow principal investigators (PIs) seeking funding to justify why they have planned for limited diversity when these mandates are not met (USHHS, NHLBI, 2011). It is also important to note that the majority of government-funded trials are epidemiologic and behavioral studies and are not designed to test investigational treatments (Getz, 2010). Although the NIH has established a policy to enforce diverse representation in clinical trials supported or funded by the NIH, this policy does not apply to industry-sponsored studies. The majority of clinical trial sponsors provide details on the demographic profiles of the participants in their NDAs, but the FDA has recently recognized improvements are still needed and enacted the Food and Drug Administration Safety and Innovation Act (FDASIA) in 2012. Section 907 of the FDASIA, “Reporting of Inclusion of Demographic Subgroups in Clinical Trial and Data Analysis in Applications for Drugs, Biological Products, and Devices,” sets forth requirements for reporting to Congress the extent to which clinical trial participation by demographic subgroups, including sex, age, race, and ethnicity, is included in NDAs that are submitted to the FDA. Section 907 of the FDASIA also requires an analysis of the extent to which the inclusion of safety and effectiveness data by demographic subgroups is included in product labeling (Food and Drug Administration Safety and Innovation Act, 2012). The FDA has developed an action plan as part of the FDASIA to be rolled out over the next several years in an attempt to encourage diverse participation in biomedical research (USHHS, FDA, 2014). While the efforts of “The FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data” encourage inclusion of minorities in clinical trial research, it is not mandated, though it includes an initiative to improve

the availability and transparency of reporting to the public the demographic composition by subgroup in clinical trials for FDA-approved medical products (USHHS, FDA, 2014). Since 2015, this information is publically available in the Center for Drug Evaluation and Research's (CDER's) Drug Trial Snapshots Summary Report (USHHS, FDA, 2019). Unfortunately, post-hoc subgroup analyses conducted on clinical trial data to ascertain differential responses to an investigational medication based on race typically cannot be conducted because the sample size of the minority participants is often too low to achieve adequate power (Cooper & Psaty, 2005). The FDA's August 2013 report, "Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved Medical Products," includes an analysis of demographic subgroup data provided in NDAs during 2011. The report noted that while approximately half of the applications included race subset data in labeling, only a few included efficacy and safety subset analyses. Furthermore, the analysis of subgroup data reveals that racial subgroups are underrepresented and race composition is not always consistent with disease prevalence in the US population. For example, while more than 13% of African American adults has diabetes, only 2% of study participants in the type 2 diabetes mellitus (T2DM) studies included in the report are African American. Similar to the findings by Cooper and Psaty (2005), the inclusion of patient subgroup data did not provide sufficient data for meaningful analysis or to detect effects in different subgroups because of low sample size limitations (USHHS, FDA, 2013; USHHS, FDA, 2014). These findings also are confirmed by a literature review conducted by Chen, Lara, Dang, Paterniti, and Kelly (2014). Chen et al. (2014) found that between 1.5% and 57% of clinical trial publications report their study sample by race and ethnicity; however, a much lower percentage include an analysis of results by racial or ethnic subgroups.

Recent public policy initiatives encourage inclusion of racially and ethnically diverse populations in industry-funded clinical trials. In 2016, the FDA issued guidance for industry for the “Collection of Race and Ethnicity Data in Clinical Trials.” Within this guidance, the FDA states their expectations that “sponsors enroll participants who reflect the demographics for clinically relevant populations with regard to age, gender, race and ethnicity. A plan to address inclusion of clinically relevant subpopulations should be submitted for discussion to the Agency at the earliest phase of development and, for drugs and biologics, no later than the end of the phase 2 meeting” (USHHS, FDA, 2016, p. 3). For clarity, this guidance by the FDA does not issue a mandate but does provide expectations regarding trial enrollment. In addition, in fulfillment of a stipulation within the FDA Reauthorization Act of 2017 (FDARA) regarding expanded access, in 2019 the FDA issued draft guidance for industry, “Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs.” The primary focus of this guidance is to broaden eligibility criteria in clinical trials to better reflect the population most likely to receive the drug. For example, patients with concomitant illnesses generally are excluded from participation based on the inclusion and exclusion criteria set forth by the researchers (USHHS, FDA, 2019 June).

Statement of the Problem

Despite efforts of the NIH Revitalization Act of 1993 (2001) and FDASIA (2012), disparities exist in clinical trial participation with African Americans, Asian Americans and Hispanic/Latino Americans underrepresented in most studies (Chen, Lara, Dang, Paterniti, & Kelly, 2014; CISCRP, 2017; Diehl et al., 2011; Duda et al., 2011; Martin, Negron, Balbierz, Bickell, & Howell, 2013; The Society for Women’s Health Research & FDA, 2011). Historically, both non-minority and minority women have been underrepresented in clinical

research studies (Bennett, 1993; Killien et al., 2000; Murthy, Krumholz, & Gross, 2004). This is a significant problem because minority women are disproportionately affected by disease (USHHS, NIH, NCI, 2019; USHHS, Healthy People 2020, 2014). Participation disparities are evident in both government-funded and industry-funded trials. The literature varies with regards to minority participation in government-funded clinical trials. Some sources indicate that overall minority enrollment in NIH-funded studies is closely proportional to the US population (CISCRP, 2017; NIH, 2013c; The Society for Women's Health Research & FDA, 2011). In fact, the NIH (2013c) reports that 36% of minorities were enrolled in government-funded clinical research in 2012. According to the US Census Bureau (2012), minorities represented 37% of the US population at that time. However, there are also several examples of government-funded trials in which minorities are underrepresented, despite the fact that the majority of NHLBI PIs with active studies believe it is important to include racial and ethnic minority groups as participants in their research (Corbie-Smith, Durant, & St. George, 2006). For example, in 2005, Fisher et al. (2005) conducted a government-funded trial to assess the effect of tamoxifen as a preventive therapy for breast cancer in 13,388 patients. Of these patients, 96.5% of the participants were white, whereas only 3.5% were African American or an unspecified minority. Furthermore, in a 2004, Murthy, Krumholz, and Gross (2004) conducted a clinical trial that analyzed enrollment in National Cancer Institute (NCI)-funded trials. They concluded that fewer Hispanics and African Americans participate in cancer clinical trials as compared with the percentage of cancer incidence among those populations in the United States. This is further confirmed by a 2010 Institute of Medicine (IOM) report, which stated that almost 90% of clinical trial participants enrolled into publically funded NCI clinical trials prior to 2006 were white when comparing enrollment by race. Furthermore, 8% of the NCI trial participants were African

American and less than 3% were Asian American (IOM, 2010). Enrollment by ethnicity prior to 2006 was 94.4% non-Hispanic white and 5.6% Hispanic. Enrollment of minority populations into NCI clinical trials improved slightly in 2013 with 25% minority participation, yet these trials are still falling short of enrollment that is representative of the US population (National Academies of Sciences, Engineering, and Medicine, 2016). Chen et al. (2014) also found that only 1% of NCI-sponsored clinical trials focus primarily on racial or ethnic minority populations. Instead, the focus is placed on cancer types and not the populations who are disproportionately affected by those cancers.

Racial and ethnic minorities are underrepresented in most industry-sponsored studies, as well. For example, in a 2006 study sponsored by the pharmaceutical manufacturer GlaxoSmithKline comparing the efficacy of different treatments in recently diagnosed type 2 diabetes patients, 88% of the trial participants were white. Yet, more than 13% of African American adults as well as 13% of Hispanic adults are diagnosed with diabetes (Viberti et al., 2006; USHHS, CDC, 2020). Additionally, according to the 2019 CDER Drug Trial Snapshots Summary Report in which 48 newly approved drugs were reviewed, 72% of the trial participants on average were white. Of note, these were global trials and only 40% of the demographic data is based on US participation (USHHS, FDA, 2019). Overall, 83% of domestic industry-funded trial participants are non-Hispanic white, considerably greater than the proportion of the US population that they represent (CISCRP, 2017; The Society for Women's Health Research & FDA, 2011; US Census Bureau, 2012). Speakers participating in the "Dialogues on Diversifying Clinical Trials" workshop convened by the Society for Women's Health Research and the FDA (2011) highlighted the under-representation of minorities in clinical trials. Clinical trials have representation from 1% of the Hispanic population, yet 16% of the US population was Hispanic

at that time. African Americans comprise 5% of clinical trial participants, much less than the 12% of the US population they represented at the time (Coakley et al., 2012; The Society for Women's Health Research & FDA, 2011). Asian Americans are also underrepresented in clinical trials. Kwiatkowski, Coe, Bailar, and Swanson (2013) conducted a systematic review of both federally funded and industry funded clinical trials and reported that among the cancer treatment clinical trials that reported on race and ethnicity between 2001 and 2010, 3% of trial participants were Asian American. This is a dramatic increase from 1990-2000 when only 0.04% of cancer treatment trial participants were Asian American, yet, according to the US Census Bureau (2019), 6% of the US population is Asian. These facts indicate that clinical trial participation is not representative of the US population or the prevalence of the disease being studied.

The biopharmaceutical industry is currently the largest funder of drug R&D, and as of 2008, accounted for 90% of all spending on clinical trial testing of investigational drugs and devices in the United States (Getz, 2010; PhRMA, 2016 April). Members of Pharmaceutical Researchers and Manufacturers of America (PhRMA) alone invested nearly \$80 billion in R&D in 2018 (PhRMA, 2019). Since 2006, there has been a 43% increase in industry-sponsored trials, while at the same time a 24% decrease in NIH-funded studies (Ehrhardt, Appel, & Meinert, 2015; Johns Hopkins Bloomberg School of Public Health, 2015). Industry researchers conducted more than 6,000 clinical trials in the United States in 2013, whereas the NIH provided funding for just over 1,000 trials that same year (Ehrhardt, Appel, & Meinert, 2015; PhRMA, 2015 March; USHHS, NIH, 2018, June). Therefore, a significant majority of clinical trials are sponsored by the biopharmaceutical industry and, as such, investigators are not mandated to

include participation from diverse populations. Accordingly, this study addresses the underrepresentation of racial and ethnic minority populations enrolled in clinical trials sponsored by the biopharmaceutical industry.

Purpose of the Study

While the underrepresentation of racial and ethnic minority participants in industry-funded clinical trials is a problem, historically, there have been occasions of successful enrollment of diverse populations. Notably, NitroMed, Inc., a privately held pharmaceutical company that is no longer in existence (businesswire, 2008; Mitchell et al., 2011), successfully enrolled 1,050 African American participants into their African American Heart Failure Trial (A-HeFT). The participating sites actively recruited only African Americans. However, the specific recruitment strategies leading to the successful recruitment of this minority group are not discussed in the literature, nor are details on recruitment strategies related to any other industry-related trial recruiting minority participants discussed in the literature. The purpose of this study is to understand the socio-ecological elements that are involved in the active implementation of racial and ethnic minority recruitment practices for biopharmaceutical-funded trials in the United States.

Conceptual Framework

A conceptual framework to view phenomena enables a systematic exploration of situations in order to better understand and explain the dynamics of events (USHHS, NIH, NCI, 2005). The conceptual framework used as a lens for this study is the socio-ecological model (McLeroy, Bibeau, Stecker, & Glanz, 1988). Describing the study of an organization as a system helps to better understand the applicability of the socio-ecological model for this study. Aristotle claimed that “the whole was more than the sum of its parts” and that knowledge is derived from

understanding of “the whole.” This worldview laid the foundation for the organization of general systems theory by Ludwig von Bertalanffy in which he recognized that investigating single parts and processes cannot provide a complete explanation of phenomena. Rather, the ensemble of the components and the relations existing between their interactions must be understood in order to derive the properties and modes of action of higher levels from their components (von Bertalanffy, 1950; von Bertalanffy, 1972).

Systems can be defined as either open or closed. In an open system, there is an inflow and outflow of energy to the environment, resulting in a change to the components. An open system moves towards a steady state through the continuous inflow and outflow of energy with the environment. In contrast, there is no energy exchange from the environment in closed systems and eventually a state of equilibrium is reached. The biggest difference between open and closed systems is characterized by the concept of equifinality. In an open system, an end state can be reached by many potential means, meaning that similar results can be achieved with different initial conditions and in different ways. Whereas closed systems cannot behave equifinally because the final state of the system is dependent on the initial components, which lead to the same final result (Katz & Kahn, 1978; von Bertalanffy, 1950).

General systems theory initially was applied to biology but now extends to several other disciplines, including social sciences. The principles of general systems theory apply to all systems, defined as “a set of elements standing in interrelation among them and with the environment” (von Bertalanffy, 1972, p. 417). Systems can be distinguished as being real, conceptual or abstract. From a social science perspective, organizations are considered systems (Foster –Fishman, Nowell, & Yang, 2007; Katz & Kahn, 1978). Organizations are categorized as real systems, that is, entities that can be inferred by observation and exist independently of an

observer. However, many of the interactions between the component elements of the environmental landscape that the organization is part of are conceptual constructs. General systems theory provides a way of seeing this organized whole through the dynamic interaction of multiple factors, which von Bertalanffy suggests were previously overlooked (1950, 1972). In fact, according to open systems theory, environmental influences are necessary social system components. Therefore, to understand an organization, its environmental influences must also be considered (Katz & Kahn, 1978).

A system can be viewed as a hierarchy composed of the system itself, components of the system (subsystems) and the larger system surrounding the system (supra-system). Each level of the system is influenced by and influences other parts of the system within the hierarchy. When using a systems perspective, it is up to the researcher to define the hierarchy of systems, considered to be the “whole,” including the relationship between the system, subsystems and supra-system (Benko & Sarvimaki, 2000). When using a systems perspective, real-world complexities are viewed as whole entities embedded in context. Thinking holistically of a system as a whole with both interconnected and interdependent parts is essential with systems theory because a change in one part leads to changes in other parts and the system itself. As such, a system as a whole cannot be understood by isolating different parts of the system. Instead, synthetic thinking is used to better understand the interactions of its parts, not the actions of its parts taken separately (Patton, 2002). This allows for simultaneous analyses of relationships on and between different system levels (Benko & Sarvimaki, 2000). The context for human actions in organizations can be examined and better understood using a systems perspective, since a system change is necessary to change an individual within the system.

A system needs to be understood in its natural ecosystem, considering the ecological, cultural, political, economic and policy environments of which the system is a part.

Organizations are social systems that consist of the patterned activities of individuals and should be studied in the context of their environment relations, both the social and physical environment within the organization, as well as the environment the organization is a part of (Katz & Kahn, 1978; McLaren & Hawe, 2005; Patton, 2002). An ecological perspective includes a comprehensive context of the environment, including physical, social, cultural and historical aspects, as well as the attributes and behaviors of people within this environment. Social ecology offers a perspective for understanding these interrelations, stressing the multiple dimensions, levels and complexity of situations within the corresponding environment. Specifically, a socio-ecological model uses systems thinking in trying to understand the interacting and interdependent elements that form a whole (McLaren & Hawe, 2004; Stokols, 1992).

A socio-ecological model is a conceptual framework that focuses on the interrelationships between individuals and their social and physical environment under the premise that behavior is both affected by and affects the environmental system of which it is a part. The ecological environment is a nested arrangement of structures that can affect and be affected by individual and organizational behavior at multiple levels (Bronfenner, 1977; McLeroy, Bibeau, Stecker, & Glanz, 1988; Trickett, 2009). These levels of influence are (McLeroy et al., 1988):

1. Intrapersonal factors: characteristics of an individual such as knowledge, attitudes, behavior, self-concept and skills
2. Interpersonal factors: social network and social support systems, including family, friends and work group

3. Organizational factors: social institutions with organizational characteristics and rules and regulations for operation
4. Community factors: relationships among organizations, institutions and informal networks within defined boundaries, including face-to-face primary groups to which an individual belongs. This includes family, social networks, churches and neighborhoods, all of which may be sources of social identity and influence the community's norms and values, as well as individual beliefs and attitudes. This also includes relationships among organizations as a means to influence community awareness
5. Public policy: local, state, and national laws, policies and procedures

Application of a socio-ecological model. Grounds for using a socio-ecological model have been made for developing effective health promotion programs for overcoming public health problems. Most public health challenges are too complex to be understood using a single level of analysis and, therefore, require a comprehensive approach that includes individual, organizational, cultural, community and regulatory levels (Stokols, 1996). Historically, the socio-ecological model has been used for understanding individual behavior in an effort to develop behavior change interventions targeted at individuals and delivered through health promotion programs (ACHA, 2016; Baert, Gorus, Calleeuw, DeBacker, & Bautmans, 2016; Daley et al., 2011; Holt, Rung, Leon, Firestein, & Krousel-Wood, 2014; Mahadevan et al., 2014; McLeroy, Bibeau, Stecker, & Glanz, 1988; Sword, 1999). Applications of the socio-ecological model also have been documented in the clinical trial literature, primarily as a framework for identifying and addressing barriers to and facilitators of clinical trial participation (Chakrapani, Newman, Singhal, Jerajani, & Shunmugam, 2012; Elder et al., 2007; Frew et al., 2014; Salihu, Wilson, King, Marty, & Whiteman, 2015; Wallington et al., 2016; Wells & Zebrack, 2008).

Healthy People 2020 recognizes that the interrelationships between biological, social, economic and environmental factors influence the ability of individuals and communities to progress towards the achievement of meeting the objectives set forth for eliminating health disparities (USHHS, Healthy People 2020, 2020b).

Much of the wide application of the socio-ecological model used for developing health promotion programs focuses on analyzing behavior change strategies on an individual level in an effort to change individuals (Stokols, 1992). However, human behavior is influenced by the environmental system of which it is a part. Instead of focusing on individual behavior change, the focus should be on changing the social and physical environment that reinforces unhealthy behaviors; therefore, change may be needed at the organizational and environmental levels (McLeroy, Bibeau, Stecker, & Glanz, 1988; Stokols, 1992). Accordingly, the socio-ecological model also is used to create health promotion initiatives that focus on changing the environmental system in order to create an environment that promotes healthy behavior (Glanz & Mullis, 1988; Monahan & Scheirer, 1988; Moore, Murphy, Tapper, & Moore, 2010). One such program strived to create opportunities for the general population to follow a healthy diet. While the goal of the program initiatives was population health, the researchers used an environmental approach to target the multiple levels of an ecological model that would impact population access to following a healthy diet, rather than targeting individual behavioral factors (Glanz & Mullis, 1988). Moore, Murphy, Tapper, and Moore (2010) investigated how the availability of food at lunchtime in primary schools was influenced by different socio-ecological levels, including national policy, Local Education Authority policy, priorities and practices of catering staff within each school, as well as the social interactions between the catering staff and children. Interviews were held at an organizational level with the Local Education Authority and

primary school catering managers to better understand influencers at multiple levels of the socio-ecological framework. Monahan and Scheirer (1988) also used a social ecological approach to demonstrate that by considering a multitude of factors and sources of influence at different levels, state health department dental offices could successfully act as linking agents in the adoption of a fluoride mouth rinse program at an organizational level (public schools).

Improving population health by implementing health promotion programs through the influence of social and environmental changes acting synergistically at multiple levels of a socio-ecological framework provides a premise for exploring ways to promote participation of minorities into clinical trials using socio-ecological elements. Hawe, Shiell and Riley (2009) suggested that a public health prevention program be viewed as an intervention within the ecological system in which it was introduced. In doing so, the intervention should be viewed in the context of the setting in which it was introduced (Hawe, Shiell & Riley, 2009). Glanz and Mullis (1988), Moore, Murphy, Tapper, and Moore (2010) and Monahan and Scheirer (1988) all shared an alternative approach to improving population health by understanding the multiple levels of influence that impact providing access to the intervention. Similar to the approaches described in the literature by these authors, the socio-ecological model could guide a better understanding of the elements involved in overcoming the problem of underrepresentation of minorities in clinical trials. Specifically, if we view minority recruitment practices as a health promotion intervention to improve minority access to participate in clinical trials, clinical research staff could be viewed as the linking agent providing the vehicle for increasing minority participation. The socio-ecological model could then be used to explore how the behavior and practices of individuals involved in clinical research who actively recruit minority participants into clinical trials are influenced by and influence environmental elements. This would offer a

better understanding of the contextual factors that promote an environment inviting clinical trial participation among minorities. Understanding the multiple levels of influencers on the successful implementation of minority recruitment practices would help researchers provide opportunities for minority populations to participate in clinical trials in the future by increasing access to trials.

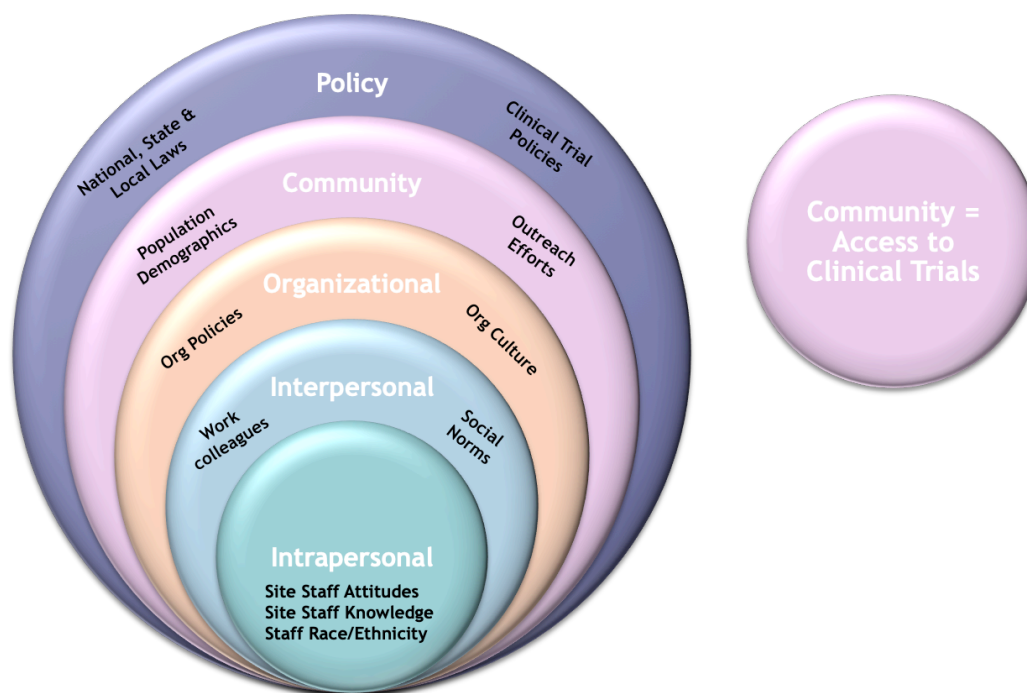


Figure 1. Application of a socio-ecological model when viewing minority recruitment practices as a health promotion intervention. Adapted from McLeroy, Bibeau, Steckler, & Glanz, 1988.

Using a socio-ecological model to explore from a provider perspective the interrelationships between individuals who are involved in clinical research and who actively recruit minority participants and environmental elements specific to recruiting minority participants into clinical trials will help frame an approach to increase minority participation. In literature reviewed, no studies were found that explored minority participation in clinical trials

using a socio-ecological model from a provider perspective. Delivery of care from the service provider viewpoint is determined by multiple factors operating within the socio-ecological framework. Healthcare utilization is understood more wholly when utilizing a socio-ecological approach (Daley et al., 2011; Sword, 1999). We can assume from this that similar to understanding delivery of care from a service provider perspective, we can also understand minority recruitment from a service provider perspective under the realm of a socio-ecological model.

Research Question

There is one overarching research question guiding this study:

What are the socio-ecological elements that are involved in the active implementation of racial and ethnic minority recruitment practices for biopharmaceutical-funded trials in the United States?

Utilizing the socio-ecological model as a framework, the five sub-questions address different components of the model to support the overarching research question:

1. How are **intrapersonal** site staff elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?
2. How are **interpersonal** site staff elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?
3. How are **organizational** elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?

4. How are **community** elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?
5. How are **policy** elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?

Significance of the Study

The minority population residing in the United States is continually growing, and, in fact, minorities are expected to be in the majority by 2044. Additionally, the Hispanic population is expected to grow from 17% of the population in 2014 to 29% of the population by 2060. Meanwhile, the non-Hispanic white population is projected to drop from 62% in 2014 to 44% by 2060. The African American population is expected to grow from 13% in 2014 to 14% by 2060 and the Asian population will nearly double; it is projected to grow from 5% in 2014 to 9% of the US population by 2060 (US Census Bureau, 2015). Based on these projections, the composition of the US population is drastically changing and, if these projections hold true, we will have two main population groups in 2060 (Hispanic and non-Hispanic white).

The *Healthy People 2020* goals include achieving health equity, eliminating disparities, and improving the health of all population groups (USHHS, Healthy People 2020, 2020b). Despite the goals of Healthy People 2020 and other such initiatives, health disparities still exist and disproportionately affect members of racial and ethnic minority populations. In fact, minorities have the highest rates of incidence and mortality of chronic disease (USHHS, CDC, 2009), and minority women are disproportionately affected by disease (USHHS, CDC, 2011a). According to the Racial and Ethnic Approaches to Community Health across the U.S. (REACH U.S.) Risk Factor Survey results, residents of minority communities have a lower socioeconomic status, more barriers to healthcare access, and greater risks for and burden of diseases compared

with the general populations living in non-minority communities (USHHS, CDC, 2011a). Health disparities among minority populations not only apply to differences in disease prevalence, but also to the severity and rate of progression of disease (Ejiogu et al., 2011; USHHS, CDC, 2013a). Several examples of disease-specific healthcare disparities include:

- *Healthy People 2020* includes objectives to reduce the prevalence of hypertension among adults to 26.9% and increase blood pressure control among adults with hypertension to 64.1% (USHHS, Healthy People 2020, 2020c). However, the rate of controlled blood pressure is lower among Hispanics (34.4%) and non-Hispanic blacks (42.5%) than non-Hispanic whites (52.6%) (USHHS, CDC, 2013a).
- When looking at coronary heart disease (CHD), the *Morbidity and Mortality Weekly Report (MMWR)* reported that death rates from CHD and stroke are declining, but there are still disparities in the rate of death from these events in racial and ethnic groups (USHHS, CDC, 2013a).
- Cardiovascular disease (CVD) is the leading cause of death in the United States and non-Hispanic black adults are at least 50% more likely to die prematurely of stroke or heart disease than non-Hispanic whites (USHHS, CDC, 2013a).
- Adult diabetes is also higher among Hispanic and non-Hispanic blacks than among non-Hispanic whites. (USHHS, CDC, 2013a). For example, more than 13% of Hispanic adults in the United States have type 2 diabetes, compared with 7.9% of non-Hispanic white adults (USHHS, CDC, 2020).

- Older blacks and Hispanics are disproportionately more likely to have Alzheimer's disease than whites. In fact, older blacks are twice as likely and older Hispanics are one and one half times as likely than older whites to suffer from the disease (Alzheimer's Association, 2020).
- Overall cancer incidence is highest among African Americans compared with all other racial and ethnic groups, and the death rate from cancer is higher for African Americans than for whites. The higher incidence and death rates of cancer among African Americans (and Hispanics) can be contributed to lack of medical coverage, unequal access to healthcare services and cancer treatments, lower socioeconomic status and barriers to screening (USHHS, NIH, NCI, 2019).
 - Although the incidence rate of breast cancer is similar in African American and white women, African American women are most likely to die from the disease (USHHS, NIH, NCI, 2019).
 - American Indian/Alaska Native and Hispanic women experience the highest cervical cancer incidence rates, yet African American women have the highest death rates from cervical cancer compared with all other racial and ethnic groups (USHHS, NIH, NCI, 2019).
 - Similarly, due to genetic factors, African American men are more than twice as likely than white men to die from prostate cancer (USHHS, NIH, NCI, 2019).
 - African American men have the highest incidence and death rates for lung cancer (USHHS, NIH, NCI, 2019).

Not only do health disparities cause greater risk for disease, disparities in healthcare access and quality create an additional cost burden on the system. According to a study by the Joint Center for Political and Economic Studies, “eliminating health inequalities for minorities would have reduced indirect costs associated with illness and premature death by more than \$1 trillion between 2003 and 2006...and reduced direct medical care expenditures by \$229.4 billion for the years 2003 to 2006 ” (LaVeist, Gaskin, & Richard, 2009).

Despite the fact that the United States has a growing minority population that faces a disproportionate rate of healthcare disparities, minority populations are significantly underrepresented in industry-funded clinical trials. As previously discussed, 83% of industry-funded clinical trial participants are non-Hispanic white, leading to a pool of trial participants who are not representative of the US population or the disease being studied (Bennett, 1993; CISCRP, 2017; Coakley et al., 2012; Cooper & Psaty, 2005; Diehl et al., 2011; Duda et al., 2011; Killien et al., 2000; Martin, Negron, Balbierz, Bickell, & Howell, 2013; Murthy, Krumholz, & Gross, 2004; The Society for Women’s Health Research & FDA, 2011; USHHS, FDA, 2013; USHHS, FDA, 2014; US Census Bureau, 2015). One reason leading to this problem is that 90% of clinical trial funding testing investigational medicines and devices in the United States is through industry and, as such, a significant majority of clinical trials do not mandate diverse participation (Getz, 2010; PhRMA, 2016 April; USHHS, FDA, 2014).

This is especially important with the implementation of the Affordable Care Act (ACA). It was expected that many of the 46 million previously uninsured nonelderly Americans would have access to healthcare and prescription medicines as a result of the ACA, a majority of which were expected to be minority populations, especially Hispanics (The Henry J. Kaiser Family Foundation [KFF], 2013a; KFF, 2013b; KFF, 2019). In 2010 when the ACA was signed into

law, approximately 50 million nonelderly Hispanics were residing in the United States. Prior to the ACA, 33% of nonelderly Hispanic individuals did not have health insurance, making this group of more than 15 million people the highest uninsured minority racial or ethnic group within the United States (KFF, 2020). It was expected that the majority of these uninsured individuals and families would have access to healthcare as a result of the ACA (KFF, 2013a). As of 2016, over 19 million uninsured people gained coverage under the ACA. There was a greater decline in the uninsured rate among African Americans and Hispanics than among whites (KFF, 2019). The result is that minorities increasingly have access to prescription medications primarily tested on adult white males (Killien et al., 2000). While significant progress has been made, there are still healthcare coverage disparities. According to the Kaiser Family Foundation (2020), 19% of nonelderly Hispanics and 11.5% of nonelderly African Americans remain uninsured, compared with 7.5% of nonelderly whites.

Given the growing minority population in the United States, coupled with the disproportionate rate of lack of healthcare access and healthcare disparities, it is important to understand how new medications may affect various populations. The current rate of minority participation in clinical trials does not allow for understanding genetic differences in treatment (Cooper & Psaty, 2005; USHHS, FDA, 2013; USHHS, FDA, 2014; Hershman et al., 2003; Rotger, Csajaka, & Telenti, 2006). There are differences in drug metabolism and toxicity in diverse racial and ethnic groups (Brody & Hunt, 2006; Cohn et al., 2004; Hershman et al., 2003; Rotger, Csajaka, & Telenti, 2006; Temple & Stockbridge). Therefore, there is an unmet need for evidence-based treatments that are relevant for all applicable populations.

In summary, public health is “the science and art of promoting health, preventing disease and prolonging life through the organized efforts of society.” This includes creating supportive

environments for health (WHO, 1998). Sallis, Bauman, & Pratt (1998) recommend environmental and policy interventions based on ecological models as a potential means to influence health behavior at a population level. Using the socio-ecological model to structure public health behavior change initiatives targeting the environmental system in order to create an environment that promotes healthy behavior have proven successful (Glanz & Mullis, 1988; Monahan & Scheirer, 1988; Moore, Murphy, Tapper, & Moore, 2010).

To achieve the *Healthy People 2020* goals of eliminating health disparities, several objectives need to be met. One *Healthy People 2020* imperative is to improve access to quality healthcare services, by increasing the proportion of people who receive appropriate evidence-based clinical preventive services (USHHS, Healthy People 2020, 2020d). Without testing medications on those who ultimately will be prescribed them creates a dilemma in that minority populations are not receiving quality healthcare or evidence-based services when genetic differences in drug metabolism are not accounted for. A lack of a diverse representation in industry-funded trials means that minority populations need to be better represented (USHHS, FDA, 2014). Given the disparities in minority enrollment into industry-funded trials, it is clear that industry just has not been able to address this need appropriately. Examples in the literature of successful recruitment of minorities into NIH-funded studies, which will be discussed in the next chapter, provide optimism that parity in trial participation can be achieved. Obtaining perspectives from industry-funded clinical research staff members who specifically focus on recruiting minorities will provide other researchers with guidance for accruing minority participants. Therefore, this study will address this significant health problem of underrepresentation of minorities in clinical trials by facilitating a better understanding of elements involved with actively recruiting minority participants into industry-funded clinical

trials. Additionally, this study will provide unique insights from published studies that relate to minority recruitment factors of success involving NIH-funded trials. To the researcher's knowledge, there is no published peer-reviewed data on successful minority recruitment strategies involving industry-sponsored trials.

Operational Definitions

The following definitions are important to understanding this study:

1. Health disparity is defined as “a particular type of health difference that is closely linked with social, economic and/or environmental disadvantage. Health disparities adversely affect groups of people who have systematically experienced greater obstacles to health based on their racial or ethnic group; religion; socioeconomic status; gender; age; mental health; cognitive, sensory, or physical disability; sexual orientation or gender identity; geographic location; or other characteristics historically linked to discrimination or exclusion” (USHHS, Healthy People 2020, 2020a).
2. Minority is defined as a race and ethnicity other than non-Hispanic white (United States Census Bureau, 2011).
3. “Hispanic” or “Latino” refers to “a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin regardless of race” (United States Census Bureau, 2011).
4. Informed consent is defined as a “person’s voluntary agreement, based upon adequate knowledge and understanding, to participate in human subjects research or undergo a medical procedure” (USHHS, NIH, 2013b).

5. Health literacy is defined as “the degree to which an individual has the capacity to obtain, communicate, process and understand basic health information and services to make appropriate health decisions” (USHHS, CDC, 2019).
6. Betancourt, Green, Carrillo and Ananeh-Firempong (2003) define cultural competence in health care as “understanding the importance of social and cultural influences on patients’ health beliefs and behaviors; considering how these factors interact at multiple levels of the health care delivery system; and, finally, devising interventions that take these issues into account to assure quality health care delivery to diverse patient populations.” Specific to research centers, “cultural competence requires that they have a defined set of values and principles and demonstrate policies, structures, practices, behaviors and attitudes that enable them to work effectively cross-culturally” (Wallington et al., 2016).
7. Clinical trial is defined as “a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.” Biomedical clinical trials of an experimental drug, treatment, device or behavioral intervention may proceed through four phases:
 - **Phase I.** Investigators test a new biomedical intervention in a small group of [healthy volunteers] (e.g., 20-80) for the first time to determine efficacy and evaluate safety (e.g., determine a safe dosage range and identify side effects).
 - **Phase II.** Investigators study the biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and further evaluate safety.

- **Phase III.** Investigators determine efficacy of the biomedical or behavioral intervention in large groups of people (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions, as well as monitor adverse effects and collect information that will allow the interventions to be used safely.
 - **Phase IV.** These studies are conducted after the intervention has been marketed and are designed to monitor the effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use (USHHS, NIH, 2013a).
8. Principal Investigator (PI) is defined as the individual who is responsible and accountable for conducting the clinical trial. The PI assumes responsibility for analyzing the research data and reporting results (USHHS, NCI, n.d.).
 9. Study Coordinator is defined as a specialized research professional who supports, facilitates and coordinates the daily clinical trial activities under the direction of the PI (Washington University in St. Louis, 2009).
 10. US biopharmaceutical industry: companies engaged in researching, developing, manufacturing and marketing drugs and biologics for human or veterinary use. Both pharmaceutical and biopharmaceutical manufacturers are classified as biopharmaceutical companies (United States Department of Commerce, 2016; United States Department of Commerce, 2020).

11. Health promotion: “the process of enabling people to increase control over, and to improve their health,” (World Health Organization [WHO], 1998); health promotion is further defined by WHO, indicating that it moves beyond the focus on individual behavior towards a wide range of social and environmental interventions.

Chapter II

LITERATURE REVIEW

Findings from the literature search demonstrate that recruiting a representative number of racial and ethnic minority participants into clinical trials continues to be a challenge, especially in biopharmaceutical-sponsored trials (Baquet, Commiskey, Mullins, & Mishra, 2006; CISCRP, 2017; Diehl et al., 2011; Duda et al., 2011; Killien et al., 2000; Mak, Law, Alvidrez, & Perez-Stable, 2007; Martin, Negron, Balbierz, Bickell, & Howell, 2013; Murthy, Krumholz, & Gross, 2004; Simon et al., 2004; The Society for Women's Health Research & FDA, 2011). Furthermore, literature discussing minority recruitment from the perspective of industry-funded trials is not available, further contributing to the uniqueness of this study and the need to share experiences of those industry researchers who are contributing to minority recruitment with the wider research community. Several themes emerged from the literature related to clinical trial recruitment trends that further explain the disparities in minority participation and the gaps in the literature that this study is addressing. A discussion on the findings from the literature review follows.

Clinical Trial Recruitment Themes

Clinical trial recruitment disparities. Minorities are not informed of clinical trials or asked to participate as often as whites (Baquet, Commiskey, Mullins, & Mishra, 2006; Simon et al., 2004). For example, in an analysis comparing independent predictors of clinical trial recruitment between respondents who identified themselves as being either African American or white, Baquet et al. (2006) found that African Americans were significantly less likely to be recruited to a clinical trial than their white counterparts. Simon et al. (2004) had similar findings. They found that African American breast cancer patients were half as likely to be offered a

clinical trial compared with their white American counterparts (21% and 42%, respectively), and only 22% of minority women from other racial groups were offered participation. In their analysis, the researchers found that the most common reasons for not being offered clinical trial participation were PIs' perceptions that they were "likely to be ineligible," "lack of available protocols for disease stage," and "concern about compliance." African American patients were more likely to be considered ineligible than white or other race patients (61% and 53%, respectively). The most frequent reasons cited by investigators for why African American patients were considered likely to be ineligible and not offered a trial were poor performance status and inadequate organ function, whereas white and other race patients were considered ineligible because of prior or current treatment, or they were seeking a second opinion only. Adams-Campbell et al. (2004) also found that a major reason for excluding African American patients from cancer clinical trials was because of existing comorbidities. All of the five patients listed by Simon et al. (2004) who were not offered enrollment in a trial because the PI considered them likely to be non-compliant were African American.

The largest magnitude of cancer burden disparities is among racial and ethnic minority populations (USHHS, NIH, NCI, 2019). In an analysis conducted by Diehl et al. (2011), the researchers found that studies for early-stage cancers were less likely to recruit African American and Hispanic American participants. For example, African American and Hispanic Americans in an early-stage breast cancer study comprised less than 10% of participants. Two advanced-stage breast cancer studies, however, included larger proportions of African American and Hispanic American participants (15% and 28%). This suggests a disparity in cancer screening and early detection efforts in minority populations, which ultimately decreases the

number of minorities who are considered eligible to participate in studies with early-stage disease inclusion criteria (Diehl et al., 2011).

While most clinical trial result publications do not specify enrollment by race and ethnicity, of those that do, the majority do not offer enrollment to minority populations. Oftentimes, these recruitment disparities lead to a misdirected conclusion that racial and ethnic minorities are less willing to participate in clinical trials. For example, Wendler et al. (2006) analyzed consent rates by race and ethnicity of those individuals who were actually invited to participate in a coronary artery surgery study that enrolled 99% non-Hispanic white patients and 1% minority patients. Although only 1% of the clinical trial participants were minority patients, individuals from minority groups actually agreed to participate at a significantly higher rate than non-Hispanic white patients who were asked to participate.

Clinical trial participation disparities. Baquet, Commiskey, Mullins, and Mishra (2006) utilized telephone interviewing to determine attitudes, awareness, and knowledge of clinical trials, as well as examine predictors of clinical trial recruitment and participation for adults residing in Maryland's underserved geographic areas. The researchers conducted an analysis that compared respondents who self-identified their race as either African American or white who were recruited into clinical trials. They looked at nine factors considered as enabling factors to clinical trial participation, including reimbursement, insurance coverage, transportation, childcare, greater knowledge, time constraints, anonymity, follow-up care and additional medical care. For most of these enabling factors, they found that African Americans were less likely than their white counterparts to be influenced to participate. Factors contributing to clinical trial participation among African Americans and those self-identifying as "other" for race included provision of childcare, not having to provide names, and provision of

transportation. They also found that those who were African American and of middle income (annual income between \$15,000-\$50,000, as categorized by the authors) were significantly less likely to participate in clinical trials. Their findings indicate that the reported low rate of recruitment and participation in clinical trials may help to explain the health disparities observed among minorities, underserved and rural communities in Maryland (Baquet, Commiskey, Mullins, & Mishra, 2006).

Similarly, a study conducted by Simon et al. (2004) resulted in similar findings related to minority participation in clinical trials. They found that the most common reason for both white and African American women who were offered participation in a breast cancer trial but didn't enroll was because they refused to participate. However, a small percentage of white women did not enroll because they did not meet the study's eligibility criteria. Conversely, all of the African American patients who were offered participation but did not enroll had refused participation. In a study analyzing factors influencing enrollment into cancer studies among patients with advanced cancer, Jimenez et al. (2013) found that race/ethnicity predicted trial enrollment, with white patients more likely to be enrolled.

Minority interest. Though there are participation disparities in clinical trials, the literature also supports the finding that eligible African American and Hispanic American patients tend to enroll in clinical trials when given the opportunity (Diehl et al., 2011; Jimenez et al., 2013; Simon et al., 2004; Wendler et al., 2006). For example, Simon et al. (2004) did not find race to be a significant factor associated with breast cancer clinical trial enrollment among those who were offered a clinical trial. This suggests that more minority women may enroll if provided an opportunity; however, they are not always given the opportunity (Baquet, Commiskey, Mullins, & Mishra, 2006; Diehl et al., 2011; Simon et al., 2004). Albrecht et al. (2008) found

that, in general, patients at two NCI centers were not offered a clinical trial 76% of the time, even though they were referred as being potentially eligible. Of those patients who were offered a clinical trial, 77% actually enrolled. Although separate enrollment rates were not calculated based on race, 17% of the study sample was African American patients. Since 13% of the US population is African American, trial participation at these two centers was representative of the African American population in the United States (US Census Bureau, 2015). Similarly, Adams-Campbell et al. (2004) found that the enrollment rate among eligible African American cancer patients at one cancer center was 60%, indicating a high rate of interest in trial participation in this population. In fact, Markman, Petersen, and Montgomery (2008) studied whether there was a difference in interest rate among various populations with cancer in learning about cancer clinical trials. They found that minority respondents (categorized as African American, Hispanic and Asian American) expressed a greater interest than whites in learning about clinical trials. Furthermore, Cook, Kosoko-Lasaki, and O'Brien (2005) found that while only 5% of minority respondents participating in a survey indicated they were ever asked to participate in a healthcare study, 60% responded that they would participate if they were asked.

While Baquet, Commiskey, Mullins, and Mishra (2006) found that African Americans who were recruited to clinical trials were significantly less likely to participate, they also found that males from a race other than white or African American were significantly more likely to participate in a trial. Diehl et al. (2011) analyzed enrollment data from 10 cancer clinical trials and found that African American and Hispanic patients were represented across the trials. However, the extent of their participation was not representative of the US population, especially among Hispanics. Jimenez et al. (2013) found race and ethnicity to be a significant predictor of clinical trial enrollment; specifically, patients who were white were significantly more likely to

enroll. However, after controlling for socioeconomic and clinical factors, race and ethnicity was no longer associated with trial enrollment. This suggests that minority patients are just as likely as white patients to enroll in clinical trials. This finding is substantiated by the “Strategies for Ensuring Diversity, Inclusion, and Meaningful Participation in Clinical Trials” workshop proceedings in which acclaimed researchers devoted to reducing racial and ethnic disparities in healthcare indicated that based on their experiences, minorities are actually just as likely as majority populations to participate in clinical trials when given the opportunity (National Academies of Sciences, Engineering, and Medicine, 2016). After reviewing records of patient screening data for more than 4,500 patients who declined to participate in a cancer clinical trial, Langford et al. (2014) found no differences in enrollment, refusal rates, or “not having a desire to participate in research” based on race or ethnicity. Based on a study conducted by Wendler et al. (2006), there is evidence to suggest that individuals from minority groups are actually more willing to participate in clinical or surgical intervention studies than non-Hispanic white patients. Wendler et al. (2006) analyzed consent rates of more than 14,000 individuals who were eligible and invited to participate in clinical and surgical intervention trials and found that consent rates of minority populations were higher than those of non-Hispanic whites. Hispanics in particular had statistically significant higher overall consent rates. Additionally, Brooks et al. (2015) found that up to 83% of minority patients who were eligible for a clinical trial chose to enroll, while only 45% of eligible white patients enrolled.

Barriers of minority participation. There is an abundance of literature on the barriers specific to participation for minorities in clinical trials. In a systematic review conducted by Ford et al. (2008), barriers specific to underrepresented populations in clinical trials were categorized according to a conceptual model that was used to illustrate factors that were related to enrollment

in a clinical trial. To make a decision about enrolling, an individual needs to be aware of the trial, as well as be provided with an opportunity to participate. As previously discussed, minorities are not made aware of or asked to participate in clinical trials at the same rate as white patients (Baquet, Commiskey, Mullins, & Mishra, 2006; Simon et al., 2004). This results in minority patients experiencing a lack of awareness and lack of access to trials. Thus, Ford et al. (2008) categorized barriers based on awareness, opportunity and decision about participation. The socio-ecological model also can be used as a framework for categorizing barriers to minority participation, as previously documented in the clinical trial literature (Frew et al., 2014; Salihu, Wilson, King, Marty, & Whiteman, 2015; Wells & Zebrack, 2008). It is important to note that while the categorization of barriers to minority participation in clinical trials using the socio-ecological model provides insight into multiple levels of influencers on an individual patient level, this is a different application of the socio-ecological model than that which was used to guide this study. However, since the utility of this categorization is beneficial for a comprehensive understanding, the barriers have been categorized according to the socio-ecological model as follows:

Intrapersonal barriers. Barriers to clinical trial participation on an individual patient level comprise characteristics of the individual, including demographic characteristics, knowledge, attitudes, beliefs and skills (Baquet, Commiskey, Mullins, & Mishra, 2006; Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Ejiogu et al., 2011; Ford et al., 2008; Ford et al., 2013; Martin, Negron, Balbierz, Bickell, & Howell, 2013; McLeroy, Bibeau, Stecker, & Glanz, 1988; Roberson, 1994; Simon et al., 2004; Swanson & Ward, 1995). Examples of these intrapersonal barriers include:

- Demographic characteristics, including being of a racial/ethnic minority descent and having a lower socioeconomic status. Socioeconomic barriers at an intrapersonal level include cost of participation, lack of transportation and low levels of education (Baquet, Commiskey, Mullins, & Mishra, 2006; Ejiogu et al., 2011; Ford et al., 2008; Ford et al., 2013; Simon et al., 2004; Swanson & Ward, 1995)
- Misunderstandings due to health illiteracy and misunderstanding the concept of informed consent (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Cortes, Drainoni, Henault, & Paasche-Orlow, 2010; Swanson & Ward, 1995)
- Awareness barriers, including a lack of knowledge surrounding the need for medical research and about what clinical trials are and a lack of awareness of clinical trial opportunities (Ejiogu et al., 2011; Ford et al., 2008; Leiter, Diefenbach, Doucette, Oh, & Galsky, 2015; Ramirez et al., 2008; Roberson, 1994; Simon et al., 2004)
- Individual beliefs and attitudes, including:
 - Fear of being used as a guinea pig (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Ford et al., 2008; Ford et al., 2013; Roberson, 1994)
 - Time demands and perceived interference of participation with other personal responsibilities (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Ford et al., 2008; Martin, Negron, Balbierz, Bickell, & Howell, 2013)
 - Fear of exportation (Ford et al., 2013)
 - Lack of perceived benefit of participation (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Ejiogu et al., 2011; Ford et al., 2008)
 - Lack of interest (Martin, Negron, Balbierz, Bickell, & Howell, 2013)

- Skepticism due to uncertainty or negative connotations of clinical trials (Durant et al., 2014)
- Perceived stresses of burdensome procedures or adverse effects (Ford et al., 2008)

Interpersonal barriers. Barriers on an interpersonal level include influences of an individual's social network and social support system, including family, work and friendship networks and healthcare providers (McLeroy, Bibeau, Stecker, & Glanz, 1988; Salihu, Wilson, King, Marty, & Whiteman, 2015). Interpersonal barriers include:

- Negative experience of a potential participant's family member with the healthcare system (Ford et al., 2008; Swanson & Ward, 1995)
- Family concerns about research trials (Ford et al., 2008)
- Work obligations and an inability to get the time off of work (Ford et al., 2008)
- Communication barriers, including misunderstandings due to language barriers and poor doctor-patient communications (Ford et al., 2008; Ford et al., 2013; Swanson & Ward, 1995; Williams & Corbie-Smith, 2006). Additionally, skepticism about trial participation is commonly mistaken by research staff as distrust whereas education on clinical trials could help to alleviate some concerns of potential participants (Durant et al., 2014)
- Patients' lack of trust in their physicians (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999)
- Cultural differences between researchers and participants (Ford et al., 2013; Williams & Corbie-Smith, 2006)

- Attitudes of healthcare providers: minority patients are oftentimes not informed of a study when their primary physician mistrusts research or perceives limited scientific value, perceives their patients as mistrusting research, doesn't want to commit the additional time to explain the study or complete paperwork, and/or objects to referring their patients to other physicians conducting a study (Howerton et al., 2007; Ramirez et al., 2008; Ramirez et al., 2012; Salihu, Wilson, King, Marty, & Whiteman, 2015)
- Lack of provider awareness about clinical trials (Howerton et al., 2007)

Organizational barriers. An organization is defined as a social institution with organizational characteristics and rules and regulations for operation. Barriers on an organizational level include influences of organizations, including the healthcare system, and how policies and structures in place within organizations and the healthcare system influence an individual's behavior (McLeroy, Bibeau, Stecker, & Glanz, 1988; Salihu, Wilson, King, Marty, & Whiteman, 2015). Organizational barriers include:

- Lack of access to health care or not having health insurance (IOM, 2003; Swanson & Ward, 1995; USHHS, CDC, 2011a)
 - After controlling for insurance status, Jimenez et al. (2013) found that after controlling for health insurance, African American, Hispanic and Asian patients were just as likely as their white counterparts to enroll in an advanced-stage cancer clinical trial. However, not all health insurers cover the costs of clinical trial participation. After reviewing data from patients consented into a cancer clinical trial at the Sidney Kimmel Comprehensive Cancer Center over a 3-year period, researchers determined that 13.6% of

consented patients were denied coverage by their insurer (Klamerus et al., 2010). While federal law now requires health insurers to cover routine costs in clinical trials under ACA, exceptions to this law may result in coverage gaps. For example, health plans that existed when the ACA was enacted are not required to cover routine patient costs in clinical trials (USHHS, NIH, NCI, 2020)

- Lack of access to research centers: minorities are less likely to have access to research centers where clinical trials are commonly offered (Boden-Albala et al., 2015; Diehl et al., 2011; Durant et al., 2014)
- Organizational barriers related to the clinical research sites, including:
 - Lack of access to the study population (Durant et al., 2014; Ejiogu et al., 2011; Swanson & Ward, 1995; Williams & Corbie-Smith, 2006)
 - Lack of experience in recruiting racial and ethnic minorities (Ejiogu et al., 2011; Williams & Corbie-Smith, 2006)
 - Researcher beliefs and biases, which influence the effort researchers exert in addressing barriers to minority recruitment. For example, a researcher's perception of the potential harm or benefit a trial could have to patients, as well as a researcher's perception of participants' distrust of research (Ejiogu et al., 2011; Ford et al., 2008; Simon et al., 2004; Stone, Mauch, & Steger, 1998; Swanson & Ward, 1995; Williams & Corbie-Smith, 2006)
 - Organizational climate, lack of resources and limited funding to support minority recruitment efforts (Joseph & Dohan, 2009)

- Study design: eligibility criteria precludes minorities from being eligible due to disproportionate comorbid conditions (Adams-Campbell et al., 2004; Ford et al., 2008; Swanson & Ward, 1995)
 - Adams-Campbell et al. (2004) conducted a study to systematically evaluate the influence of the study design on the recruitment of African Americans into cancer clinical trials being conducted at one large cancer center. Of the African American patient population studied, nearly one-fourth was ineligible to participate in an existing clinical trial because of comorbidities. Langford et al. (2014) also found that being of non-Hispanic black race was significantly associated with not meeting eligibility criteria due to existing comorbidities. Given that health disparities disproportionately affect racial and ethnic minorities (USHHS, CDC, 2011a; USHHS, CDC, 2011b), it is likely minorities also have a disproportionate burden of comorbidities excluded by study protocols, which results in a lack of opportunity to participate
- Members of racial and ethnic minority groups are underrepresented in the healthcare workforce, leading to a shortage of minority physicians involved in clinical research. Ramirez et al. (2008) found that half of the Latino physicians who participated in their survey indicated they had never been involved in a clinical trial, compared with one-third of white physicians. This is an important finding since the inclusion of minority investigators and research staff is associated with successfully recruiting minority study participants (Ford et al., 2013; Swanson & Ward, 1995; The Society for Women's Health Research & FDA, 2011; Williams & Corbie-Smith, 2006)

Community barriers. Community is not only defined by individuals sharing common demographic or geographic characteristics, but also includes mediating structures such as family, social networks, churches and neighborhoods, all of which may be sources of social identity. Community is also defined by relationships among organizations within a geographical region. Community barriers include:

- Cultural beliefs and attitudes
 - Lack of trust in the healthcare system and clinical research, particularly due to past history of unethical conduct in clinical research involving minorities (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Ejiogu et al., 2011; Ford et al., 2013; Roberson, 1994; Swanson & Ward, 1995; Williams & Corbie-Smith, 2006)
 - One such example was the Tuskegee Study that started in 1932 with the US Public Health Service and the Tuskegee Institute and enrolled poor African American men who were told they were being treated for ‘bad blood.’ The men agreed to be treated for their ‘bad blood’ but were never properly informed about the study to provide their informed consent. Instead, they had been misled about the study and were not informed that they had syphilis in order to allow the researchers to record the natural history of syphilis in African American men. Furthermore, once penicillin was found to be successful in treating syphilis in 1947, it was never offered to the study participants. The study lasted until 1972, when the US government

deemed the study to be unethical and announced the end of the study (USHHS, CDC, 2013b)

- Another example is known as the Puerto Rican “Tuskegee.” In the 1950s to the early 1960s in a remote farming town in Puerto Rico, women were given a “magic pill.” They were told the pill would keep them from having children they could not support. Unbeknownst to these women, they were actually subjects in research testing of the world’s first birth control pill. Doctors provided hundreds of women among Puerto Rico’s poorest agricultural class with these free pills that contained three times as much hormone as the versions currently on the market. Although the pills kept the women from getting pregnant, they also came with a multitude of side effects and, more importantly, without the informed consent of the women taking the pill (Quintanilla, 2004).
 - Cultural beliefs about illness and disease, such as distinguishing between “hot” and “cold” diseases and preferences for folk healers and herbal remedies (Juckett, 2013; Swanson & Ward, 1995)
- Lack of available public transportation to the research site for attending study visits (Ejiogu et al., 2011; Ford et al., 2008; Swanson & Ward, 1995)

Public policy barriers. Barriers at a public policy level include local, state, and national laws and policies, such as:

- The mandate to include women and members of minority groups as participants in clinical research applies to NIH-funded trials only (USHHS, NIH, 2001)

- The federal law under the ACA requiring health insurers to cover costs for routine procedures in clinical trials grants an exception to Medicaid plans and grandfathered health plans that were in existence when the ACA became law (USHHS, NIH, NCI, 2020)

A few of these barriers were found to be specific to Hispanics (Martin, Negron, Balbierz, Bickell, & Howell, 2013; Roberson, 1994). Roberson (1994) found that ethnic background, lack of information and mistrust are perceived barriers specific to recruitment among the Hispanic population. Lack of interest and time commitment were cited as the most common barriers to recruitment for African American and Hispanic women in a postpartum depression study (Martin, Negron, Balbierz, Bickell, & Howell, 2013). Ford et al. (2013) found that Spanish-speaking clinicians are crucial to the successful recruitment of Hispanic patients, since they are more likely to be trusted by their Hispanic patients. Study materials need to be translated into Spanish, keeping in mind patients with low literacy levels. Researchers also need to reassure patients that immigration status will not be documented (Ford et al., 2013).

Strategies specific to addressing barriers. Martin, Negron, Balbierz, Bickell, and Howell (2013) successfully recruited minority women (African American and Latina) into a postpartum depression prevention study by using a feedback-responsive recruitment strategy. Their approach involved immediately responding to identified recruitment barriers that evolved throughout the enrollment period by revising their recruitment messages. This strategy resulted in a decreased refusal rate to participation of 40% to 19%. Lack of interest and time commitment were identified as the two most common barriers to participation. The researchers addressed concerns for time commitment by offering alternative methods for completing follow-up interviews that better fit within the women's schedules. To help overcome lack of interest, they

changed their recruitment message and presented the study to potential participants as a way to teach them about postpartum mothers' health so their input could be used to benefit other African American and Latina women in the future. This shared goal of helping others helped increase recruitment, which is consistent with research that demonstrates altruism as a main reason for participating in clinical trials (Bevan, Chee, McGhee, & McInnis, 1993). A study conducted by Smith et al. (2007) found that African American women are motivated by the desire to help their community or other people of their color.

In a study conducted by Ejiogu et al. (2011), barriers that disproportionately affect participation in clinical trials by minorities and the socioeconomically disadvantaged were targeted in order to overcome recruitment challenges and successfully recruit for a longitudinal study. The study examined how race and socioeconomic status influence the development of age-related health disparities. They targeted biracial (African American and non-Hispanic white) and socioeconomically diverse participants. The researchers identified barriers that were specific to this study and its targeted participants by meeting with local stakeholders, health professionals, government officials, as well as establishing a community advisory board that included church leaders, neighborhood activist leaders and local residents. To address the barriers, the researchers created a recruitment and retention plan that included deploying mobile medical research vehicles (MRVs) parked in the participants' neighborhoods in Baltimore, Maryland, and offering transportation to the MRVs. They also educated members of the community advisory boards about health disparities and the need for research in their communities to gain feedback on the study methods and local barriers, as well as to gain community support. They coordinated surveillance of the MRVs with the Baltimore Police Department and developed a cultural proficiency curriculum for site staff. The investigators also

established active community citizenship through their participation in local festivals and community social events. Finally, they adapted the study design to include medical benefits as a means to motivate participants who didn't have access to healthcare. Their recruitment strategy paid off. Of the 3,722 participants recruited, 2,200 (59%) were African American and 1,522 (41%) were white (Ejiogu et al., 2011). They designed the study based on the recruitment strategy, which is an important consideration because this is typically not common practice since recruitment strategies are often an after-thought. Williams and Corbie-Smith (2006) have found that recruitment strategies need to be established prior to beginning enrollment in order maximize their success. When they are altered during the recruitment period, they are less successful in recruiting minority participants.

Value investigators place on minority recruitment. The literature indicates that physicians' attitudes toward participating in clinical trials directly impacts enrollment in general, likely due to the value and importance they place on clinical trials. Further, those physicians who have more positive feelings towards clinical trials are more active in enrolling patients (Jacobs et al., 2014). However, there is an ethnic disparity among physicians in regard to their attitudes toward clinical trials. Twice as many Latino physicians as white physicians disagree that the scientific value of clinical research outweighs the risks (18% vs. 9%, respectively) (Ramirez et al., 2008). This may contribute to the underrepresentation of Latino researchers, as well as the underrepresentation of minority clinical trial participants, since Latino physicians are more likely to treat Latino patients. This is important because having Spanish-speaking research staff who look like the population they are trying to recruit has been successful in recruiting Hispanic women (National Academies of Sciences, Engineering, and Medicine, 2016). Therefore,

improving minority physician attitudes towards clinical trials could improve minority participation.

Results of studies have determined that PI attitudes play a significant role in minority recruitment. The value investigators place on minority recruitment has been found to be a key contributor toward the success or failure of recruiting minority participants into clinical studies (Williams & Corbie-Smith, 2006; Wright et al., 2001). For example, Williams and Corbie-Smith (2006) found that investigators who valued the inclusion of minority participants in clinical research were more successful in recruiting minority participants. In their study, Williams and Corbie-Smith (2006) surveyed PIs to gain their perspectives on recruiting minority participants into clinical trials to identify factors associated with success in this area. The majority of PI respondents (90%) were white but the majority of them reported including minorities on their research team. Notably, 73% of the investigators surveyed self-reported success with recruiting minority participants into a trial. PIs who considered minority participation in research as important, who didn't need to make midstream modifications to their recruitment strategy and who reported fewer recruitment barriers reported being successful in minority recruitment. Although including minority recruiters, investigators and/or project managers as part of the site staff was associated with reported minority recruitment success, the race of the PI was not associated with reported minority recruitment success. Of the sites that didn't make midstream changes to their recruitment strategy, 76% reported success in recruiting minority participants, whereas only 59% of those sites that made changes midstream to their recruitment strategy were successful in recruiting minorities.

Durant et al. (2007) conducted a survey of PIs to evaluate the attitudes and experiences of those who receive federal funding in recruiting minorities and women in clinical trials. The

purpose of their study was to determine the recruitment goals that investigators set for minority recruitment, the percentage of PIs that failed to reach their goals, and whether or not PI and study characteristics and PIs' perceptions of minority recruitment were associated with their failure to meet minority recruitment goals. The majority of the PIs surveyed were white males with a mean age of approximately 50 years. The most common methods of recruitment used among the PI respondents were clinic or hospital-based recruitment, word of mouth, flyers and physician referral. The authors found that many PIs did not set recruitment goals for individual minority groups. Goals were set more frequently for African Americans (91%) and whites (88%); 67% of PIs self-reported setting recruitment goals for Hispanics and 55% for Asian Americans. Mean recruitment goals were highest for whites (71%), compared with mean recruitment goals of 33% for African Americans, 21% for Hispanics and 10% for Asian Americans. Although investigators who receive federal funding are required to meet minority enrollment targets, this study reinforces the fact that many of these investigators do not set minority recruitment goals. In another study that explored researcher strategies to incorporate the NIH's policy to include a representative proportion of minorities in NIH-funded clinical trials, only half of the respondents indicated they proactively set recruitment goals for minority inclusion (Boden-Albala et al., 2015). Durant et al. (2007) also found that PIs were more likely to fail to meet their racial and ethnicity demographic-specific recruitment goals set for African Americans (51%), Asian Americans (55%) and Hispanics (44%) compared with goals set for whites (30%). Failure rates in meeting recruitment goals were significantly higher for African Americans and Asian Americans as compared with failure rates in meeting recruitment goals for white participants. Many factors were found to be associated with failing to meet recruitment goals, but they were varied, and none were consistently associated with failing to meet recruitment goals across

different racial and ethnic groups. Sixty percent of PIs had not yet completed study enrollment for their most recent federally funded trial, which could contribute to not meeting their minority recruitment goals. The factors found to be associated with failing to meet recruitment goals for African Americans were related to investigator and study characteristics, as well as PI perceptions. These factors included PIs conducting an observational study, completed study enrollment, or the perception of PIs that there would be a large number of barriers to minority enrollment (Durant et al., 2007). The fact that a perception of recruitment barriers was associated with failing to meet recruitment goals corroborates the findings of Williams and Corbie-Smith (2006) who reported fewer perceived recruitment barriers were associated with greater success in minority recruitment (Williams & Corbie-Smith, 2006).

Durant et al. (2007) also found that having more than 20 years of funding as a PI was associated with a lower chance of failing to meet recruitment goals for African Americans. This may be due to greater experience in conducting and recruiting for clinical trials. None of the factors that were analyzed were independently associated with failing to meet recruitment goals for Hispanics. The value investigators place on minority recruitment plays a role in successfully recruiting minority participants (Williams & Corbie-Smith, 2006) but whether or not this value is associated with setting individual minority recruitment goals is unknown.

Interestingly, sites in the ALLHAT with a large African American patient population recruited African Americans at the same rate as those sites without a high percentage of African American patients. Though the reasons behind these similar recruitment rates were not articulated, the authors speculated that they were due to the motivation and training of investigators to recruit diverse patients, as well as the existing physician-patient relationship at those sites that successfully recruited African American participants (Wright et al., 2001). These

findings demonstrate that recruiting minority participants into clinical studies is achievable when investigators are motivated and place value on recruiting minorities and suggests that these sites were specifically focusing on and actively recruiting minority participants. Since more than half of the ALLHAT participants were minorities (Pressel et al., 2001), the research also suggests that minorities are willing to participate when given the opportunity, similar to findings from Diehl et al. (2011), Jimenez et al. (2013) and Simon et al. (2004). This is also important to recognize because of a sponsor's focus and priority to expedite trial enrollment in order to conduct a study in the shortest amount of time possible (Getz, 2012; IMS Health, 2012; USHHS, OIG, 2000). The findings from Wright et al. (2001) provide evidence that recruiting minority participants when the right sites are involved is not time-consuming.

African American and Hispanic participants likely will enroll in clinical trials when given the opportunity (Diehl et al., 2011) and minorities are interested in learning about clinical trials (Markman, Petersen, & Montgomery, 2008). These findings suggest that minority participation may increase when value on the importance of including minority participants in clinical research is instilled in more investigators. Therefore, if guidance or successful experience with minority recruitment is shared among the research community, it may increase the value that investigators place on recruiting minority participants and, ultimately, result in an increased number of minority participants enrolling in clinical trials.

Organizational context. Organization contextual factors can impact the enrollment success of clinical trials among the general population. Specifically, those organizations that provide support and offer incentives to physicians to enroll patients, as well as mandate minimum enrollment targets, accrue more patients. While these organizational contextual factors increase enrollment, they were not found to directly influence physician attitudes toward clinical

trials. Physicians' positive attitudes toward participating in clinical trials did, however, have a direct positive effect on enrollment (Jacobs et al., 2014). McMullen, Griffiths, Leber, and Greenhalgh (2015) explored factors related to high-recruiting and low-recruiting practices (within the general population) and found that high-recruiting practices were innovative and characterized by strong leadership, good managerial relations, dedicated resources and provision of staff training. Adams, Caffey, and McKevitt (2015) found that research staff perceived organizational factors to contribute more to recruitment success than the study itself (in general). These factors included commitment by the research team, the value of research recognized within the organization and having sufficient resources. In a systematic literature review conducted by Fletcher, Gheorghe, Moore, Wilson, and Damery (2012), the researchers found that providing research-dedicated staff, enrollment incentives and additional training led to increased recruitment rates. They also found that being part of a practice active in research is connected with positive recruitment results. These findings relate to clinical trial recruitment in general, and further studies are needed to determine if the same factors apply when recruiting minorities. However, there is a small pool of literature on organizational contextual factors specific to minority recruitment.

When exploring organizational barriers to minority participation in cancer clinical trials, Joseph and Dohan (2009) found that organizational climate and research infrastructure impacts minority recruitment. Specifically, a lack of resources created a climate in which clinical trials were made a low priority, such as providers who are already being stretched to see patients and having recruitment activities occupying exam rooms that were needed for patient care. Limited funding for research left providers with a small research staff and a lack of resources to translate patient-facing materials that described studies that were being conducted to patients.

Furthermore, the interdisciplinary structure of the clinic was such that patients did not have a dedicated provider, which resulted in a lack of continuity of care and limited individual provider awareness of specific trials. These factors led to staff having an unfriendly attitude toward clinical trials, which shaped the culture of the clinic to prioritize clinical care over research. These findings by Joseph and Dohan (2009) support other findings that research center infrastructure and experience impact the successful enrollment of minority participants (Etkin, Farran, Barnes, & Shah, 2012). PIs' perceived importance of minority inclusion is also associated with minority recruitment success rates (Williams & Corbie-Smith, 2006), which would likely impact organizational climate.

As previously discussed, factors related to the investigator site that negatively impact minority recruitment include lack of access to the study population, lack of experience in recruiting racial/ethnic minorities, lack of information about effective strategies and cultural differences between research staff and participants (Williams & Corbie-Smith, 2006). On the other hand, several studies suggest that characteristics related to specific research sites may have contributed to their successful enrollment of minorities into clinical trials. Jimenez et al. (2013) found that white race was not a significant predictor of clinical trial enrollment after controlling for recruitment site. One recruitment site in particular in this study was a statistically significant confounder to predicting enrollment based on race and ethnicity. More than half of the study participants in the ALLHAT were African American and those sites with a large African American patient base recruited at the same rate as sites that did not have primarily African American patients (Wright et al., 2001). These examples suggest that there is something different about these sites from the other sites in terms of recruiting minority participants and that, perhaps, they are specifically focusing on minority recruitment. In a study conducted by Duda et

al. (2011), the lack of consistency with recruitment strategies employed across different research sites led the researchers to believe that the success specific sites had with recruiting minority patients was related to characteristics of the investigator sites themselves. More research is needed in this area to determine the specific organizational characteristics that may contribute to successful minority recruitment.

Health literacy. Health literacy is defined as “the degree to which an individual has the capacity to obtain, communicate, process, and understand basic health information and services to make appropriate health decisions” (USHHS, CDC, 2019). Although general literacy and health literacy are not the same, even people with strong literacy skills and high education levels have trouble understanding health information. For instance, 15% of high school graduates have limited health literacy (US Department of Education, Institute of Education Sciences, 2006). General literacy is defined by the US Department of Education, Institute of Education Sciences (2006) as “using printed and written information to function in society, to achieve one’s goals, and to develop one’s knowledge and potential.” This includes reading, writing and basic mathematical and speech comprehension skills. Thus, general literacy is the foundation for health literacy because literacy provides the skills that enable individuals to understand and communicate information within a health context (IOM, 2004).

On average, Hispanic adults have lower health literacy than any other racial or ethnic group and white adults have the highest health literacy compared with adults of other races or ethnicities. Sixty-six percent of Hispanic adults have either below basic or basic health literacy skills, indicating limited health literacy, and 41% do not have the skills to perform simple everyday literacy activities. Fifty-eight percent of African American adults have limited health literacy, compared with 28% of white adults (US Department of Education, Institute of

Education Sciences, 2006). Individuals with limited health literacy have less knowledge about their medical conditions and management of their disease (IOM, 2004). For example, Williams, Baker, Parker and Nurss (1998) found that functional health literacy levels in patients with a chronic disease were correlated with knowledge and management of their disease—patients with limited health literacy cannot optimally manage their disease. Patients with limited health literacy also are less likely to use preventive services, since they are more likely to enter into the healthcare system at a more advanced stage of their disease (IOM, 2004). Paasche-Orlow and Wolf (2007) suggest that access and utilization of the healthcare system is decreased in individuals with limited health literacy due in part to a limited ability to navigate the complexity of the healthcare system. In a systematic literature review conducted by Koskan, Friedman and Messias (2010), the researchers found that Hispanics with lower levels of health literacy were less likely to be screened for the presence of diseases. It is no surprise that limited health literacy is a barrier to clinical trial participation among minorities (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Swanson & Ward, 1995). Barriers with entering the healthcare system as indicated by the IOM (2004) and Paasche-Orlow and Wolf (2007), as well as the limited knowledge of chronic disease in individuals with lower health literacy levels, may be part of the reason behind lower clinical trial participation. Further, Hispanic ethnicity and lower levels of education have been found to be independently associated with decreased levels of clinical trial awareness (Leiter, Deifenbach, Doucette, Oh, & Galsky, 2015). In a study conducted by Duda et al. (2011), the researchers found that the minority participants who enrolled in the National Lung Screening Trial were disproportionately less well educated and more economically disadvantaged than whites, both of which are factors contributing to limited literacy (IOM, 2004). Although distinct from general literacy, basic literacy skills are required for health

literacy, and the percentage of adults with proficient health literacy increases accordingly with each higher level of educational attainment beyond high school (IOM, 2004; US Department of Education, Institute of Education Sciences, 2006). In fact, approximately half of US adults lack the basic literacy skills required for full participation in American society. Since basic literacy skills are a building block for health literacy, a large proportion of the US population, a disproportionate amount of which are racial and ethnic minorities, therefore, has limited health literacy. Both being a member of a racial and ethnic minority and lower education levels have been found to be associated with limited health literacy (IOM, 2004). This poses a problem with informed consent when sites need to educate patients with low education or limited health literacy on study details and requirements and any potential risks of participating in the study. The readability levels of informed consent documents for clinical trials are higher than the average reading level of most adults in the United States, and the majority of clinical trial participants do not fully understand the study information presented to them during the consent process (Cortes, Drainoni, Henault, & Paasche-Orlow, 2010; Flory & Emanuel, 2004; Helgesson, Ludvigsson, & Stolt, 2005; IOM, 2004). In fact, after using health literacy principles to redesign a surgical consent form, the percentage of patients who actually read the form increased from 25% to 91% (Lorenzen, Melby, & Earles, 2008). Even so, following industry recommendations for improving comprehension of a consent form for a hypothetical study did not always result in comprehension among Spanish-speaking individuals with low literacy or lack of familiarity with research. Researchers should incorporate interactive consent discussions into their consent processes to better ensure comprehension by all potential research participants (Cortes, Drainoni, Henault, & Paasche-Orlow, 2010; Flory & Emanuel, 2004). Additionally, the teach-back method can help the researcher determine the patient's understanding of the

information being presented (Lorenzen, Melby, & Earles, 2008). Furthermore, individuals with limited health literacy are less likely to ask questions of their provider and admit that they have a poor understanding of the discussion. Physicians are often unaware of any misunderstandings (IOM, 2004). This could result in patients not taking their study medication or performing any at-home study requirements as instructed, since patients with limited health literacy remember and understand less than half of what they are told by their physicians (IOM, 2004).

The skill of healthcare professionals in communicating health information also contributes to health literacy (IOM, 2004). The Agency for Healthcare Research and Quality (AHRQ) has recognized that in order to address the needs of patients with limited health literacy, organizations need to become health literate. Ways to promote health literacy within a healthcare practice include improving communication (spoken and written), providing patients with empowerment to control their disease and implementing patient support systems (AHRQ, 2010). According to the participants of an IOM roundtable on health literacy, a health literate organization is “an organization that makes it easier for people to navigate, understand, and use information and services to take care of their health” (Brach et al., 2012). Livaudais-Toman, Burke, Napoles, and Kaplan (2014) conducted a study to assess the organizational health literacy of clinical trial sites and characteristics associated with health literate behaviors, measured by communication (written and verbal) and outreach efforts. Less than half of the sites surveyed offered supplemental information about clinical trials (such as frequently asked question sheets to help potential participants better understand clinical trials), and only 22% of sites offered supplemental materials in languages other than English. Only one-fourth of sites offered translated materials to facilitate recruitment and patient navigation to trials. The provision of translated materials does not, however, solely fulfill health literacy requirements, since

individuals with limited English proficiency may have limited health literacy (IOM, 2004). Sixty-five percent of sites offered professional interpretation services, a finding that is disappointing given the National Standards on Culturally and Linguistically Appropriate Services (CLAS) in Health Care policy that healthcare organizations must offer and provide language assistance services, at no cost, to each patient with limited English proficiency (Livaudais-Toman, Burke, Napoles, and Kaplan; USHHS, Office of Minority Health, 2018). Additionally, less than half of the sites engaged in community outreach efforts, a strategy that the authors categorized as an organizational health literate characteristic and that others have found to be successful in recruiting minority participants (Etkin, Farran, Barnes, & Shah, 2012; Livaudais-Toman, Burke, Napoles, and Kaplan). Findings by Livaudais-Toman et al. (2014) suggest that clinical research sites are not addressing the health literacy needs of their patients.

It is also important to note that culture influences how individuals interact with the health care system. Cultural differences may have an effect on the communication and understanding of health information, and an individual's ability to make appropriate healthcare decisions is based on their cultural beliefs (Ingram, 2012; IOM, 2004). As a result, culture is a component influencing the health literacy skills of an individual. As such, cultural competence skills and knowledge are required for healthcare professionals to be able to provide care as part of a health literate organization (IOM, 2004).

Cultural competence. Cultural competence is a required skill set among physicians for them to deliver high quality care to patients successfully, helping to reduce racial and ethnic disparities in healthcare (Betancourt, 2004; Betancourt, Green, Carrillo, & Ananeh-Firempong, 2003). Cultural competency requires that organizations have a congruent set of values, behaviors, attitudes, practices, policies and structures that enable them to adapt to diversity and

deliver services in order to work effectively cross-culturally (Cross, Bazron, Dennis, & Isaacs, 1989). In order to be culturally competent, healthcare professionals must be aware of the values and belief systems of different cultures, have knowledge of cultural world views, possess the skills to collect health information in a culturally sensitive manner and encounter patients from culturally diverse backgrounds with cross-cultural interactions. Lastly, they need to have a desire to engage in the process of cultural competence (Campinha-Bacote & Campinha-Bacote, 1999; IOM, 2004). A culturally competent healthcare system is one that acknowledges and incorporates the importance of culture and adapts services to meet specific cultural needs based not only on health beliefs and behaviors but also on social factors (Betancourt et al., 2003).

Purnell et al. (2011) published guidance for assessing an organization's cultural competence in the delivery of culturally competent healthcare, of which the key components are administration and governance, education, language services and staff competencies. For example, a culturally competent healthcare organization has a mission statement and philosophy that address diversity; they partner with ethnic community agencies to engage the local community in activities, such as community health screenings; advertisements and health promotion campaigns are representative of the diversity and languages of patients and placed where they will reach patients in the local community; resources are allocated to diversity training for all levels within the organization; recruitment of staff reflects the diversity of the community; and staff are knowledgeable of their patients' cultures. Further, Brach and Fraserirector (2000) suggest that if an organization exhibits cultural competency techniques they could effectively change both physician and patient behavior, resulting in improved communication, a better understanding of patients' cultural behaviors, increased trust and improved patient education on their disease and treatment options. This would ultimately yield greater access to appropriate healthcare services among minorities.

Poor doctor-patient communications, cultural differences between researchers and participants, mistrust, lack of patient knowledge about clinical research as a potential treatment option and limited access to healthcare services are all barriers to minority recruitment (Baquet, Commiskey, Mullins, & Mishra, 2006; Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Ejiogu et al., 2011; Ford et al., 2008; Ford et al., 2013; IOM, 2003; Leiter, Diefenbach, Doucette, Oh, & Galsky, 2015; Roberson, 1994; Simon et al., 2004; Swanson & Ward, 1995; USHHS, CDC, 2011a; Williams & Corbie-Smith, 2006). These findings, therefore, suggest that a healthcare organization employing cultural competency techniques also would yield greater access to clinical trials among minority populations.

Cultural competence also needs to be prevalent in protocol design and study initiation (Diehl et al., 2011). For example, Adams et al. (2004) found that exclusion criteria prohibited the eligibility of many African Americans from cancer trials due to the disproportionate incidence of comorbidities in that population. Characteristics of African Americans and other minorities must be taken into consideration when developing study designs and eligibility criteria. The capacity to acquire cultural knowledge about patients is a crucial component of cultural competence attributed to recruiting minority populations into clinical trials (O'Brien et al., 2006). Examples in the literature describe successful recruitment of diverse patients into clinical trials by acquiring cultural knowledge about patients they are targeting and incorporating that knowledge into the study design and recruitment plan (Ejiogu et al., 2011; Wallington et al., 2016). Wallington et al. (2016) used a cultural competence conceptual framework to integrate culturally competent strategies into the study design, such as using diverse staff from the local community, ensuring all staff were trained on the elements of cultural competence, as well as reviewing all study procedures, consent documents, data collection tools and recruitment materials for health

literacy and cultural suitability. Additionally, Ejiogu et al. (2011) found that culturally sensitive researchers, support of the local community, and designing their study to overcome known barriers to minority participation in clinical research all contributed to the successful recruitment of minorities. As part of their recruitment plan, cultural proficiency training was instituted to help researchers and site staff recognize how their personal biases could influence their interactions with potential patients who were of a different culture. As a result of these considerations, the recruitment success in the study was partly credited to the diverse research staff and the cultural proficiency training program that provided continuous training to the researchers throughout the study.

Cultural competency also plays an invaluable role in the informed consent process with a multicultural audience, as evidenced by Simon and Kodish (2005). In reviewing a series of informed consent discussions for participation in clinical trials for pediatric leukemia, Simon and Kodish found that information quality and the disclosure process regarding the clinical trial was significantly better for white parents than it was for minority parents. This included informing parents about the right to withdraw from the trial, details about the benefits and risks, as well as details about any expected pain or discomfort that may result from the investigational medication. Simon and Kodish attributed the disparity in clinical trial information communicated to the parents of minority patients to assumptions made by the researchers about these parents' information needs and preferences based on their race or ethnicity and socioeconomic status.

The ACA includes provisions for recruiting and thorough training of the healthcare professional workforce in an effort to improve access to and delivery of care for all individuals, especially those who face healthcare disparities, such as minorities (KFF, 2013a; KFF, 2013b; Sultz & Young, 2014). One such provision provides support for cultural competence training of

healthcare professionals (KFF, 2013a). However, additional cultural competency training is needed as several investigators reported deficiencies in this area (Diehl et al., 2011; O'Brien et al., 2006). Lack of researcher training in communication techniques that are culturally appropriate is a known barrier to recruitment (Baquet, Commiskey, Mullins, & Mishra, 2006), yet Boden-Albala et al. (2015) found that only 36% of investigators required cultural competency training for staff as part of their strategy to adhere to the NIH's minority inclusion policy.

Cultural, community and site-specific recruitment strategies. Direct community involvement by researchers who tailor their strategies to align with the culture of the community have proven to be successful in recruiting minority participants into clinical trials (Duda et al., 2011; Ejiogu et al., 2011; Etkin, Farran, Barnes, & Shah, 2012; Germino et al., 2011; Wallington et al., 2016). Germino et al. (2011) described a successful recruitment strategy for recruiting young African American breast cancer survivors into an interventional study designed to help women deal with fears and communication issues around their breast cancer and identify positive directions for their lives. The recruitment strategy involved engaging community stakeholders to address barriers to recruitment specific to the study population and community. The over-arching recruitment objectives were focused on increasing familiarity of the study in the targeted communities through community outreach, partnering with African American churches and community organizations, increasing the availability and accessibility of study information, and using cultural brokers to help accomplish their goals. One of the strategies used for increasing the availability and accessibility of study information included using African American recruiters who made calls from their homes in the evening so their name appeared on the caller ID rather than a private or unknown number. They also collected data in the participants' homes to help

make participation more convenient. Through the implementation of these culturally informed strategies by Germino et al. (2011), the recruitment rate of younger African American breast cancer survivors increased 373% in just under 1 year, with the steepest rise in recruitment occurring after all strategies were in place and operating simultaneously.

Community involvement by researchers conducting the Telephone Resources and Assistance for Caregivers (TRAC) study resulted in an exceeded minority enrollment target of 30%. Researchers used social marketing and a community-based approach to develop their recruitment plan for this interventional study that enrolled sedentary caregivers of patients with Alzheimer's disease in an attempt to increase caregiver physical activity. The researchers collaborated with community leaders and organizations and maintained a strong presence at community events. They also cast a broad net into the community, making relationships with senior centers, faith-based organizations and adult day care programs. They attributed their success in recruiting for this study to the infrastructure and experience of the research center, as well as the collaborative partnerships and relationships they developed in the community through their community engagement and giving in the form of educational programs (Etkin, Farran, Barnes, & Shah, 2012). Similarly, Wallington et al. (2016) conducted community advisory boards to gain entry into the community and also used the knowledge they gained about the patients they were targeting and the community they live in to guide their research design. As a result, they experienced a 62% increase in African American participants across the non-interventional trials they were conducting.

Interestingly, the African American Study of Kidney Disease and Hypertension (AASK) trial utilized community-based screening and outreach strategies as part of their recruitment efforts and found it to be ineffective in recruiting African American participants. This may be

due to a lack of awareness in the community about the relationship between hypertension and renal dysfunction. Additionally, many people were not aware they have the disease that was being studied (renal insufficiency due to hypertension) (Phillips et al., 2004). This suggests that while community-specific recruitment strategies can be successful, their success is dependent on the disease being studied and cannot be generalized as an effective recruitment strategy across all studies.

Duda et al. (2011) conducted a study to determine the impact of targeted recruitment strategies on recruiting minority participants into the National Lung Screening Trial. Seven institutions from the American College of Radiology Network were selected to be the intervention sites, which created their own targeted minority recruitment strategies. These seven sites, which were situated in culturally diverse communities, were selected based on their performance in overall recruitment and their past success in recruiting minority participants. Their site-specific recruitment strategies varied from direct mailing, advertising, printed brochures, disseminating information at community events and enlisting cultural insiders. Of the 18,842 participants enrolled in the study, 1,576 (8.4%) were from racial and ethnic minority populations. Of the 1,576 minority participants enrolled, 1,223 (77.6%) were from one of the seven sites that had implemented a targeted minority recruitment strategy. These seven sites with targeted recruitment strategies enrolled significantly more racial and ethnic minority participants than those without targeted minority recruitment strategies. Specifically, they enrolled a higher percentage of African American (9.5% vs. 2.0%), Asian (0.9% vs. 0.3%) and Hispanic (1.7% vs. 0.9%) participants. Duda et al. (2011) found that the rate of minority recruitment increased quickly after the targeted recruitment strategies were implemented at those seven sites with dedicated strategies, while the rate of minority recruitment was relatively stable across all other

sites. Although minority recruitment increased significantly after the targeted recruitment strategies were implemented, recruitment methods varied and there wasn't a common strategy that worked consistently well across all seven sites with targeted recruitment. Additionally, these seven sites were selected because they were already enrolling minority participants. Therefore, the impact of their targeted strategies for boosting minority recruitment is speculative and could be due to characteristics of the site itself.

In a study by Harris et al. (2003), the researchers used both proactive and reactive recruitment strategies to enroll African American participants into a smoking-cessation clinical trial, which eventually led to successful recruitment due to their flexibility in changing the recruitment strategy mid-stream. For the proactive methods, study staff personally recruited participants from the existing patients and staff at an African American health center in which the study took place. Reactive strategies consisted of community outreach via a targeted media campaign and included ads in the form of television, radio and print. Minority recruitment was considered prior to study design, and many factors were taken into consideration in developing the study design to increase recruitment of African American participants. For example, all staff members were African American, the study setting was a health center that was trusted by the African American community and incentives and reimbursement were offered. Only proactive strategies were implemented at the start of the study, but since recruitment goals were not being met, the researchers put reactive strategies in place. Once the reactive strategies were implemented, recruitment significantly increased and was found to be more successful in recruiting participants ($n = 534$) over the proactive strategies ($n = 66$). Just over one-fourth of all enrolled participants were recruited on the 5% of screening days in which the media outreach took place. Additionally, people screened during the reactive phase were more likely to be

eligible and enroll in the study. Presumably, this was due to those who responded to the media outreach pre-screening themselves based on their review of the eligibility criteria and who also were more likely to be ready to quit smoking. After comparing the demographic information between participants recruited using both methods, Harris et al. (2003) found that participants recruited in the proactive phase were more socially and economically disadvantaged than those recruited in the reactive phase. This is likely because the community health center serves an African American population with a 93% rate of incomes below poverty level, compared with the metropolitan area surrounding the clinic, in which 28% of the African Americans had incomes below the poverty level in that year. From this, it may be assumed that proactive strategies may be more successful in studies looking to recruit lower-income African American participants. The investigators learned that ensuring the recruitment strategy could remain flexible when designing the trial was imperative to successful recruitment. When the proactive recruitment strategies were unsuccessful, alternative methods were used via the reactive strategies to successfully recruit minority participants (Harris et al., 2003). One difference between the success reported by Harris et al., (2003) and Williams and Corbie-Smith (2006) in making midstream modifications to the recruitment strategy is that the smoking-cessation trial described by Harris et al., (2003) took into consideration a flexible recruitment strategy upfront when designing the trial.

Brown et al. (2012) conducted a recruitment experiment to determine whether sending personalized recruitment letters and including ethnic-specific health information in the letter increased the response rate of minorities recruited for a weight-management trial for obese women. The response rate was 34.4% higher among the women who received letters that included health information specific to ethnic minority women than among those women who

received generic letters. However, personalized letters did not result in a higher response rate. In this weight management trial, 33.7% were minorities. Of the minority women enrolled in the trial, 68.9% were recruited using direct mail letters. Of these women, 75.8% were sent a letter addressed to them and 24.2% were referred into the trial by a family member or friend who received the letter (Brown et al., 2012). This suggests that direct mail letters are a successful technique for recruiting minority women into clinical trials.

A personalized letter containing a statement regarding heart disease statistics for the general American population sent along with a recruitment flyer mailed to Hispanic employees of Stanford University was found by Kiernan, Phillips, Fair, and King (2000) to result in a significantly higher response rate (7.8%) to a dietary intervention study than the Hispanic employees who received only the recruitment flyer without the personalized letter (2.1%). This study's findings are in direct conflict with the study findings by Brown et al. (2012) who found that a personalized solicitation letter did not result in a higher response rate. Kiernan, Phillips, Fair, and King (2000) have found that a personalized approach to minority recruitment was successful and employees were four times more likely to respond and be eligible for participation if they received a flyer along with a personalized letter than those who only received a flyer. Kiernan et al. (2000) also found that the response rate among Hispanic employees who received the recruitment flyer in addition to a personalized letter containing heart disease statistics specific to Hispanics was higher (9.1%) than those who received the flyer with the personalized letter containing statistics pertaining to the general American population (6.5%). Although this finding wasn't significant, it aligns with the finding from Brown et al. (2012) that providing ethnic-specific disease information yields a higher response rate from minorities.

The examples of successful minority recruitment that were just discussed are very specific to the community in which the study was taking place. Additionally, the recruitment strategies were not consistent across all sites. As demonstrated by the unsuccessful community outreach strategies described by Phillips et al. (2004), these cultural-, site- and community-specific strategies employed cannot be generalized across all studies. This leads to a discussion on the lack of evidence-based minority recruitment strategies.

Lack of evidence-based minority recruitment strategies. There is still a lack of evidence-based strategies for minority recruitment. The successful examples discussed involved a combination of several different recruitment strategies. A gap in the evidence remains as to the effectiveness of any single strategy (Duda et al., 2011; Ejiogu et al., 2011; Etkin, Farran, Barnes, & Shah, 2012; Germino et al., 2011; Harris et al., 2003). For example, Duda et al. (2011) found that the site-driven recruitment plans implemented in their study resulted in an increased number of minority participants enrolled. However, although minority recruitment increased significantly after the targeted recruitment strategies were implemented, there wasn't a common strategy that worked consistently well across all seven sites with targeted recruitment. Additionally, these seven sites were selected because they were already enrolling minority participants (Duda et al., 2011). The success that Duda et al. (2011) found may be due to the investigator sites themselves and their experience rather than an individual recruitment strategy. Their targeted strategies also required staff to devote a significant amount of time to recruitment efforts, taking away from their clinic responsibilities. It is also important to note that these sites received infrastructure support by the NIH for disseminating information in minority communities.

Germino et al. (2011) employed a population-specific approach to recruitment that will require systematic testing of the strategies implemented in order to know which individual

strategies were successful in recruiting and retaining younger African American breast cancer survivors into the study. The researchers' approach expanded on the existing literature on the importance of community engagement in research. Through a combination of factors, such as addressing barriers to research participation, taking into account cultural preferences, as well as bridging gaps across cultures and communities through the use of cultural brokers, they were able to successfully recruit African American women into this study. Although the researchers were successful in recruiting minority women participants, the strategies were very specific to the community and they can only deduce that the combined strategies were successful. Germino et al. (2011) did not evaluate the effectiveness of the strategies on an individual level. The strategies employed also required extra time commitment not typically provided by investigator sites.

Similarly, a limitation of the study conducted by Harris et al. (2003) is that they did not systematically test the successful recruitment strategies. The majority of enrolled participants were recruited through the radio ($n = 209$), followed by referrals from a friend ($n = 152$). The manner in which participants' friends found out about the study in order to make the referral is unknown. For instance, study staff members may have approached them during the proactive stage, or they could have heard about the study through the media campaign. Additionally, referral by a friend was found to be similar to the reactive strategies in the ability to recruit a population that was eligible for and more likely to enroll in the study. Although Harris et al. (2003) demonstrated successful recruitment strategies, it will be important to further test these strategies to understand which can be attributed to successful recruitment.

Ejiogu et al. (2011) demonstrated how recruiting minority and socioeconomically disadvantaged participants can be successful by infiltrating the community to better understand

the needs of the targeted patient population and gaining the support of community stakeholders. However, they used a combination of several strategies that would need to be evaluated in order to determine which strategy or strategies were successful in recruiting minority participants. Their recruitment efforts were directed towards the specific barriers of the targeted population in that particular community. Specific strategies that are successful in one community may not work in another because each community and culture has its own unique barriers. Similarly, Wallington et al. (2016) successfully recruited African American participants into non-interventional cancer clinical trials by employing cultural- and community-specific strategies that were relevant to a specific population in the Washington, DC metropolitan area. The authors recognized that strategies might need to vary when recruiting participants from other racial and ethnic groups and in other geographic locations (Wallington et al., 2016).

While recruitment for the TRAC study was successful in exceeding the minority recruitment target, it was largely due to the geographical area in which the study was conducted and the inclusion of a research center that was already well established in the local community. In fact, the researchers were not successful in recruiting minority participants from communities in which the center did not already have established relationships (Etkin, Farran, Barnes, & Shah, 2012). The extent of community engagement and involvement that was practiced in this study is beyond the traditional realm and resources of industry investigators. Likewise, the hands-on approach discussed by Ejiogu et al. (2011) that involved direct community engagement by the site staff and PIs, including the creation of a community advisory board, is not common practice in industry-sponsored studies. Instead, the focus is on reducing R&D costs, while completing a trial in the shortest amount of time possible to expedite the drug development process (Kermani & Bonacossa, 2003; National Academies of Sciences, Engineering, and Medicine, 2016;

USHHS, OIG, 2000). However, this level of involvement greatly contributed to these studies' minority recruitment successes. The sustainability of this approach is yet to be documented among industry-funded studies.

Lack of evidence-based minority recruitment strategies in benchmark trials. There are three benchmark trials that focused specifically on ethnic minority populations: AASK, the African American Heart Failure Trial (A-HeFT) and ALLHAT (Taylor & Wright, 2005). A brief description of each follows, as well as a discussion on the lack of evidence-based minority recruitment strategies or lack of sustainable strategies for these benchmark trials. These examples provide further evidence of a need to better understand what contributes to successfully recruiting minority participants into industry-funded clinical trials. Even with these trials that specifically required a large number of minority participants, variability in recruitment approaches and success rates among the government-funded trials and lack of information on recruitment approaches used in the industry-sponsored trial demonstrates that more research is required in this arena.

AASK. The AASK trial was conducted to compare the effectiveness of different treatments in African American patients with renal insufficiency due to hypertension. The AASK trial was funded by the National Institute of Diabetes and Digestive and Kidney Disease, as well as by NIH grants. Financial support and drug donations were also provided by Pfizer, AstraZeneca and King Pharmaceuticals (Phillips et al., 2004). Before beginning enrollment into the AASK study, a pilot study was conducted to determine the feasibility of the proposed recruitment, retention and data collection procedures. The pilot study enrolled 94 African American participants, most of whom were recruited through the primary recruitment strategy of clinic-based chart screening and referrals (67%). Four secondary recruitment strategies were also

encouraged: mass mailing campaigns, mass media campaigns, community-based screening and referrals of relatives and friends of existing patients. The contributions and effectiveness for each of the secondary recruitment strategies varied widely by research site. Screening through clinical practice provided only 17% of the participants for pre-screening, yet yielded 67% of the randomized participants. Mass mailing provided the most interested patients for pre-screen (44%), but only 15% of the patients recruited through mass mailings were randomized. Of note, 75% of the participants were men (Whelton et al., 1996).

The most-effective recruitment strategy for recruiting patients into the AASK trial was the same as in the pilot study—screening patients in clinical practice. This included pre-identifying prospective patients through chart reviews, as well as primary care provider referrals. Eighty-three percent of patients were recruited for a screening visit through this method and provided 58% of the randomized patients. However, this required a total of 558,295 chart reviews to randomize 635 patients, requiring a tremendous amount of resources from the clinics. The number of chart reviews per randomized patient varied widely among the 21 clinics, ranging from 42 to 6,381 charts reviewed per site, averaging 879 charts reviewed per randomized patient. This was a much less effective strategy in the full trial than in the pilot study and also not likely to be feasible from a resource perspective in an industry-sponsored study without additional support. Similar to the pilot study, there was variability in the use and effectiveness of the other recruitment strategies across the 21 clinic sites. As previously discussed, community recruitment was not an effective strategy for this study. This was likely because patients with hypertension and renal dysfunction are asymptomatic with low awareness of these diseases in the community. This suggests that community-based approaches are dependent on the disease being studied and cannot be generalized as being effective in all populations, diseases or communities. Recruitment

in general proved to be challenging and the recruitment period was extended by 1 year in order to meet the recruitment goal (Phillips et al., 2004).

The African American Heart Failure Trial (A-HeFT). Another benchmark trial focusing on minorities was A-HeFT. A-HeFT was sponsored by NitroMed, Inc., a privately held pharmaceutical company that is no longer in existence (businesswire, 2008; Mitchell et al., 2011). Amid much controversy, the first race-specific drug, BiDil, was approved by the FDA in 2005 based on the results of A-HeFT. BiDil was approved for the treatment of heart failure in African American patients when added to standard therapy. It was approved after demonstrating effectiveness and showing a mortality benefit in African American patients during A-HeFT, which recruited over 1,000 African American participants (Brody & Hunt, 2006). The decision to conduct the study only in African American participants was justified by both NitroMed and the FDA due to the fact that the post hoc subgroup analyses from two similar studies conducted previously indicated that African American and white patients had a different response to BiDil. There was an effect in treatment in African American patients, yet little or no effect in white patients using the fixed-dose combination of two generic drugs to study the effects against placebo and an existing treatment. Based on this fact, the FDA had reason to believe that a large study that included both African American and white participants wouldn't detect a treatment effect in white patients. Coupled with the well-known disparities in heart failure rates that African American patients suffer from more so their white counterparts and the infeasibility of a mixed-race study that would be too large and take too long to conduct (from a cost and time perspective to get a needed drug to market), the decision to only include African American participants was made (Temple & Stockbridge, 2007). An abundance of literature discusses A-HEFT, including the controversy the study sparked over the rationale for including only African

American participants and using race and ethnicity to categorize participants to test response to drugs. However, no literature discussed the recruitment strategies employed to recruit the 1,050 African American participants. This is likely due to the fact that this was an industry-sponsored study and not supported by NIH grants. However, this important study provides more evidence on the genetic differences in response to different treatments and, therefore, reinforces the importance of clinical trial participation parity.

ALLHAT. The third benchmark trial, ALLHAT, was funded by the NHLBI. Financial support was also provided by Pfizer to provide additional recruitment resources to study sites. The study medications were supplied by three pharmaceutical manufacturers: Pfizer, AstraZeneca, and Bristol-Myers Squibb (Wright et al., 2001). The primary goal of ALLHAT was to evaluate different treatment regimens to examine the reduction of CVD incidence between the different treatment arms in 40,000 patients with hypertension aged 55 or older in a racially diverse group, 55% of which needed to be African American (Wright et al., 2001). Initial recruitment strategies implemented by the Recruitment and Eligibility Subcommittee included mass mailings, as well as encouraging sites to conduct chart reviews, obtain physician referrals and conduct community screening activities. Some sites also advertised locally. Enrollment into ALLHAT was slower than projected, which resulted in several study design and recruitment strategy changes being implemented in an effort to recruit the required 40,000 patients. These changes included increasing the number of sites from 270 to 600, including expanding the geographic region to Canada and Puerto Rico; extending the recruitment period by 1½ years (which resulted in extending the follow-up period by an additional year in order to achieve sufficient power); opening up the eligibility criteria to also include smokers and reducing the minimum age requirement from 60 to 55 years; increasing site reimbursement for patient

enrollment; providing funding for additional site resources; and instituting a national advertising campaign (radio, print and direct mail letters). Similar to what was reported by Harris et al. (2003), a flexible approach is sometimes required. These changes all ultimately led to the successful recruitment of 42,419 participants, 54% of whom were minorities. African Americans represented 36% of the study participants; however, the goal of recruiting at least 55% African American participants was not achieved. As demonstrated by Durant et al. (2007), recruitment goals set for African Americans are not likely to be achieved.

Minority participation in ALLHAT is still considerably higher than most studies, but, unfortunately, an analysis of effective strategies specific to recruiting minority participants was not conducted. Since it was a practice-based study and nearly all of the participating patients were from the practices that were involved in the study, it is expected that the minority participants primarily were recruited because sites with a large minority patient group were selected. For example, the addition of Puerto Rican sites also yielded a high number of minority participants (Pressel et al., 2001). However, the ALLHAT sites with a high African American patient population recruited at the same rate as those sites recruiting other populations. Wright et al. (2001) contributed the parity in recruitment rates to investigator motivation, training and existence of a trusting relationship between investigators and their patients, instead of on the diverse demographic patient population of these sites. While this is promising, it contributes to the fact that not only is there a lack of understanding of evidence-based minority recruitment strategies, but also a lack of understanding of the interacting components and characteristics that may contribute to an investigator site successfully enrolling minority participants.

Lack of evidence-based minority recruitment strategies summary. In summary, many studies in the literature focus on the barriers to minority participation in clinical trials and not the

successful strategies. The successful examples of minority recruitment discussed in the literature involved government-funded studies and employed strategies that not only would be costly and difficult for industry to adopt without a system change but also vary across different studies, sites, patient populations and communities. Even the benchmark studies that specifically required minority participation reinforce the fact that there is a lack of evidence-based minority recruitment strategies.

Summary of the Literature

Disparities exist in clinical trial participation, with racial and ethnic minority populations underrepresented in most studies (Diehl et al., 2011; Duda et al., 2011; Killien et al., 2000; Martin, Negron, Balbierz, Bickell, & Howell, 2013; Murthy, Krumholz, & Gross, 2004; The Society for Women's Health Research & FDA, 2011). There are many reasons for this disparity as many barriers have been identified that preclude minorities from participating in clinical research studies. Some of these barriers include individual patient beliefs and concerns about participating in research; lack of awareness of clinical trials; lack of trust in the healthcare system; cultural differences between researchers and patients; as well as doctor-patient communication barriers (Ejiogu et al., 2011; Ford et al., 2012; Ford et al., 2013; Swanson & Ward, 1995; Williams & Corbie-Smith, 2006). However, minorities are interested in learning about clinical trials and tend to enroll when they are given the opportunity (Diehl et al., 2011; Jimenez et al., 2013; Markman, Petersen, & Montgomery, 2008; Simon et al., 2004; Wendler et al., 2006). Research sites may be better equipped to provide greater access to clinical trials to minority populations when they follow guidance suggested for delivering culturally competent healthcare services and exhibit culturally competent techniques (Brach and Fraserirector, 2000; Purnell et al., 2011).

Based on findings from a prior study, another area that could help to improve access and provide minorities with opportunities to enroll is working toward increasing the value investigators place on minority clinical trial participation, since this has been found to play a role in the success of recruiting minority participants into clinical trials (Williams & Corbie-Smith, 2006). This is important because minorities are less likely to be offered a clinical trial than their white counterparts (Baquet, Commiskey, Mullins, & Mishra, 2006; Diehl et al., 2011; Simon et al., 2004). It has been found by some researchers that PIs' perceptions of minority patients being ineligible, noncompliant or disinterested provide explanation for this disparity in recruitment practices (Durant et al., 2007; Eggly, Barton, Winckles, Penner, & Albrecht, 2015; Howerton et al., 2007; Simon et al., 2004). Furthermore, many PIs, including those receiving NIH-funding, do not set minority recruitment goals (Boden-Albala et al., 2015; Durant et al., 2007). While the literature describes PI attitudes and perceptions in relation to minority recruitment, it is also important to understand characteristics and perceptions of other research site staff members who often play a critical role in clinical trial recruitment. This is an area in which there is an opportunity for contribution to the literature.

Research center infrastructure and experience has also been found to impact the successful enrollment of minority participants (Etkin, Farran, Barnes, & Shah, 2012; Joseph & Dohan, 2009). For example, study site staff inexperience with the recruitment of minorities is a barrier to minority recruitment, as is clinical research sites inability to address the health literacy needs of patients (Ejiogu et al., 2011; Livaudais-Toman et al., 2014; Williams & Corbie-Smith, 2006). Many organizations, even those receiving NIH-funding, are limited in their focus on minority recruitment because of infrastructure barriers and the additional cost of translating materials (Durant et al., 2014; Joseph & Dohan, 2009).

Existing literature suggests that characteristics related to both specific research sites and individual investigators may have contributed to their successful enrollment of minorities into clinical trials (Boden-Albala, 2015; Duda et al., 2011; Jimenez et al., 2013; Joseph & Dohan, 2009; Williams & Corbie-Smith, 2006; Wright et al., 2001). More research is needed in this area to determine what those specific characteristics may be, including site staff perspectives and characteristics and how they may play a role in minority recruitment. For example, cultural, community and site-specific minority recruitment strategies have proven successful in NIH-funded trials (Duda et al., 2011; Ejiogu et al., 2011; Etkin, Farran, Barnes, & Shah, 2012; Germino et al., 2011; Wallington et al., 2016). There still remains a lack of evidence on what specifically contributes to successful minority recruitment because while success has been experienced, it was the result of a combination of several strategies. These strategies were also specific to the local communities in which the studies were being conducted and may or may not be generalizable to other geographic areas. Success also may have been due to characteristics of specific research sites and/or researchers themselves, leading to an unclear explanation as to what the specific elements are that led to their success (Duda et al., 2011; Ejiogu et al., 2011; Etkin, Farran, Barnes, & Shah, 2012; Germino et al., 2011; Harris et al., 2003; Wallington et al., 2016). Additionally, as the examples discussed were from NIH-funded studies, they have a minimum requirement for enrolling racial and ethnic minority participants as a stipulation of receiving funding (USHHS, NIH, 2001). Hence, these successful examples discussed could be due to additional funding and support sites received to amplify their recruitment efforts.

Exploring environmental elements that may be involved with minority recruitment holistically, including research site staff perceptions and organizational characteristics, among other factors from an ecological perspective, will contribute to filling these gaps in the literature

and facilitate a more comprehensive understanding of what specific elements are involved in the active recruitment of minority participants into industry-funded clinical trials. This will also provide a significant contribution to the literature since the existing peer-reviewed literature describing minority clinical trial recruitment is solely related to NIH-funded trials. Additionally, it offers a wide view for understanding environmental factors more wholly from the perspective of healthcare professionals involved in clinical research. Once these factors are better understood, industry stakeholders involved with clinical research can better support minority recruitment initiatives.

Chapter III

METHODOLOGY

The purpose of this study was to understand the socio-ecological elements that are involved in the active implementation of racial and ethnic minority recruitment practices for biopharmaceutical-funded trials in the United States. A qualitative design was selected utilizing semi-structured, in-depth interviews in order to allow participants to “express their own understandings in their own terms” to appropriately capture their perceptions and experiences (Patton, 2002, p. 348).

Study Design

The study design is a descriptive, exploratory, general qualitative study. A general qualitative study “involves collection of data in an effort to characterize human experience as it occurs naturally” to capture participants’ perspectives (Portney & Watkins, 2000, pp. 14-15). When conducting qualitative research, the researcher is the key instrument and attempts to identify the complex interactions of factors within the context of the data to gain an in-depth understanding of how a phenomenon is experienced by individuals (Creswell, 2013). The study is descriptive in that it involves describing what is prevalent regarding a phenomenon as it naturally occurs to create a better understanding (Bickman & Rog, 2008; Kumar, 2011; Portney & Watkins, 2000). This research is also exploratory as it involves examining a phenomenon in which little is known and “explores its dimensions, including how it relates to other factors” (Kumar, 2011; Patton, 2002; Portney & Watkins, 2000, p. 14). This design was selected to study this topic because of the gap in the literature on the specific elements involved when a research site is actively focused on minority recruitment, including site staff member and organizational characteristics. This understanding is best achieved when participants are allowed to express

their own perspectives and experiences rather than fitting them into the researcher's pre-defined categories (Patton, 2002). This study design allowed for gaining insight into the personal perceptions, experiences and behaviors of individuals who work at a clinical research site regarding trial recruitment and what factors play a role in their actions regarding minority recruitment. Semi-structured, in-depth interviews were conducted to achieve this.

Research questions. Since this research study utilized a qualitative design, there are no hypotheses accompanying the research questions. One overarching research question guided the study:

- What are the socio-ecological elements that are involved in the active implementation of racial and ethnic minority recruitment practices for biopharmaceutical-funded trials in the United States?

This research question is important because it addresses the gap in the literature on what specific elements contribute to successfully recruiting minority participants into industry-funded clinical trials from a socio-ecological perspective. To support the overarching research question, five primary research questions guided the study:

1. How are intrapersonal site staff elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?
2. How are interpersonal site staff elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?
3. How are organizational elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?
4. How are community elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?

5. How are policy elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States?

These five primary research questions address different components of the socio-ecological model, the conceptual framework that guides this study. The exploratory and descriptive nature of the overarching research question fit the exploratory and descriptive study design and the qualitative data analysis methodology as discussed in the literature and that was utilized to analyze the data in this study.

Sample Selection

Purposive sampling was used to identify potential participants based on the inclusion and exclusion criteria. In qualitative research, information-rich samples are typically selected purposefully by the researcher on the basis of specific criteria that will allow for studying this topic in-depth to learn about issues of central importance to the purpose of the study (Patton, 2002; Portney & Watkins, 2000). Snowball sampling was also utilized. It was suggested that those individuals contacted may pass along the study solicitation to other potential candidates who are involved with minority recruitment for clinical trials (Patton, 2002; Portney & Watkins, 2000). In this research study, participants were involved with actively recruiting racial or ethnic minorities for biopharmaceutical-sponsored clinical trials. As this study was bound to be US-specific, participants needed to reside in the United States. Other inclusion criteria included being 18 years of age or above and having the ability to understand and speak English.

The sample frame from which to recruit was established from publicly available data that identifies clinical trial research staff based on the medical conditions in which they specialize, as well as geographic location. The PI used the publicly available data to create a targeted recruitment list inclusive of clinical trial research staff located in geographic areas of the United

States with a large ethnically diverse population, as well as those involved with clinical trials in disease areas that disproportionately affect racial and ethnic minority populations.

Sample size. The study required a sample size of 15 individuals who provided their insights on and experiences with recruiting minority participants into clinical trials. These 15 individuals provided adequate information to “elucidate the particular” in reaching an understanding (Creswell, 2013, p. 157). G*Power is not used to calculate sample size in qualitative studies. Instead, data are collected until the categories and themes become saturated, meaning that fresh data no longer gleans new insights (Creswell, 2014). As such, there are no sample size limitations in qualitative inquiry and, instead, participants should be selected to provide information-richness to the study findings (Patton, 2002). Patton (2002) recommends specifying minimum samples “based on expected reasonable coverage of the phenomenon” (p. 246). The goal is to fulfill the intent of qualitative research to explain the particular in depth, and not to generalize (Creswell, 2013; Merriam, 1998). Typically, a sample size between 10 and 15 individuals provides in-depth coverage of the phenomenon to reach redundancy in qualitative research (Creswell, 2013; Lincoln & Guba, 1985). According to Guest, Bunce and Johnson (2006), interviewing 12 participants is sufficient when it is a relatively homogeneous group and the goal is to describe a shared perception or behavior. Therefore, as this was a qualitative study utilizing interviews, inclusion of 15 participants is in accordance with guidance that has been established by qualitative experts. Additionally, data saturation was achieved during this study as these 15 individuals provided adequate information to reasonably describe the elements of actively implementing minority recruitment practices in order to reach an understanding.

Sampling Procedure. As previously mentioned, the PI used publicly available data to create a targeted recruitment list. Upon Institutional Review Board approval, the PI emailed the

Study Solicitation to individuals on the target recruitment list. The Study Solicitation provided instructions for individuals interested in participating to confirm their interest, as well as offer the opportunity to pass along the invitation to other individuals who may qualify for participation. Individuals confirmed their interest in participating by clicking on a hyperlink that was provided in the Study Solicitation that directed interested individuals to a registration form for them to indicate that they would like to be contacted by the PI for study participation, provide preferred contact details and answer an eligibility screening question. If interested individuals met the online eligibility criteria, they were contacted by the PI to further confirm eligibility and to schedule a date and time to participate in a telephone interview. The PI re-contacted individuals who did not respond to the Study Solicitation after 1 week by sending a solicitation reminder via email and/or placing a telephone call. A last reminder for any remaining individuals who did not respond took place 3 weeks following the initial Study Solicitation. Prior to the telephone interview taking place, the PI emailed the participant the Informed Consent Form (see Appendix B) and provided a personal fax number for returning the signed consent form prior to the start of the interview.

The recruitment period was 5 months in duration, during which time a total of 165 individuals were invited for study participation. Of those 165 individuals, 25 declined participation; three accepted and then were no longer reachable; six had incorrect contact details listed in the publicly available data and were not reachable; two accepted but were ineligible; 94 did not respond; and the maximum number of follow-up attempts were reached for 20 individuals. Following this recruitment process, 15 individuals participated in this study.

Data Collection

Data was collected using semi-structured, in-depth telephone interviews. A semi-structured interview format was used to allow respondents to more freely share their perceptions and experiences, while still allowing flexibility for probing for additional information as needed. Specific interview questions were used as a guide to interview the participants (see Appendix A). While the development of the interview guide was informed by the socio-ecological model, the questions were constructed to be broad to allow for more freedom of response by the participants. Certain steps were taken for the conduct of the interviews, as described next.

Interview process—before the interview. In qualitative research, the researcher is the instrument. Therefore, it is important that the researcher is attentive to and discloses his or her personal perspectives and experiences with the phenomenon under study that may affect data collection, analysis and interpretation (Lincoln & Guba, 1985; Merriam, 1998; Patton, 2002). In this study, the credibility of the researcher was substantiated through the PI's reflexivity/positioning statement (see Appendix C) indicating her position in terms of her experiences with the topic being explored in this study prior to conducting any interviews. Reflexivity is when qualitative researchers position themselves by becoming self-aware of the origin of their perspective. This involves becoming conscious of the biases, values and experiences that they bring with them, including how that shapes data collection and interpretations of the data (Creswell, 2013; Patton, 2002). Prior to conducting each telephone interview, the PI assigned the individual a participant number to be used to identify the participant during the transcription and data analysis phase to maintain confidentiality. As previously mentioned, the PI obtained a signed informed consent from each participant prior to the start of the interview.

Immediately before the interview started, the PI explained the goals of the research, assured the interviewee that responses would remain confidential and asked for permission to audio record the interview.

Interview process—during the interview. Upon permission, the telephone interviews were recorded utilizing the audio recording functionality from freeconferencecall.com. An Olympus Digital Voice Recorder model number WS-853 was used to serve as a back-up recording mechanism. Interview questions were asked one at a time using the interview guide, asking probing questions as relevant and providing transitions between major topics. The PI tried to remain neutral and unbiased and took brief notes during each interview. Each interview was approximately 1 hour in duration.

Interview process—after the interview. Due to the nature of the topic being studied, questions related to the study participant's demographic characteristics, as well as characteristics related to the organization in which he or she worked at the time of the interview, were asked at the end of the interview (see Appendix A). After the interview, the researcher took notes regarding the interview.

Data Analysis

While data collection and data analysis are simultaneous processes in qualitative research, formal data analysis commenced once data saturation had been reached (Creswell, 2014; Merriam, 1998). Data analysis for this study was conducted as follows.

Transcription. Each recorded interview was transcribed verbatim, increasing reliability. A transcription key was used to capture voice inflection and emphasis participants placed on their words. All personally identifiable information was removed and confidentiality of the participants was maintained by referring to each participant only by his or her participant

number. After transcription, the transcripts were checked to make sure no obvious mistakes were made during the transcription by playing the recording back and ensuring that it matched the transcription.

Organizing the Data. The raw data was organized by creating a “database” in which to store all information collected. This included interview transcripts, participant demographic information and any researcher notes or reflections on the interviews (Creswell, 2013; Merriam, 1998). Atlas.ti data analysis software was utilized for this purpose (Frieze, 2019).

Reading and Memoing. The PI immersed in the data by reading transcripts in their entirety and reviewing all data collected, writing notes in the margins as applicable (Creswell, 2013; Merriam, 1998; Patton, 2002). This process allows the researcher to get a general sense of the information collected and reflect on the overall meaning (Creswell, 2014).

Coding and Categorizing. The next step was coding and categorizing. First, the PI formed codes by assigning a label to meaningful, recurrent segments of data (Patton, 2002). Codes were formed inductively based on information that emerged from the data (Creswell, 2013; Patton, 2002). The socio-ecological model was then used to categorize codes by each level of the model. All of the data for three interview transcripts were coded initially in order to develop a preliminary codebook that included definitions and examples for all of the codes created. A codebook is a set of codes with accompanying definitions and examples in order to guide data analysis and maintain consistency when coding the data (DeCuir-Gunby, Marshall, & McCulloch, 2011; Miles & Huberman, 1994). According to Creswell (2013), it is recommended to develop a codebook from three interview transcripts prior to obtaining inter-coder agreement. Prior to obtaining inter-coder agreement, intra-coder agreement was achieved by the PI re-coding a portion of an interview transcript and comparing it with the previously coded portion to assess

the level of consistency in coding (Miles & Huberman, 1994). Inter-coder agreement was then established by having an independent reviewer with expertise in qualitative data analysis audit the codes by coding data from a portion of a transcript independently, using the preliminary codebook that was developed. The independent reviewer and PI met to compare their analyses, discuss discrepancies and come to a consensus (Miles & Huberman, 1994). Both intra- and inter-coder agreements were achieved within the recommended ranges, which are between 80% and 90% (Creswell, 2013; Miles & Huberman, 2014). The codebook was refined based on the inter-coder review process and was then used as a guide for assigning codes to the data for the remaining transcripts (Creswell, 2013). The codes were continuously reviewed and defined throughout the coding process (Miles & Huberman, 1994). After all of the data were coded, major categories were developed based on patterns that emerged from the coded data (Creswell, 2013). As with the codes, the categories were classified by the socio-ecological model levels.

Establish Themes. Overarching themes were developed by further classifying several categories that formed a common idea and analyzing them to look for consistency and repetition in order to establish patterns and create the overarching themes (Creswell, 2013). The themes were categorized by each of the socio-ecological model levels.

Interpretation. Lastly, the PI interpreted, or made sense of, the data using themes to explain findings (Taylor-Powell & Renner, 2003). The socio-ecological model was used as a lens to interpret findings and explain the results. The interpretation was grounded in the larger research literature on this topic (Creswell, 2013).

Trustworthiness

Validity and reliability are specific to quantitative studies. As this is a qualitative study, trustworthiness standards need to be achieved instead. Trustworthiness demonstrates rigorous

methods were used for doing fieldwork in an attempt to assess the accuracy of findings as best described by the researcher and participants (Creswell, 2013; Patton, 2002). In other words, trustworthiness demonstrates that the researcher followed protocol and standards for conducting qualitative research such that the findings reported by the researcher accurately describe what the participants shared. According to Lincoln and Guba (1985), the criteria for establishing trustworthiness in qualitative studies are through establishing credibility, transferability, dependability and confirmability. Each of these concepts is described next.

Credibility. Credibility in qualitative research is the equivalent to internal validity in quantitative research and demonstrates that findings are worth paying attention to, based on establishing confidence in the truth of the findings (Lincoln & Guba, 1985). Credibility was achieved in this study through the following courses of action:

- Member checking was used during the telephone interviews to ensure the PI accurately interpreted the interviewee's statements (Creswell, 2013; Lincoln & Guba, 1985; Merriam, 1998)
- Independent reviewer examination was conducted to audit findings (Merriam, 1998)
- In addition to the themes that were formed, discrepant information that ran counter to the themes was also presented (Creswell, 2014)

Transferability. Transferability in qualitative research is the equivalent to external validity in quantitative research and refers to the extent to which findings have applicability in other contexts (Lincoln & Guba, 1985). Transferability was achieved in this study through the following course of action:

- Rich, thick description was provided when conveying the findings in order to make transferability judgments possible for the reader (Creswell, 2013; Lincoln & Guba, 1985).

Direct quotations from the interview data have been shared in Chapter IV to provide context to the themes that were derived from the data.

Dependability. Dependability in qualitative research is the equivalent to reliability in quantitative research and demonstrates that findings would be repeated if the inquiry were replicated (Lincoln & Guba, 1985). Dependability was achieved in this study through the following courses of action:

- Data collection procedures were guided by the study design, research questions and interview guide
- The interviews were recorded and transcribed verbatim (Creswell, 2013)
- Findings and interpretations were supported by the data collected (Lincoln & Guba, 1985; Merriam, 1998)
- A study database was developed to store all raw data (Creswell, 2013; Merriam, 1998)
- An audit trail maintained a chain of evidence that demonstrated how data were collected, how categories were derived and how decisions were made in deriving study findings (Lincoln & Guba, 1985; Merriam, 1998)
- A codebook was created to maintain consistency when coding the data (Creswell, 2014; Miles & Huberman, 1994)
- Inter-coder agreement was established by using an independent reviewer to analyze and code transcripts, as well as to audit the creation of categories (Creswell, 2013)

Confirmability. Confirmability in qualitative research is the equivalent to objectivity in quantitative research and refers to the degree to which findings are determined by the respondent's and not the researcher's biases (Lincoln & Guba, 1985). Confirmability was achieved in this study through the following courses of action:

- An audit trail maintained a chain of evidence that allowed data to be traced back to its original source (Lincoln & Guba, 1985; Merriam, 1998)
- Credibility of the researcher was maintained through reflexivity/positioning, becoming self-aware of personal bias (Creswell, 2013; Lincoln & Guba, 1985; Merriam, 1998; Patton, 2002)

Chapter IV

RESULTS

The results will be presented in two sections. At the end of each interview, several demographic questions related to characteristics of the interview participants, as well as the organization in which he or she worked at the time of the interview, were asked. Those results will be shared first. Second, the themes involved with active minority recruitment practices that emerged for each level of the socio-ecological model will be shared.

Demographics

The participants in this study were asked 19 demographic questions following the telephone interview. Table 1 provides a summary of the results related to characteristics of the interview participants.

Table 1

Interview Participant Demographics

Participant Characteristics	<i>n</i>	%
Clinical Research Experience		
1-5 years	1	7%
6-10 years	2	13%
11-15 years	5	33%
16-20 years	3	20%
Over 20 years	4	27%
Minority Recruitment Experience		
1-5 years	4	27%
6-10 years	1	7%
11-15 years	6	40%
16-20 years	4	27%
Over 20 years	0	0%
Duration at Site		
1-5 years	3	20%
6-10 years	4	27%
11-15 years	6	40%
16-20 years	1	7%
Over 20 years	1	7%
Current Role		
Owner ^a	3	20%
Principal Investigator ^a	3	20%
Research/Recruitment Lead	10	67%
Executive Director	1	7%

Interview Participant Demographics

Participant Characteristics	<i>n</i>	%
Patient-Facing Role		
Yes	14	93%
No	1	7%
Spoken Language other than English		
Yes	6	40%
No	9	60%
Spoken Language Other than English		
Spanish	2	13%
French	1	7%
Russian	1	7%
Chinese	1	7%
German	3	20%
Gender		
Male	8	53%
Female	7	47%
Ethnicity		
Hispanic, Latino or Spanish origin	2	13%
Not Hispanic, Latino or Spanish origin	13	87%

Interview Participant Demographics

Participant Characteristics	<i>n</i>	%
Race		
White	9	60%
Black or African American	3	20%
Asian	2	13%
Native Hawaiian or Other Pacific Islander	0	0%
American Indian or Alaska Native	0	0%
Mixed	1	7%

^aSome participants indicated they are both an owner and Principal Investigator.

The majority of participants (33%) have between 11 and 15 years of clinical research experience, as well as minority recruitment experience (40%). Forty percent of participants also indicated that they have been with their current organization between 11 and 15 years. However, it is important to note that of the participants who responded that his or her clinical research experience, minority recruitment experience or duration at his or her organization was between 11 and 15 years, it was not consistently 11-15 years across all three responses. Some participants focused on minority recruitment for longer than they have been with their current organization, for example.

The current role of the interview participants is as follows:

- Three participants own their organization that they opened specifically to improve access to clinical trials to minority patients—two own dedicated research institutions and one owns a community physician practice
- Three are PIs, two of which are also owners

- The majority of participants (10 out of 15) are responsible for overseeing recruitment activities within their organizations
- One participant is an executive director

Only one participant is not in a patient-facing role. During analysis, it became evident that this participant's responses did not consistently fit with the themes emerging for the other roles.

Six participants speak a language other than English fluently. These languages include Spanish, French, Russian, Chinese and German.

There were nearly as many female participants (47%) as male participants (53%), which is the exact same overall percentage of trial participants by gender in industry-funded trials reported by CISC RP (2017).

Participants were also asked if they consider themselves to be of Hispanic ethnicity, as well as which racial designation best describes them. Questions were asked in alignment with the FDA's guidance for industry on collecting race and ethnicity information in clinical trials (USHHS, FDA, 2016). Since respondents were asked to respond to both the race and ethnicity questions, some respondents indicated that they are of Hispanic ethnicity and white race. Figure 2 provides an overall representation of race and ethnicity in the study. Minority representation is 53%, considerably higher than the minority population in the United States, as well as representation in clinical trials (CISC RP, 2017; US Census Bureau, 2019). This may be explained by the fact that participants are researchers themselves focusing on minority recruitment and, therefore, likely interested in the topic of this study.

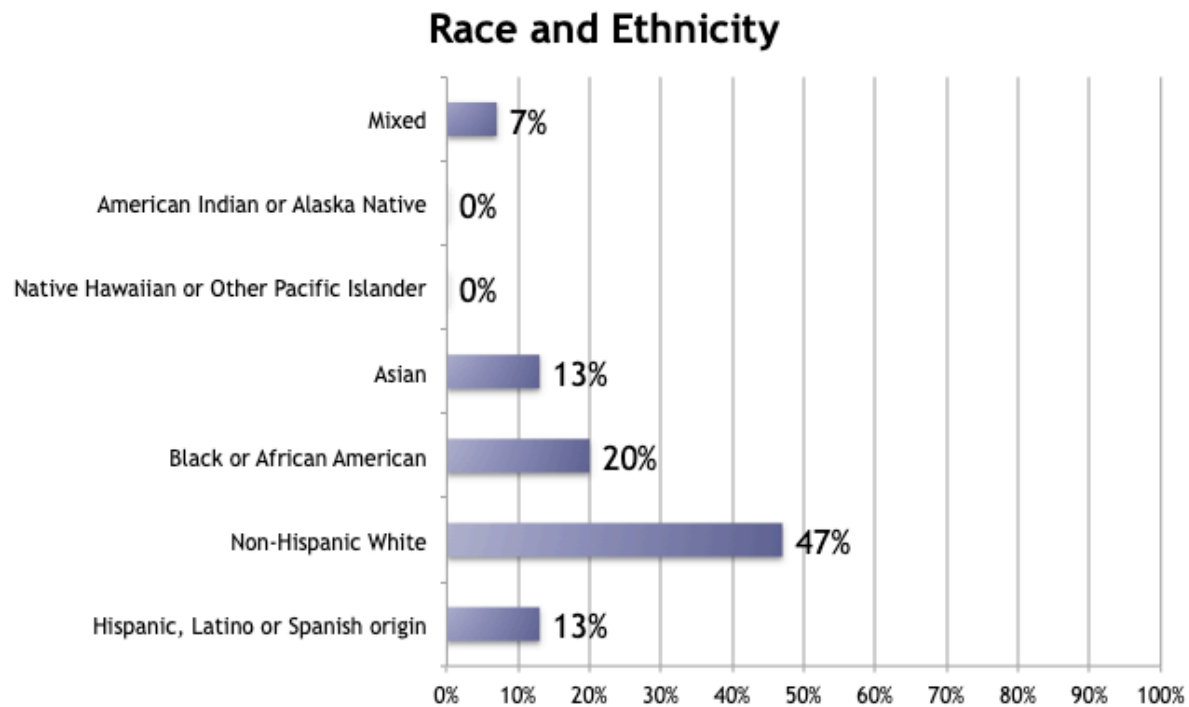


Figure 2. This bar chart illustrates the representation of race and ethnicity in the study. Participants were asked to provide a response to both race and ethnicity questions.

Table 2 provides a summary of the results related to characteristics of the organizations in which interview participants worked at the time of the interview.

Table 2

Organizational Demographics

Organizational Characteristics	<i>n</i>	%
Type of Organization		
Dedicated research institution	8	53%
Academic medical center	2	13%
Community physician/medical practice	3	20%
Public hospital	2	13%
Geographical Area of Clinical Trial Setting		
Urban	8	53%
Suburban	7	47%
Rural	0	0%
Trial Funding ^a		
Biopharmaceutical Sponsors	15	100%
NIH	3	20%
Therapeutic Area/Disease State of Trials ^a		
Cardiovascular	6	40%
Diabetes	7	47%
Neurology	5	33%
Oncology	5	33%
Urology	3	20%
Multi-therapeutic	4	27%
Racial/Ethnic Minorities Included on Research Team ^{a,b}		
Principal Investigator	10	67%
Sub-Investigator	10	67%
Recruiter	14	93%
Study Coordinator	11	73%
Study Nurse	9	60%
Minority Recruitment Goal Setting		
Yes	6	40%
No	7	47%
Cultural Competency Training Required		
Yes	6	40%
No	8	53%
% Minority Participation in Trials		
10% or less	3	20%
11-25%	2	13%
26-40%	3	20%
41-55%	1	7%
56-70%	2	13%
71-85%	0	0%
86-100%	3	20%

Organizational Demographics

Organizational Characteristics	<i>n</i>	%
% Minority Participation Representation of Community Demographics		
Less	4	27%
Same	6	40%
More	4	27%

Note. Due to missing responses, *n* values may not sum to 15 and percentages may not equal 100.

^aDue to multiple responses per participant, *n* values may exceed 15 and percentages may exceed 100.

^bRecruiter, Study Coordinator and Study Nurse are the same role in some organizations.

More than half of the interview participants (53%) work for dedicated research institutions, 20% of participants work for a community physician/medical practice, 13% of participants work for an academic medical center and 13% work for a public hospital. This reflects the trend with the investigator site landscape for industry-sponsored studies, which has shifted away from academic medical centers toward private practice or dedicated research sites used exclusively for research (USHHS, OIG, 2000; IOM, 2012). Private-practice community physicians and research institutes have replaced academic medical centers as the majority of industry-sponsored sites, increasing from 37% in 1994 to 74% in 2004 (Steinbrook, 2005). Increasingly, however, there has become a significant shortage of community physicians conducting clinical trials since 2009, moving towards an ever-increasing number of research institutions conducting industry-sponsored clinical trials. Part of the reason for this is the increasing complexity of procedures included in trial design, making conducting the study within the trial infrastructure a burden for community physicians and academic medical centers (IOM, 2012).

The geographic area of each organization's clinical trial setting is either urban (53%) or suburban (47%). None of the participants reported having a clinical trial setting in a rural area.

As part of the eligibility criteria, all participants need to be recruiting racial or ethnic minorities for clinical trials in which biopharmaceutical sponsors are the funding source. Three participants work for organizations that also receive NIH funding in addition to biopharmaceutical funding for the trials that their organizations conduct.

The therapeutic areas and/or disease states of trials that the participating organizations conduct include cardiovascular, diabetes, neurology, oncology, urology and multi-therapeutic, meaning that they conduct trials across a multitude of indications. The clinical trial experience of participating organizations in these disease areas is to be expected since minority patients are disproportionately affected by CVD, diabetes, Alzheimer's disease, cancer and urologic conditions, such as prostate cancer (Alzheimer's Association, 2020; USHHS, CDC, 2013a; USHHS, NIH, NCI, 2019).

The majority of study sites (93%) have included members of racial and ethnic minorities as part of their research teams. Only one participant responded that minority staff are not part of the research team; however, minority staff are part of the regular practice at that organization. Recommendations from the literature indicate that important components for overcoming distrust are ensuring research staff are the same race or ethnicity and speak the same language as the patients they are trying to recruit (Germino et al., 2011; Ford et al., 2013; Hinton et al., 2010). While 93% of the participants reported their organizations have minority recruiters, a lower number reported having minority PIs or Sub-Investigators (67%). Although some minority patients prefer to be treated by physicians of similar racial or ethnic backgrounds, minority recruiters also have been found to contribute to the successful enrollment of minority participants (Cook, Kosoko-Lasaki, & O'Brien, 2005; Ejiogu et al., 2011; Germino et al., 2011). In fact, Williams and Corbie-Smith (2006) found that the inclusion of minority recruiters, not PIs, was

associated with reported success of minority recruitment. This suggests that while including racial and ethnic diversity on the research team is important, the race of the PI alone may not be an essential component.

Nearly half of the organizations that participants work for do not set recruitment goals for racial and ethnic minority groups (47%), a finding that corroborates with the existing literature. In fact, recruitment goals for individual minority groups are not often set, even for NIH-funded studies (Boden-Albala et al., 2015; Durant et al., 2007).

More than half of the organizations (53%) do not require staff to take cultural competency training. Ensuring researchers are culturally sensitive has been found to be a contributing factor in the successful recruitment of minorities (Ejiogu et al., 2011). Although cultural competency is not often instituted as a training requirement among PIs conducting NIH-funded trials, it has been recommended as a best practice for minority recruitment by these researchers (Boden-Albala et al., 2015). When asked if staff members are required to take cultural competency training, a couple of study participants indicated that may be something they may incorporate in the future. Participant #3 said:

No but that's something I would like to do... that's a good question...as of today – no but that is something that I have considered to incorporate into my research uh process and it's a good question actually...

Participant #13 also shared:

No? No, it's a good idea though. That's not really been um an issue that's arisen but that would be a good idea 'cuz I never I mean I understand my competency on to other backgrounds but I haven't really evaluated any others. There's never really been a reason to...but it makes sense. Ya, I'm gonna write that down.

Eight participants reported that the percentage of minorities who participate in trials conducted by their organizations is 40% or above. This is unique among industry-funded research sites in that minority recruitment is on par with minority representation in the US population, which is currently 39% (US Census Bureau, 2019). This finding indicates that these participants recruit considerably more minorities than other organizations conducting industry-funded trials, since overall only 17% of trial participants in industry-sponsored studies are minorities (CISCRP, 2017). Four of these participants went on to report that they recruit more minority participants in their studies on average than the population demographics of their nearby community. This could be another indicator that researcher and organizational characteristics may play a role in recruiting minorities.

Themes

The second part of the results that will be discussed are the themes involved with active minority recruitment practices that emerged for each level of the socio-ecological model during the data analysis process.

First, the application of the socio-ecological model used for this study is explained. Because the study explored how the behavior and practices of individuals involved in clinical research who actively recruit minority participants are influenced by and influence environmental elements, this puts the research site staff at the intrapersonal level of the model. Therefore, the intrapersonal level encompasses characteristics of the study participants only, including their knowledge, attitudes, perceptions, behavior and demographics.

The interpersonal level is related to the interpersonal relationships of the study participants. The interpersonal level includes characteristics or interactions related to the interview participants' co-workers, colleagues and social networks.

The organizational level is defined as the research sites in which the study participants belong. This includes organizational characteristics such as policies, culture, processes, structure and mission.

Community is related to the community surrounding the study participants' research sites. The community level encompasses information related to patients; patients' social networks; local community stakeholders or organizations; and any outreach efforts conducted by the study participant or his or her research site that took place in the community.

Policy is related to national, state or local laws, as well as clinical trial policies. The policy level includes items such as government regulations on clinical trials; federal guidance related to clinical trial conduct; regulations, policies or expectations set forth by the trial funder (i.e. NIH or pharmaceutical sponsor); and the healthcare system.

In addition, because the study was designed to better understand perceptions and experiences of research site staff, most of the discussions and subsequent themes from data analysis were related to the intrapersonal and organizational levels of the socio-ecological model. Therefore, results are presented in the order of the socio-ecological model levels in which more themes emerged. First, findings in response to Research Question #1 are shared related to intrapersonal site staff elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States. Second, organizational findings related to Research Question #3 at the organizational level of the socio-ecological model are discussed. Next, community elements in response to Research Question #4 related to the community level of the socio-ecological model are discussed. Research Question #2 related to interpersonal site staff elements at the interpersonal level of the socio-ecological model is addressed next. Lastly, policy elements related to Research Question #5 are discussed.

There are 20 overarching themes that emerged from the interview data during the data analysis process. Table 3 provides an overview of these themes involved with active minority recruitment practices, along with corresponding levels of the socio-ecological model and corresponding research questions that are addressed.

Table 3

20 Themes Involved with the Active Implementation of Minority Recruitment Practices Emerged During Data Analysis that Represent Each Level of the Socio-Ecological Model

Research Question	Socio-Ecological Model Level	Theme
#1	Intrapersonal	Research is important
#1	Intrapersonal	Important to increase minority participation in clinical trials
#1	Intrapersonal	Frustration with barriers to recruiting minority participants
#1	Intrapersonal	Personal commitment to recruiting minority participants
#1	Intrapersonal	Satisfying work
#1	Intrapersonal	Evolving personally
#3	Organizational	Mission related to improving healthcare through clinical research
#3	Organizational	Mission guides recruitment efforts
#3	Organizational	Organizational commitment to minority recruitment related to providing community education
#3	Organizational	Organizational commitment to minority recruitment related to organizational structure
#3	Organizational	Culture of inclusion
#3	Organizational	Minority recruitment practices evolving based on learning

20 Themes Involved with the Active Implementation of Minority Recruitment Practices Emerged During Data Analysis that Represent Each Level of the Socio-Ecological Model

Research Question	Socio-Ecological Model Level	Theme
#4	Community	Should have access but don't: not just about location
#4	Community	Efforts to instill trust
#4	Community	Cultural sensitivity
#4	Community	Encouraging active role in healthcare and trial participation
#2	Interpersonal	Teamwork
#2	Interpersonal	No peer influence
#5	Policy	Lack of diversity emphasis
#5	Policy	Diversity emphasis attempts

Six intrapersonal themes that are involved with the active implementation of minority recruitment practices.

Research is important. The first theme at the intrapersonal level is research is important. Participants shared their personal point of view related to his or her perspective that clinical research is important. As participant #16 said:

... if research is done well it it's a win-win-win for everybody. It's a win for the patient, it's a win for the research team, and it's a win for...the pharmaceutical company that's sponsoring it and for the public in general.

In addition, participant #12 shared, “I think it’s a positive thing. I encourage everyone to do a research study...I really do, I think you get great...care...you’re helping out society...it’s all good.”

Participants also discussed how research is important in the context of believing what they do is important. Participant #3 shared, “I think what...I do is important. You know I think it’s important for the value of...the scientific validity of new drugs and uh new drug development...”

Important to increase minority participation in clinical trials. The second theme at the intrapersonal level is that participants not only believe that research is important, but they also believe that it is important to increase minority participation in clinical trials. Participants discussed this in relation to why they feel minority inclusion is important, including for generating generalizable knowledge in understanding if a drug is safe and effective in different populations. Participant #1 said:

Research for me is that you know we’re here to seek generalizable knowledge that’s what we’re trying to learn how this medication or medications or device works and we need more you know minorities to participate.

In addition, participant #3 shared:

...it’s important to understand...if we can extrapolate the data to... the general practice I think as a physician and I don’t think a lot of physicians think about this but you know I thought about it for a long time...when I’m looking at a drug you know for example when I’m looking at a blood thinner right an anticoagulant you know I’m looking at the studies that were done and you know that only had a few if any minority participation,

how can I say that this drug is safe? How can I say it's effective? You can't say that until the only way that's going to change is to get more representation in trials.

Participant #2 expanded on this by sharing:

... like I said we wanna start looking at precision medicine and how medication helps a person, people with the same indication but of different genders, races, age groups, you know it's very, very important that we include all people... in those studies...

Having equitable access to treatment options available in clinical research was also discussed as a reason why participants feel it is important to increase minority participation in trials. Participant #2 went on to say, "I also think it's extremely important for the patients in our health system to have access to the clinical innovations, the research innovations that are there."

Frustration with barriers to recruiting minority participants. The next theme is frustration with barriers to recruiting minority participants. Participant #7 said:

I really wanna see um basically effort at the end of the day...we are smaller companies and... we really wanna see industry-wide more...towards this and giving more help and support to encourage minority...group to participate in...pharmaceutical trials...but it just I feels like it's more frustration from my end... I wanna encourage them but I don't have the enough energy and effort...I'm too small... to change the whole big...picture...so that's just my frustration...I feel personally it's important to cover...all the diversity group, majority or minority, but um big picture wise, industry wise, it seems that they all ignore that part.

Frustration with barriers related to study design or lack of supportive materials that prevent access were also discussed. Participant #14 shared:

...this is a big issue, all of our trial materials need to be translated into different languages. And the fact that these consents for the most part are not translated routinely into Spanish, into other languages, is ridiculous...it should be a knee-jerk thing. You have a Spanish version, you have an English version, you have a Spanish version, you have an English and it's really only based on a lot of the sites depending where they are, maybe you know we'll we'll only do it then. Well if you know you have a... urban site like Chicago where you want to go ahead and do a trial and you have nothing translated in Spanish, you're not gonna do it because...you're then asking only for English speakers, ok and I think this is something that we have to really understand. You are excluding people because you will not...go ahead and translate a consent into the language and/or the study materials and/or the study questions...

Additionally, participants discussed communication barriers with patients, as well as expressed frustration with barriers preventing appropriate communication with patients.

Participant #14 shared:

I think there's a lack of understanding from the investigators um to understand the culture and the community itself and you know I have I have heard investigators say that's not my job that is my study team's job, that's the nurse's job, it's the social worker's job, it's the researcher's assistant's job, and I would argue and say no, actually it's your job. Um you are the PI and you are the person conducting the trial and if you have no interest or to even understand how the community operates - what are some of the barriers they face, um what their world looks like then you really shouldn't be doing a lot of these trials um that require um you know you actively recruiting... and I see this consistently where the community feels this. And the community is very smart and the community will say you

know the investigator never even came over here. You know, the study team only came. Or the investigator didn't have time to talk about results or midway...or...anything about the disease that's being studied and I think that's really sad and I think that's the reason why a lot of our minority recruitment is hurting. Um because the investigators itself and again I mean the PI um needs to be much more engaged in understanding his or her community in a real way, not just from what his people tell him or her about the community.

Personal commitment to recruiting minority participants. The fourth theme at the intrapersonal level is personal commitment to recruiting minority participants. Participants in this study demonstrated having a personal commitment to minority recruitment by initiating self-directed action for this purpose. Participant #3 said:

...about 14 years ago I went out in private practice and started my own research company and...I was focused primarily on recruiting uh patients from...racial minority ethnic communities uh then trying to improve outcomes in clinical research, participation of research...

In addition to initiating self-directed action, participants also demonstrated commitment by displaying determination or dedication towards recruiting minority participants. Participant #10 said:

I believe in medicine that works for everyone...I've made a commitment to...try and make that happen by hiring um people A) who are from the communities that we're trying to reach and B) who have a real desire to work in those communities and get those individuals engaged with science.

Participant #5 also discussed this idea:

A lot of people the moment I tell them um I'm in clinical research they say "oh how many people died in a study?" At the beginning it was for me shocking that people would even ask because for me it was a given that everybody out there knows that nobody actually nobody should die in a clinical trial, right? Uh and that's why we have all those regulatory authorities and all of this but guess what? People do not know and there is still this mentality in particular uh nowadays with... technology and social media if something bad happens it's immediately spread all over the world but all the good things that happened are not out there so therefore we have to fight against this myth that clinical research is something very bad... there are people that abuse the system and then its it's a slap in the face for the entire clinical research community trying to do our best because they did not play by the rules so we go back to the starting point and have to explain that the moment it's properly done the entire system tries to keep everybody volunteering in the system as safe as we can. We are not careless in this industry and this is something we have to explain there. And I will not give up doing this.

Satisfying work. The fifth theme at the intrapersonal level is satisfying work. Participant #15 shared:

I mean, it's kinda funny um maybe I'm telling you too much but... I'm 65 and I um everybody says to me "are you, when are you gonna retire?" ...I'm not ready to retire, yet I think about it because you know of course it's I can think about it but...I enjoy research and I enjoy this job...

Participants shared their job satisfaction in relation to having positive feelings from helping patients. For example, participant #16 said, "...you know the whole idea is to help people. I mean I love what I do."

In addition to being satisfied with their jobs, participants feel rewarded by their efforts that help patients. Participant #13 said:

I think it's very exciting...because it's something that you're actually able to possibly help somebody with as well as help a lot of other people with it. You know it's really rewarding experience just to be part of that. Um especially whenever you can talk to somebody who you know that could possibly benefit from this trial 'cuz...it'd be better for them I've met this fellow...he was supposed to be taking metformin every day twice a day. He was taking it once a week, he was borrowing it from his neighbor....I said listen, you need to come in and meet this doctor. Also I have some trials you might be good for. He didn't qualify for the trials 'cuz of his his hemoglobin A1c was way too high 'cuz he wasn't treated. Uh but the doctor was actually able to get him samples of the..medicine he needed uh to the point to where he was to actually able to get in to the threshold of what the study fit... What if I wasn't out there that day?...I'm not saying I'm the direct...reason but...the rewarding part of it is is I know because I had the opportunity to talk with him, he was actually able to take some action...and find a way to help himself...

Participant #3 also shared:

...it always makes me happy to you know I see a patient who may have had some reservations earlier on who have come in for their study visits, who are interested, who want to know the laboratory data, want to know how they're doing in the research

program... it makes me smile, it makes me happy that uh that we have not only educated a patient, patient who is had some reservations now patient is engaged, fully engaged...they're joining their follow-up visits uh and and you know at the end of the day I can sit down at my desk and say well I think we've made...a significant impact on this patient life...and just it's a good feeling for me.

Evolving personally. The sixth theme at the intrapersonal level is evolving personally. As previously mentioned, the responses for the one participant in the non-patient-facing role did not consistently fit with all of the themes that emerged from the data at the intrapersonal level. This is one example in which that participant's responses did not align. Aside from that individual, personal growth was a common theme that was discussed, with participant #3 saying:

...my feeling when I in participating in trials has made it really I think has made me a better physician, uh it's made me a better physician for my patients...in understanding their disease process, what they go through and how we can impact that in in clinical trials...

Evolving by changing perspectives was discussed in relation to becoming more sensitive to other cultures and cultural preferences. Participant #16 said:

I think I've um become just a little bit more knowledgeable and sensitive to the situations that different uh minority populations are in. Um I think over time I've learned more and so I think I'm just a little bit more sensitive to it now than I I was previously. I think that's kind of a continuous process.

In addition to changing perspectives, participants also discussed behaviors they have adapted in order to develop skills for interacting across cultures. Participant #5 shared:

I can give you a very real example. I needed to be exposed I'm a Caucasian through and through...so I have never dealt with the African American community besides having some friends and coworkers. So I personally even started...mingling this um community in a completely different way in my private time simply to learn more about the thinking and the culture of this particular group so I ended up line dancing sounds weird now...with a group of black women at the church. Why did I do this? I want to learn more about their culture and what kind of triggers them and what what they think about certain things. That's why I um even made the step into my private life um investing and learning and it's actually it it embraces my life.

Six organizational themes that are involved with the active implementation of minority recruitment practices.

Mission related to improving healthcare through clinical research. The first theme at the organizational level is having an organizational mission related to improving healthcare through clinical research. This includes healthcare for overall society, as well as at an individual patient level, by improving access to treatment options available in clinical trials. When asked to share his organization's mission, Participant #10 said, "to...treat and prevent Alzheimer's basically...we're being seen as a brand uh in the community that can deliver care...at a high-level and provide research opportunities at a high-level." Participant #3 also shared:

...when I developed it many years ago...my mission was to... recruit and to improve minority participation in clinical trials uh with the ideal to dispel misconceptions, to dispel myths, to improve outcomes in healthcare through participation in community-based research...

Mission guides recruitment efforts. The next theme at the organizational level is that the organization's mission guides recruitment efforts. Participant #10 said:

So...that idea that we have a mission to prevent and treat is is part of what we market and what we for lack of a better word sell to people that that being active in research is part of that ongoing process of treatment or prevention...whether you get better...or not it's part of the hope and the... intrinsic value...as a human being that...if you...have dementia for example being part of the solution ultimately.

In addition, participant #3 shared the following when asked about team members, indicating that the organization's mission is prevalent in the ways of working across the organization:

... they're engaged...they understand what our mission is and they're engaged... as engaged and as I am in in getting patients involved in studies, getting the patients engaged..."

Organizational commitment to minority recruitment related to providing community education. The third theme at the organizational level is organizational commitment to minority recruitment related to providing community education. Disease and general clinical trial education needs to be provided to minority communities prior to presenting a specific trial opportunity. As participant #14 said:

We've always talked about wellness first and we've always talked about how do we maintain where we're at so we so the decline that we know can happen can be lessened. So it's educating first. That then is built on, once we have that established, then we build on discussing recruitment into trials for specific...trials. This trial is for memory decline, this trial is for Alzheimer's, this trial is for stroke, this trial is for Parkinson's. Then we

start to build on that but the foundation always is how do we understand aging, how do we prevent the declines that we know can happen...

Additionally, the education needs to be culturally appropriate. Participant #10 shared:

...somewhere along the way we decided we needed to make that much more culturally appropriate um it had been uh developed basically with a bunch of rich older white um folks...in these sort of relatively affluent...retirement communities. And when we were talking with various community groups and other people we were realizing this didn't make any sense for um other groups and we wanted to ask those groups...what they wanted to learn about and how-what was the best way to deliver that? So we started... to try this in some black churches um and we...asked them, "...what of these pieces of [[Alzheimer's Disease prevention disease education]] do you want to learn, are there anything different?" um and then we also went into uh a couple of Latino serving organizations and asked them to help us refine it as well. And we got very different answers from each group... So we we took [[Alzheimer's Disease prevention disease education]] and we modified it to meet those um different demands...and then um uh started delivering that in those communities um as a first entry point to get people to know us as a center and build a little bit of trust by delivering some um education and service maybe connecting people with um resources in that area um off-line or things like that. So it was it was very little about recruitment and very much about exposure in the community.

Building on the needs to provide culturally appropriate disease and general clinical trial education prior to presenting a specific study opportunity, this requires a long-term investment.

As participant #6 said:

...and this is where many people make a mistake you know how do you recruit patients for a trial? You recruit patients for a trial, this...particular demographic by first educating them. By offering them something valuable that they can use without the pressure of or without the you know the pressure or the um the need to even have to discuss a study. You know...when you do this in in an effective manner, it means that you have to put up a lot of resources and quite honestly, many businesses are not willing to invest over the long term and this is where they go wrong. People want to see numbers on a spreadsheet and that's just not the case...when you're dealing with a certain demographic you cannot be there for that trial for just that study, your investment has to go beyond that, beyond the study number one and then before the study even starts, ... there's an initial investment that you have to make long before that so you can't look at numbers on a spreadsheet to determine that you know that that piece of advertisement worked – it doesn't work that way. Not...for the kinds of patients that we see.

Organizational commitment to minority recruitment related to organizational structure. The fourth theme at the organizational level is organizational commitment to minority recruitment related to organizational structure, which needs to be made conducive for recruiting minority participants. This includes hiring diverse staff from the local community, ensuring that staff members are able to speak the same language of the patients that are being recruited and adjusting hours of operation. Participant #10 said:

...we do make an effort to have people um who uh have comfort and knowledge uh of the communities we're trying to...recruit from um so you know for lack of a better way to say it this is sort of how the field says it - you want to have people in your organization

who look like the people you're trying to recruit right and who sound like the people you're trying to recruit and who grew up in the neighborhoods and...places.

While participants discussed their organization's commitment to creating an organizational structure in order to be better at recruiting minority participants, they also recognized room for improvement. Participant #10 went on to say:

...who could uh provide the full infrastructure that's needed it's not just recruitment I've gotta have um a a doctor to do physical exams who um can speak Spanish for example,...a Study Coordinator who uh can explain all of the procedures and do help with all the scheduling um who speak Spanish if that's the only language... I can make small investments for recruitment but to really fully get people into trials it is a very there's a critical mass...of investment...the center has to make um across the board in in all aspects of what we do...I can't just piece meal it 10% here, 10% there, for a 10% Latino population. I've gotta have a full-time person who can do uh who can do that, multiple full-time people who can serve that whenever we need it. And that's that's hard.

Surprisingly, participants discussed their organization's commitment towards overcoming barriers to making structural changes just as often as discussing barriers that prevent their organizations making structural enhancements. Participant #6 said:

And so a couple of years ago you know we made the investment of opening up our clinic on Saturday, which was a hard thing for us to do because you know from a business perspective it's an expensive thing to do Saturdays. You know additional staffing, physician time, you know you have limitations in terms of how...late you can see patients because of courier issues, I mean there's just a multitude of things and so it requires an up-front investment and a continued sustained approach...

Culture of inclusion. The fifth theme at the organizational level is culture of inclusion with regards to diverse inclusivity in clinical research, as participant #5 said:

So you know living in an area here where we have um a population heavily mixed with minority groups we have all of those people here and the kind of uh communication we have even on our lunch breaks or whatever now, it's different. We are listening to each other to learn about each other and our cultural backgrounds. That hopefully helps us to understand the motivation of minority groups better um to possibly being a part of clinical research.

Some participants discussed having a culture of inclusion derived from leadership support or directive. Participant #2 shared:

I think one of the more important things the aspects of how we recruit is that everyone is should have access to clinical research within our health system. It is imperative that everyone have an opportunity to take advantage of health alternatives and that's just a thought from um the top of the administration down to you know the clinical research program.

Additionally, participant #15 shared:

...our hospital system I mean...their whole mission is to serve anyone that comes through the doors...that kinda drives how you know research mindset is that everybody qualifies for a study and we don't care you know.

Minority recruitment practices evolving based on learning. The final theme at the organizational level is minority recruitment practices evolving based on learning. Participants discussed how their research organization's approach to minority recruitment evolves based on

lessons learned. Participant #3 said, "...you know we're continually evolving and uh trying to get understanding of what would help more..." Participant #6 also discussed this idea:

Well it's changed over time. You know, it's evolved over time and part of...that is because you know we don't have um how can I explain it – it's changed over time because as you start to gain the confidence and you start to to learn more about you know what what people want and what they respond to, you have to kind of customize as you go along.

Past experiences shape future recruitment approaches. As participant #5 said:

We were supposed as many other sites worldwide this year to enroll in a pharmaceutical...study uh to enroll people with a different uh ethnical background so um we were looking for Hispanics, for Asians and for African Americans. Um we thought living in a hot spot of a very mixed culture here um around San Diego would make it easier and boy did we learn that it has nothing to do with the statistics of the population but it has more to do with I come back to the basis with trust. Cuz people of different um ethnical backgrounds have a different culture and they trust their own but not so much the rest of the world and therefore if you are not deeply rooted and have have earned your trust in this community already before you are looking for um volunteers for a clinical trial um you might not be successful and uh unfortunately this entire project has been pulled by the by the uh pharmaceutical sponsor because uh the entire world suffered the same. So what we learned as a team is uh the entire clinical research industry invested in some education of the public over the last four decades but this education was mainly targeting Caucasian people – nobody else. And that bites us a little bit in our behind now because uh we dropped all those other people uh and they need to be educated now that

we we go to the same level of trust and have a chance to attract them volunteering in clinical research. So we adjust. So our work now with uh ethnical different communities changed dramatically so we reprioritized our efforts...

Four community themes that are involved with the active implementation of minority recruitment practices.

Should have access but don't: not just about location. The first theme at the community level is should have access but don't: not just about location. Clinical research sites do not always have access to minority patients for trials, despite having physical access based on geography. As participant #4 said, "...but if you start the trial just because uh doctor say yes yes yes I have the patient population – 80% of the time uh that means failure." This is because of the multitude of barriers to minority participation, which were previously discussed. Participant #2 said:

...and then when I got this position here where our demographic is 88% you know African American little bit easier to have – 'cuz you have that population but the difficulties are still the same because you still have more opportunities for education, more opportunities for...well more opportunities for continuous education.

Mistrust of research among minority patients was prominent in the discussions during the telephone interviews, as shared by participant #12:

...minority you just really have to I mean they still have I can't tell you how many minority men have you know come have mentioned the [Tuskegee] um incident and you know "are you using me as a guinea pig?"... probably like one out of every three brings that up to me.

Also mentioned earlier as a past experience shaping recruitment approaches, Participant #5 expanded on mistrust as a learning experience that demonstrates it takes much more to being successful with recruiting minority populations than just having physical access:

We were supposed as many other sites worldwide this year to enroll in a pharmaceutical...study uh to enroll people with a different uh ethnical background so um we were looking for Hispanics, for Asians and for African Americans. Um we thought living in a hot spot of a very mixed culture here um around San Diego would make it easier and boy did we learn that it has nothing to do with the statistics of the population but it has more to do with I come back to the basis with trust. 'Cuz people of different um ethnical backgrounds have a different culture and they trust their own but not so much the rest of the world...

Efforts to instill trust. The second theme at the community level is efforts to instill trust. Many efforts are taken by the study participants and their organizations to establish trust with minority patients. These efforts are divided into two subthemes: site staff interpersonal interactions with patients and leveraging a patient's social network.

Site staff interpersonal interactions with patients. There are several different ways in which trust is developed with minority patients that relate to research site staff interpersonal interactions with those patients. First of all, it's important to give back to the community without asking for anything in return. As participant #6 said:

We have more traction in terms of recruitment just from word of mouth because we're not seen as somebody who just takes. You know if you just take, take, take, it's gonna become apparent. You can't just target people for a study. You know you don't, you don't build trust that way. And so we've had to give, give, give, and our return quite

honestly has been ten-fold. But we haven't changed that. We put an investment into the give, give, give, first.

A way to give back to the community and establish trust is to provide personalized education to help patients understand their disease and how to manage it. Participant #6 shared:

So many of the things that we did to gain their trust first of all you know revolved around more um humanitarian kind of services so you know one of the things that um that I learned early on is that um you know people...have a sense and a fear of of the unknown and when it comes to their...own condition or disease um many of them just don't have an understanding. So one of the things that we decided early on is you know rather than to approach um people with you know with studies why don't we just dedicate the time and resources to be able to educate people on what it is that they have...

Having personal interactions with minority patients is important for instilling trust. As shared by participant #5

...the direct face to face contact with those who might to be impacted by themselves or take care of somebody who is affected. The face to face um opportunity to meet people and discuss things is the most important thing um to build the trust for sure...

Another important component for developing trust is for research staff to have a commonality with patients. This helps with making patients feel comfortable, as well as indicates to them that the trial is important, when there is someone from the same racial or ethnic background as part of the study team. Participant #3 shared:

...you know patients trust me and uh that's important...they're able to to look at me, I'm African American and I'm coming from an African American population...so you know in contrast to an academic center where they're looking at an Investigator who may not

reflect um you know their racial or social sensitivities where I may and and so there's some commonality and that that helps a lot in terms of recruiting...

Communication techniques are also important for developing trusting relationships. As

Participant #12 said:

...being a good listener...taking our time - if we have to repeat things multiple times, we repeat them. Um you know just really um if you say you're gonna call them back, even if you don't have the answer yet, you call them back. You have to...you have to build trust you have to...you just have to do that...and once they start trusting you then it's great. You know, there's no hiding. Like you just gotta make sure they know that nothing, there's nothing hidden – there's no hidden agenda, there's no we are here for you, and you know and I think once they meet us and they realize all the stuff we do for them...

In fact, participant #12 went on to share, "...these people become like family. Our patients, I mean I have so many um you know to be able to help them and you know I'm part of their lives."

Developing trust occurs over time and needs to be nurtured. It is also crucial that the PI is engaged. As participant #14 said:

...the last piece is um you know there has to be a (community) involved with in some way to ask people to come into a trial and if you don't give the education and the results back of what previous trials have shown and explain it, you're not going to get continued people to even consider coming in a trial. And that's very big in our minority populations where you know it's you you continue to see it. You know, investigators have come in and done some work and then they the community never hears from them again..., they don't talk about the results, whatever's been gleaned, and it's just moving on to the next

project. And the community's like wondering well what happened. So I think that's really key um especially in our minority populations.

Patient interpersonal influence: social network. There are a couple of ways in which trust is developed with minority patients by leveraging their social networks. First, participants discussed how patients' social networks, such as friends or family members, may refer them for a trial if they themselves are supportive or had a good experience with a trial. Some participants discussed the importance of engaging the family in recruitment and consent discussions.

Participant #12 said:

...we really encourage um the wives a lot of times are very mistrusting of us...and uh so getting um getting them to come in...when their husbands are there with us and actually talking it out all of us together um helps a lot...

Second, partnering with community stakeholders that serve as existing trusted sources of patients is a critical component for establishing trust and gaining access to minority communities. As participant #6 said:

You know...it evolved over time and really what looking back now it was a process of gaining trust...if I could target those people that were most influential – pastors,...priests within congregations, if I could get gain their trust and they in turn could introduce me to people and if I could gain their trust, then I was kind of one step closer to to being able to...draw them in...

Cultural sensitivity. The third theme at the community level is cultural sensitivity. Being aware of and respectful that cultural differences may exist is an important component when recruiting diverse populations. Participant #16 shared:

...every population is different and you have to really understand what their concerns are, and and their culture, and and try to...bridge the gap in an individual manner. I mean first of all, I I think you've just gotta respect each individual first of all. First you can't draw any conclusions you deal with that person directly and individually. Then if you're gonna try to reach out to African Americans or to Hispanics then you you have to understand how they typically view research...

Participant #14 discussed the negative impact of not recognizing or addressing the specific needs of cultural groups by stating:

...the other issue we're facing is because we are trying to recruit ethnically diverse people, and it goes back to understanding the community but it's really going back to understanding the culture. And I have seen this multiple times...if you're a PI and if you do not understand the culture and the history of this ethnic group and racial group either in the city you're in, the town you're in, or from the native country about some of the things that are very important to the group and some of the medical issues that may have happened with the group, then you're in trouble and um people sense it and they understand that...you don't know of this atrocity that may have happened to to my...people. That you know typically is said – my people. You don't know about this therefore why would...I let you do something to me if you don't even know that this happened to our group in this trial...

It goes beyond recognizing the existence of cultural differences to also understanding cultural preferences in order to effectively communicate with patients across cultures. As participant #5 said:

That hopefully helps us to understand the motivation of minority groups better um to possibly being a part of clinical research. The moment we we understand minority groups better we have a chance to target and approach them in a different way because we are thinking more out of their head then out of our head. And that makes a difference...

Participant #4 expanded on this by discussing how everyone who works for him must learn to work with different cultures:

...forget about your belief um because this trial is not about you...let's concentrate on the belief of that minority, let's try to understand their needs, let's try let's try to understand their culture...let's try to understand how can we make it better for them... let's try to to be educative as possible, let's try to find new ways to send a very strong message to them, um let's learn about them, that's my message um if you if you work for me...you have to to learn how to um work with different cultures...and leave your perception out because it's not about you. It's about the patients, it's about the different cultures.

Encouraging active role in healthcare and trial participation. The fourth theme at the community level is encouraging an active role in healthcare and trial participation. Participants discussed how they encourage patients to be engaged and take an active role in managing their health by educating them so they understand their disease and how to manage treatment options.

Participant #6 said,

...take for example a diabetic, what we found is that people...could have been diabetic for 20 years but they really do not understand what is occurring within their own bodies.

And so the first challenge is to really help them understand...

In addition, encouraging patients to take an active role in trial participation is also important, as stated by participant #1:

...I believe what works for me is give the patient enough time to go over the informed consent, let them read it, tell the patient, "look you know I need you to ask questions. I don't just want you to sign a document, I want you to ask me questions about particular adverse events. Would this happen? What is the likelihood? What's the percentage? What happened?" I mean I need this information because it keeps ME fresh as well too so I like to have the patient ENGAGED in terms of the studies that they may or may not participate in.

Participants in this study also shared how minority patients are interested in receiving disease and general trial education and understanding what it means to them, as shared by participant #14:

...the foundation always is how do we understand aging, how do we prevent the declines that we know can happen, and of late we have been focusing on racial differences that we see...and trying to understand what those racial differences are between Blacks and Whites and uh Hispanics and hopefully soon Asians...this kind of discussion is very important in the community. People want to hear it and people are very interested and wanting to know why are these differences there, what are you thinking, and how are you designing trials to address those differences...

Two interpersonal themes that are involved with the active implementation of minority recruitment practices.

Teamwork. The first theme at the interpersonal level is teamwork. Participants discussed working together as a team as a standard way of working. Participant #15 said:

I have various teams and...one person comes in...in the morning, also you have to set your roles and your schedule so that everybody's agreeable. But one person comes in in the morning and starts recruitment um starts screening every morning. Um and when she gets aggravated by doing all that, then you know then I say to the other person, "well, you know either get in a little bit earlier or as soon as you get here start doing it so that the other person the first person could do the regulatory today or do something else." Um so I think the team effort...

Several different aspects of teamwork were discussed, including taking a proactive, team approach to recruitment planning as well as involving the PI in recruitment discussions with team members. Participant #2 discussed both of these ideas:

...ya so it's it's developing a recruitment plan uh before we even start we sit down with the Principal Investigator, develop a recruitment plan on um how we're gonna chart review in our electronic medical records, the...physician's schedule um they are really involved in looking at their schedule to see if the patients...fit inclusion exclusion criteria...

Participants described learning as a team within their organizations, as shared by participant #9, "...well the first few times that we go through the process everybody learns, we definitely learn something..."

Problem solving as a team was also discussed, as shared by participant #16:

...if things aren't going well...we're just trying to work together to solve the problem so um I would say I other than maybe some disappointment when things don't go exactly according to plan we we're really just troubleshooting.

Effective communication across teams and between team members is important in order to be effective at recruitment, as mentioned by participant #16, "...we're very much a team and...we're all in the same room so...there's really kinda no barriers to conversation between us."

Participants also discussed having a team spirit, or camaraderie, as shared by participant #14:

Assuming you have people that like what they do, love being out there...have a team supporting them and then you know it's a very enjoyable experience...for everybody involved but for especially for them they feel a sense of accomplishment. They feel a sense of the giving back. They feel that this project is not just let's say your project, it's the team's project. It's a win-win.

No peer influence. The second theme at the interpersonal level is no peer influence. Participants indicated that their colleagues or peers do not influence them with regard to minority recruitment when asked one of these two questions during the interview, "what types of discussions are happening among your colleagues with regards to minority recruitment?" or "Can you share an example of when one of your colleagues encouraged you to focus on minority recruitment?" Participant #16 responded, "Hmmm. You know most of my... physician colleagues are...White, mostly male..." Participant #13 provided a similar response:

...not a lot to be honest with you...I do talk with other people in the country – I’ve a friend over in California, I have some friends down in South Florida...they run research sites and um there’s not really a lot of talk about that...

In fact, some participants shared how they are the ones actively attempting to influence others with regards to minority recruitment, as mentioned by participant #14, “...um I’m trying to think I mean it’s often the opposite...It’s me telling somebody else that they better you know get this thing going here...”

Two policy themes that are involved with the active implementation of minority recruitment practices.

Lack of diversity emphasis. The first theme at the policy level is lack of diversity emphasis by the trial sponsor or governing body. Participant #7 shared:

...I feel horrible...because for years I still don’t see...I was always curious as a researcher background before, I...always ask questions...why uh does no one see it? Is this really doesn’t matter or it’s like it does matter it’s also difficult for organization like FDA you know or like pharmaceutical company perspective is this really hard for them to encourage minority group to participate uh that’s why they just ignore it, they don’t even put a policy on it or any do anything about it, give any...additional support to the site to cover it?

Participant #2 expanded on this by stating:

... pharma companies allow too...much control from the individual sites meaning that hey if I don’t get minorities I don’t get minorities but I...fulfilled my recruitment goal. You know, in the long run that looks great on the site and it may look great for the pharmaceutical company but actually is that the best medicine that could be provided

for...the patient...for the population? ... there's an area of...opportunity there that I believe um the pharma company can can kind of control a little bit more um you know they can put regulations...

Participants in this study discussed how either they themselves, their colleagues and/or organizations are motivated to meet the enrollment goal commitment made to the study sponsor. This essentially results in a lack of diversity focus, as participant #10 shared:

But at the end of the day, I am judged by how many what my *n* is...not my *n* solely of you know well you you needed 20 and you only got four, but all four were African-American...that's okay but that means I only got paid for four people. Not 20 people.

There was one participant who was an outlier regarding this topic. Participant #3 was motivated by making a difference to a patient's life and not necessarily by the numbers:

...these are lives that it's I think its very powerful...you may have one patient you know we've had trials where I only had one patient and involved in the trial but that one patient did well. That one patient had a positive outcome and a that one patient had a positive experience and that one patient comes back and and asks us if there's other trials that that she can participate in. You know so you know that that you know that for a physician I I think that's important a lot of times we get you know we get sort of bogged down in in you know even in research we look at the numbers...

Some participants also discussed the lack of diversity focus during site selection, as participant #3 said, "...when I go to...Investigator Meetings... if there are a hundred investigators at the meeting there may be 2 or 3 minority investigators...in a clinical trial..."

Surprisingly, participants in the study who work for organizations that also receive NIH funding shared examples demonstrating a lack of diversity focus that still occurs at the NIH

level, despite the policy that has been instituted as part of the NIH Revitalization Act of 1993 (USHHS, NIH, 2001; USHHS, NHLBI, 2011). Participant #10 shared:

I've never heard of a trial being pulled 'cuz you didn't meet your underrepresented minority uh goal, right? Um nobody ever pulls a trial or scolds you or holds you accountable to those things.

Diversity emphasis attempts. The second theme at the policy level is diversity emphasis attempts made by either the trial sponsor or governing body. Participants discussed a recent shift in the trial landscape with the trial sponsor or FDA emphasizing diversity. This was discussed in relation to both the NIH and pharmaceutical organizations as the trial sponsor, as shared by participant #10:

I don't know if...that's gonna continue over the next five years. I really feel like at least at the NIH level there is beginning to be a, "this is not lip service this is important" um kind of sense...to what I'm hearing. I also think that Pharma truly has an interest in having their drug um tested in in all types... but...I don't know if they're gonna start you know really holding people accountable...I think there might be...a shift in...accountability uh beginning just now...just in the last maybe year or so.

Participant #4 discussed this recent shift to a diversity emphasis solely in the context of pharmaceutical sponsors:

I think right now there's a small uh shift and I think they're realizing this now and we're seeing more and more feasibility questionnaires um, "hey where is your access to this specific population or ethnicity group?" um I'm seeing this more on the uh mid-size, small biopharma companies but in the huge pharma companies I still haven't seen that yet...

When requirements or expectations related to diversity are put in place, this influences research sites to focus on diverse recruitment, as described by participant #5:

...from a researcher point of view and knowing that the treatment in in the indication we are operating is heavily impacted by ethnical background, so by genes, the FDA, they started already requiring not only certain age groups but certain minority groups as well because the simply the treatment of the same condition is different for different ethnical groups so therefore...there is no way around this there will be more and more protocols that will require this targeted population. It's a requirement so and therefore we have to be prepared that we have access to those uh minority groups.

Summary of Findings

In summary, several themes emerged during the data analysis process that answered the research questions, providing an explanation for the elements involved with active minority recruitment practices. Each research question represented a different component of the socio-ecological model.

Research question one: how are intrapersonal site staff elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States? Individuals who participated in this study believe that research is important. They also believe that it is important to increase minority participation in clinical trials and shared their frustration with barriers preventing that from happening. Participants in this study are personally committed to providing access to clinical trials to minority participants, which may be fueled by the satisfaction they receive from their recruitment efforts and their personal beliefs. Finally, participants discussed examples in which they have personally evolved through these efforts.

Research question two: how are interpersonal site staff elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States? At the interpersonal level, participants discussed several aspects of working as a team towards their recruitment goals. While participants in this study are not influenced by their colleagues to focus on minority recruitment, there is a social norm within their organizations of working as a team on their minority recruitment initiatives.

Research question three: how are organizational elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States? Participants work for organizations that have a strong sense of mission related to improving healthcare through clinical research. A commitment to minority inclusion is demonstrated by efforts made to provide culturally appropriate, general disease and clinical trial education to the community with an organizational structure conducive for minority recruitment. Participants represent organizations that demonstrate a culture of inclusion and continued learning for further refinement of minority recruitment practices based on learning.

Research question four: how are community elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States? Participants also discussed community elements related to how although they may have physical access to minority populations to recruit into clinical trials, factors such as mistrust and lack of awareness come into play that hinder participation. As such, several efforts are taken by participants and their co-workers to instill trust in the research process and between patients and site staff, including being sensitive to and understanding cultural preferences, as well as empowering patients to take an active role in managing their disease through education.

Research question five: how are policy elements involved in the active implementation of minority recruitment practices for biopharmaceutical-funded trials in the United States? Participants in this study are not often influenced by public policy or expectations of pharmaceutical sponsors to focus on minority recruitment. A strong sense of commitment to meeting enrollment goals contributes to a study-level focus in expediting recruitment. At the same time, participants are making long-term preparations for improving access to minority groups, which also prepares them for the cohort-specific expectations from the FDA and/or pharmaceutical sponsors that participants discussed are becoming more prevalent.

The next chapter will discuss the meaning of these findings by first comparing and contrasting with existing literature, then by using the socio-ecological model as a lens to interpret these findings, and lastly by suggesting recommendations for practice based on these findings from the data analysis.

Chapter V

DISCUSSION, RECOMMENDATIONS AND CONCLUSIONS

This qualitative study was designed to understand the socio-ecological elements involved in the active implementation of minority recruitment practices for biopharmaceutical-sponsored clinical trials. The socio-ecological model guided this study, and 20 themes emerged from the data analysis and were categorized across the socio-ecological model levels.

The following section interprets the emerging themes in relation to the literature. The meaning of these findings is then discussed in relation to the socio-ecological model. Implications for practice that have been guided by an ecological perspective and derived from the findings are provided to offer guidance and suggestions for enabling clinical research sites to effectively create an environment for recruiting minority participants. In conclusion, suggestions for future research are provided.

The literature on the topic of minority recruitment in clinical trials is in the context of NIH-funded trials, so these findings offer a new contribution to the literature related to industry-funded trials. In addition, it is important to differentiate between the support and resources that are provided to sites conducting NIH-funded studies versus those provided to industry-funded studies. In addition to individual study support, the NIH oftentimes provides funding for research activity infrastructure at sites. This includes providing strategic guidance, placing resources at sites or providing funding for hiring and training minority staff to support recruitment and educational activities (Duda et al., 2011; Cook et al., 2005; Hinton et al., 2010). The discussion that follows will focus on areas in which the study findings are similar and divergent from existing literature, outside of these differences discussed relating to the literature and support provided for NIH-funded trials.

Themes Interpreted with Literature

As previously discussed, the themes that emerged have been categorized across the socio-ecological model levels, with themes representing the “intrapersonal” and “organizational” levels found to be more prominent in this study. A reason why these two levels were more prevalent in this study is likely a result of the study design and interview questions that captured a better understanding of research site staffs’ perceptions and experiences within their organizations related to minority recruitment. Interestingly, attitudes and other intrapersonal elements regarding minority inclusion in clinical trials from a healthcare professional perspective are not widely explored in the existing literature and are limited to PI and physician attitudes, perception of barriers and extent of or lack of focus by virtue of setting and measuring progress toward minority enrollment targets (Boden-Albala et al., 2015; Durant et al., 2007; Eggly, Barton, Winckles, Penner, & Albrecht, 2015; Howerton et al., 2007; Simon et al., 2004; Williams & Corbie-Smith, 2006).

From an organizational perspective, infrastructure barriers to minority recruitment, such as inexperience and limited funding, are discussed in the literature (Durant et al., 2014; Joseph & Dohan, 2009; Williams & Corbie-Smith, 2006). However, outside of the importance of hiring a diverse research staff, organizational contextual characteristics in relation to successful minority recruitment practices are not widely described in the literature (Etkin, Farran, Barnes, & Shah, 2012; Ford et al., 2013; The Society for Women’s Health Research & FDA, 2011; Williams & Corbie-Smith, 2006). Existing literature suggests that characteristics related to research sites may have contributed to the successful enrollment of minorities into clinical trials (Duda et al., 2011; Jimenez et al., 2013; Wright et al., 2001). Participants in this study have provided context for specific organizational characteristics that contribute toward the active implementation of

minority recruitment practices, including incorporating improving access to clinical research in an organization's mission statement and nurturing a culture of inclusion.

Although the data that emerged from this study were not as prominent on the community level as the intrapersonal and organizational levels, there was still an abundance of data representing the community level of the socio-ecological model. These data were provided from the perspective of the individuals who participated in this study and was primarily related to efforts they take to engage with their local communities in efforts to build trust. Most of the literature related to minority recruitment is specific to the community level of the socio-ecological model. Many of the examples discussed in the literature share cultural or community-specific recruitment strategies that involved engaging with the local community and building trust (Ejiogu et al., 2011; Etkin, Farran, Barnes, & Shah, 2012; Germino et al., 2011; Wallington et al., 2016). The literature also provides minority patient perspectives, including motivators and barriers to clinical trial participation (Ejiogu et al., 2011; Ford et al., 2012; Ford et al., 2013; Markman, Petersen, & Montgomery, 2008; Salihu, Wilson, King, Marty, & Whiteman, 2015; Wells & Zebrack, 2008). In this study, participants discussed patient motivators and barriers to trial participation. Although this information was not collected directly from patients, the perceptions shared by this study's participants corroborates with existing literature describing minority patient perspectives regarding clinical trials. In addition to information reported in the literature, the participants in this study provided context surrounding minority patient interest in receiving disease education and learning about clinical trials. Participants discussed building long-term trusting relationships with minority communities by providing education and empowering patients to take an active role in managing their disease. Study participants also shared their experiences related to learning about other cultures through face-to-face interactions.

At the interpersonal level, only two themes emerged from this study – teamwork and no peer influence. The existing literature related to minority recruitment in clinical trials is not inclusive of the interpersonal level of the socio-ecological model from a research provider perspective. Instead, the socio-ecological model has been used in the literature for categorizing barriers to minority participation in clinical trials and describes influencers of patients' interpersonal relationships as opposed to researchers' interpersonal relationships (Salihu, Wilson, King, Marty, & Whiteman, 2015; Wells & Zebrack, 2008). Thus, the themes at the interpersonal level provide new contributions to the literature.

Similarly, two themes emerged that represent the policy level of the socio-ecological model. These two themes are lack of diversity emphasis and diversity emphasis attempts made by either the trial sponsor or governing body. Due to the application of the socio-ecological model for this study, the policy level was defined to represent both public policy and clinical trial policy or expectations set forth by trial sponsors. Therefore, any expectations or lack of expectations regarding minority enrollment on behalf of the pharmaceutical sponsor was categorized under the policy level, which broadened the opportunity for representation of this level. The clinical trial literature is not heavily saturated with policy-level representation related to minority recruitment. An abundance of literature discusses minority recruitment strategies utilized for NIH-funded studies; however, the focus of the literature is on describing the strategies used and not policy implications related to these studies having a minimum requirement for enrolling racial and ethnic minority participants as a stipulation of receiving funding (USHHS, NIH, 2001). However, some of the strategies utilized in the literature that were discussed may have been made possible due to additional funding and support. There is also literature regarding the low uptake of planning for the NIH's mandate for minority inclusion with

regards to setting minority enrollment goals, requiring cultural competency training and translating study materials (Boden-Albala et al., 2015; Durant et al., 2007; Durant et al., 2014; USHHS, NIH, 2001). Finally, lack of access to healthcare or not having health insurance are discussed as barriers to minority participation in clinical trials (IOM, 2003; Swanson & Ward, 1995; USHHS, CDC, 2011a). While not a dominant theme, participants in this study discussed lack of access to healthcare as being both a barrier and an enabling factor toward minority participation in clinical trials.

Intrapersonal themes interpreted with literature. Participants in this study demonstrated their personal commitment to minority recruitment by initiating self-directed action for this purpose. Based on the literature, underlying factors contribute to active minority recruitment efforts, specifically actively offering a trial to minority patients. For example, researcher perception of barriers influence whether or not minorities are offered trial participation (Durant et al., 2007; Simon et al., 2004; Stone, Mauch, & Steger, 1998; Williams & Corbie-Smith, 2006). PI motivation also is believed to play a role in successfully recruiting minority participants (Wright et al., 2001). Researcher attitudes influence success with minority recruitment, likely because those with positive attitudes toward minority inclusion are more active in enrolling patients (Williams & Corbie-Smith, 2006). Participants in this study not only believe that clinical research is important, but also that it is important to increase minority participation in clinical trials. Participants discussed their frustration with barriers to recruiting minority participants. Based on the findings of this study, participants' positive attitudes toward minority inclusion are fueled by their desire to ensure equitable access to treatment options available in clinical research and their frustration with barriers. These factors likely contribute to participants in this study taking an active role in minority recruitment. In addition, participants

shared their experiences that go beyond merely offering a trial and shared examples detailing ways in which they are personally committed and determined to improve minority participation in clinical trials. Participants discussed feeling satisfied with and rewarded by their jobs, more so than the industry trends reporting job satisfaction levels of clinical research professionals (Korieth and Anderson, 2015). The participants also discussed personal growth as they undergo a continuous process of learning through their recruitment efforts. By better understanding their patients' needs and perspectives, participants are better able to be effective at communicating cross-culturally. Existing literature does not discuss personal growth or change among clinical research staff. For participants in this study, continuous learning is important to being more effective in minority recruitment.

The limited literature discussing intrapersonal elements from a research professional perspective is confined to PI and physician attitudes and perceptions regarding clinical research or minority inclusion in clinical research. This study offers perspectives from other research professionals related to minority inclusion in clinical trials, outside of PIs. The majority of participants in this study have responsibility for recruitment within their organizations. They have positive perceptions regarding the importance of diversity inclusion in clinical research and are personally committed to actively implementing minority recruitment efforts. For research organizations focusing on minority recruitment, taking perspectives regarding diversity inclusion into account is an important consideration when making hiring decisions. When organizations focus on minority recruitment, hiring considerations for recruitment staff should include those who believe minority inclusion to be important and thus contribute to a culture of inclusivity within the organization.

Organizational themes interpreted with literature. One of the key elements to successfully recruiting minority participants, which is supported by the literature, is education of minority communities through providing disease and general clinical trial education prior to presenting a specific trial opportunity (Etkin, Farran, Barnes, & Shah, 2012; Regnante et al., 2019; The Society for Women's Health Research & FDA, 2011). Despite recognition of the importance of minority community education prior to study-level recruitment activities, such action is not being taken ahead of study recruitment activities nor is providing community education a common practice at the site level (Livaudais-Toman, Burke, Napoles, & Kaplan, 2014). Those research sites that are engaged in educating their local communities are providing education at the same time as trial recruitment, even when receiving NIH funding or resources (Aponte-Rivera et al., 2014; Cook et al., 2005; Germino et al., 2011; Hinton et al., 2010; Sturgeon et al., 2018). The success and sustainability of this approach to providing education to minority communities is yet to be documented among industry-funded studies. However, NIH National Institute on Aging Alzheimer's Disease Research Centers (ADRCs) and NCI-designated comprehensive cancer centers provide community education to minority communities prior to introducing a clinical trial opportunity in partial fulfillment of the requirements for being recognized as a federally designated center and maintaining federal designation status (American Cancer Society, 2014; Etkin, Farran, Barnes, & Shah, 2012; USHHS, NIH, 2018, January; Regnante et al., 2019).

Surprisingly, participants in this study discussed how their organizations have made the commitment to invest in providing general disease education to minority communities prior to discussing a study, despite the fact that this is not common practice even for NIH-funded institutions (other than the federally designed ADRCs and NCI comprehensive cancer centers

that are stipulated to do so). Educational events are costly and they yield few participants (Sturgeon et al., 2018). Additionally, pharmaceutical sponsors are focusing on expediting trial enrollment (USHHS, OIG, 2000). Sponsors provide centralized recruitment support on a study-by-study basis, leaving it up to the research sites to establish a long-term commitment to community education, should they wish to do so. The extent of community education being provided by sites that conduct industry-sponsored trials is unknown, though presumed scarce or non-existent based on the literature that depicts NIH-funded research institutions as not initiating community education at all, let alone as a long-term investment (Livaudais-Toman, Burke, Napoles, & Kaplan, 2014). This clearly differentiates the participants in this study from research staff in both NIH and industry-sponsored sites. Industry stakeholders who attended a recent workshop acknowledged that although recommended, community education prior to focusing on study recruitment is not occurring with industry-sponsored studies (The Society for Women's Health Research & FDA, 2011). Some interview respondents discussed how this concept was fairly new to them as they recently learned about the importance of community education when they started focusing on minority recruitment. They ultimately made that change to overcome barriers and commit to investing in a long-term commitment to educating their local communities and empowering patients to understand their disease and its potential treatment options and to be comfortable with the concept of participation in a clinical trial prior to presenting a specific trial opportunity.

Individuals in this study also discussed how their organization demonstrates its commitment to minority recruitment by investing in structural enhancements. As described in the literature, research center infrastructure impacts the successful enrollment of minority participants, including having the appropriate dedicated staff, resources and structure for

conducting research activities (Etkin, Farran, Barnes, & Shah, 2012; Ford et al., 2013; Joseph & Dohan, 2009; Williams & Corbie-Smith, 2006). Even with these investments and having leadership supportive of clinical research initiatives within their organizations, participants discussed continuing barriers. Many expressed the need for additional research staff members and more language capabilities, which are also discussed in the literature as limiting factors for minority recruitment (Durant et al., 2014; Joseph & Dohan, 2009). However, participants also shared examples of how their organizations have overcome barriers to improving their research infrastructures and have enhanced their capabilities to better meet the needs of diverse patients.

Participants also discussed organizational contextual characteristics in relation to implementation of minority recruitment practices, which are not widely described in the literature. Participants in this study work for organizations with a mission related to improving healthcare through clinical research, a finding that is to be expected since these organizations conduct clinical research. Improving access to clinical research is a component of the organizational mission for many of the participants' organizations. While the literature does not discuss the organizational mission statements of clinical research sites, the authors of one study reported that research activities are not sufficiently supported when clinical research is not incorporated into a research organization's mission statement (Joseph & Dohan, 2009). Findings from this study suggest that both incorporating clinical research and providing access to clinical research within a research site's mission statement are components that promote active minority recruitment efforts. This finding is supported by the fact that participants in this study discussed recruitment activities being driven by their mission. Believing in the mission was an important aspect leading to principles of working in support of carrying out their organization's mission.

Regnante et al. (2019) reported that cancer research centers recruiting a high percentage of minority clinical trial participants demonstrate an inclusive organizational culture by dedicating leadership roles to diversity and hiring minority staff. In addition to leadership support deriving a culture of inclusion, the organizational cultures related to this study's participants also portray an importance and focus on minority recruitment based on co-worker attitudes and interactions. Participants' co-workers help to create an inclusive organizational culture that is prevalent across the organization.

Another characteristic unique about the participating organizations is that they have processes that are flexible. This allows their minority recruitment approaches to change based on learnings from past experience, as individuals and their co-workers gain a better understanding of the patients being recruited and how to better adapt to those patients' cultural preferences and needs. Crosson, Lane, and White (1999) discussed how organizational learning provides a competitive advantage. Individuals who participated in this study discussed the enhancements that were made based on organizational learning that improved their organizations' competencies and allowed them to improve their recruitment of minority trial participants.

Community themes interpreted with literature. Although organizations conducting clinical research may be located in diverse communities or have a high percentage of diverse patients they manage in clinical practice, this does not equate to having access to these diverse patients for clinical research. While physical access based on geography may be apparent, many barriers preclude research organizations from the successful enrollment of minority patients into clinical trials. For example, according to one study, organizational structural barriers prevented minority enrollment into clinical research within a safety net hospital that serves a high percentage of minority patients (Joseph & Dohan, 2009). Mistrust in the healthcare system

and/or clinical research also has prevented clinical research organizations from enrolling minority patients into trials (Corbie-Smith, Thomas, Williams, & Moody-Ayers, 1999; Durant et al., 2014; Ejiogu et al., 2011; Ford et al., 2013; Roberson, 1994; Swanson & Ward, 1995).

Similarly, individuals in this study discussed how factors such as mistrust or a lack of understanding related to clinical trials come into play that prevent them from enrolling minority patients into trials, despite having physical access to patients based on geography. Despite geographical location, it still takes time and a concerted effort to overcome the multitude of barriers that prevent successful enrollment of minority participants into clinical trials.

As mistrust is a prominent barrier, participants in this study discussed the many efforts they have taken to instill trust in clinical research, as well as a relationship of trust between research staff and minority patients. Participants discussed the need for developing and fostering long-term, trusting community relationships that start prior to and extend beyond a specific study opportunity, and this is facilitated through education. Participants and their research organizations engage in these activities despite existing literature indicating that building trusting relationships through community education is not common practice outside of the federally designated ADRCs and NCI comprehensive cancer centers, as discussed previously (Etkin, Farran, Barnes, & Shah, 2012; Livaudais-Toman, Burke, Napoles, & Kaplan, 2014; National Academies of Sciences, Engineering, and Medicine, 2016; Regnante et al., 2019). Providing general and personalized disease education, coupled with health screenings, is a way to establish trust by giving back to the community without asking for anything in return. Participants discussed how their immediate motivation behind community education efforts is related to developing trust. Recruitment may be their ultimate goal in the future, but their immediate goal is to build trust with minority communities. This concept is not widely practiced and is one area

in which the participants in this study display an exceptional practice that is unique compared with other clinical research sites.

Research stakeholders have indicated that disease education is important to minority patients (The Society for Women's Health Research & FDA, 2011). Participants in this study further validated this and shared that their efforts to empower patients with knowledge and self-efficacy for managing their diseases was of interest to minority patients. In fact, when discussing patient factors that impact access to clinical trials, participants discussed how patients' engagement with managing their health positively impacts their access to trials more than being disengaged negatively impacts access. Participants rarely discussed minority patient interest in trials in relation to personal benefit, which may suggest that patients aren't as motivated by financial incentives as by becoming engaged with managing their disease. However, one of the barriers is access to information. Patients have to first be made aware of details about their disease and clinical trials as a potential option to be able to benefit from participation.

Participants also discussed the role a commonality between research staff and patients plays in developing trust. Ensuring research staff are the same race or ethnicity and speak the same language as the patients being recruited is recommended for building trust and has been successful for enrolling minorities in past studies (Germino et al., 2011; Ford, 2013; Hinton et al., 2010; National Academies of Sciences, Engineering, and Medicine, 2016). Also, participants emphasized that the PI needs to be involved with recruitment activities. Regnante et al. (2019) reported that a physician's role is important in influencing a patient's willingness to participate in clinical research. Further, trusting relationships between a physician and a patient, as well as between a physician and the patient's family members, contribute toward successfully enrolling minority patients in clinical research (Regnante et al., 2019; Wright et al., 2001). Leveraging a

patient's social network is a tactic participants discussed that helps instill trust in clinical research. Many of the successful examples of recruiting minorities that have been discussed in the literature involve developing community partnerships with key stakeholders as a necessary component for building trust among minority communities (Germino et al., 2011; Ejiogu et al., 2011; Regnante et al., 2019). Participants in this study shared that they partner with community stakeholders that have already been established as trusted sources within minority communities, such as pastors and minority association leaders. Some participants discussed this approach as being their first step in gaining access to minority communities. Interestingly, while this was discussed as an important component among participants in this study, as well as reported by some of the literature reporting on NIH-funded studies, this approach does not appear to be prevalent among industry-funded clinical research sites. According to a white paper published by a trade organization representing clinical research sites, the Society for Clinical Research Sites, only half of individuals representing research sites that responded to a survey related to success factors in recruiting diverse patient populations in clinical studies indicated that they had community connections. Yet, individuals representing sites with more community connections self-reported more success with enrolling diverse patients into clinical trials than the individuals from sites without community connections (Pierre, 2018). Mistrust or disapproval of clinical research by a patient's social network is a known barrier to minority recruitment (Ford et al., 2008; Swanson & Ward, 1995). Therefore, it would be prudent for researchers to educate and build trust among a patient's social network, including leveraging already trusted sources. One way participants mentioned that this is achieved is by including family members in recruitment and consent discussions.

Finally, culturally sensitive researchers provide a valuable role in the successful enrollment of minorities in clinical trials, especially since cultural differences have an effect on the communication and understanding of health information (Ejiogu et al., 2011; Ingram, 2012; IOM, 2004). However, formalized cultural sensitivity or cultural competency training is not always instituted (Boden-Albala et al., 2015). Only six of the 15 participants in this study reported having formal cultural competency training requirements at their organizations. Participants, however, discussed their personal and organizational commitments to actively implementing minority recruitment practices regardless of whether or not formal cultural competency training was a requirement within their organizations. Furthermore, formalized cultural competency training was not a factor in recruiting minorities in equal or greater proportion to the US population in this study. This is in discordance with the findings of the author of a recent industry white paper who reported that cultural competency training was a contributing factor that enabled sites to have more success with enrolling diverse participants. The author also reported that those research sites in which none to most of the staff were culturally competent had less success with recruiting diverse patient populations (Pierre, 2018). As a measure of ensuring that staff members are culturally competent, research sites may want to consider integrating cultural brokers into their research teams. Serving as a connecting link between research staff and the communities they serve, this strategy has been found to enhance trust, promote cultural understanding among team members and ultimately improve access to minority populations (Germino et al., 2011). Rather than discussing formalized cultural competency training, participants in this study discussed how understanding and being sensitive to other cultures does not necessarily come from institutionalized training. Instead, they

discussed the importance of face-to-face interaction with community members and being immersed in their culture.

Interpersonal themes interpreted with literature. Ejiogu et al. (2011) described empowering research staff members to take an active role in study-related decision-making by soliciting opinions from staff members to inform strategy decisions. This way of working that was implemented by the study's PIs motivated research staff to engage in study activities and also promoted staff retention. It was one of many components that led to the successful implementation of this longitudinal study in which racially and socioeconomically diverse participants were recruited. While not an overarching theme, some participants in this study discussed team member satisfaction in relation to being provided autonomy in decision-making. The importance of working as a team was a key theme that was divergent from the existing literature. Many different aspects of teamwork were discussed, including proactive team planning, involving the PI in recruitment activities, learning and problem solving as a team, having effective communication across and among teams, as well as having team camaraderie. These characteristics of participants' interpersonal relationships and interactions among their co-workers provided insight into their organizational cultures and the high regard placed on working as a team. Teamwork was important for informing the implementation and refinement of minority recruitment practices in this study.

Individuals in this study conveyed their personal beliefs in the importance of increasing minority participation in clinical trials. Through the efforts they take, they also demonstrate a personal commitment to providing minority populations with greater access to clinical trials. Peer influence is not a factor in these actions that individuals in this study take to promote diverse inclusion in clinical trials. This finding is unique in that the clinical trial literature related

to minority recruitment does not discuss social influence on minority recruitment efforts. Additionally, the clinical trial literature related to the socio-ecological model is primarily categorizing motivators and barriers to minority recruitment by providing insights related to a patient's intrapersonal perspectives and interpersonal influences, and not perspectives and interpersonal influences among research staff (Frew et al., 2014; Salihu, Wilson, King, Marty, & Whiteman, 2015; Wells & Zebrack, 2008). The finding that individuals in this study are not influenced by their peers with regard to their efforts taken to actively recruit minority trial participants demonstrates that the commitment of these individuals may be due to personal attitudes and enabled by organizational contextual factors and teamwork. Although social influence related to colleagues external from participants' organizations was not prevalent, participants' co-workers within their research organizations contribute to a culture of inclusion. A combination of the study participant's attitudes and their co-worker attitudes contribute to a social norm within their organization of focusing on minority recruitment.

While external social influence is not a factor in promoting active minority recruitment efforts, participants with a role of PI and/or owner of a research site instead discussed actions they take in attempts to encourage their peers in relation to minority recruitment. Interestingly, these individuals discussed providing education to their colleagues on clinical research and the importance of having diverse representation in clinical trials. Education is also a key practice among study participants in their efforts to improve minority participation in trials and build trust. As previously mentioned, the clinical trial literature does not cover social influence on minority recruitment efforts, so this finding suggests a new contribution to the literature as an area for future research with a larger sample size.

Given the lack of influence or even discussions taking place among the participants' peers, it is evident that clinical research professionals are not widely focusing on minority recruitment. Additionally, according to the literature, many minority physicians do not view clinical research as beneficial (Ramirez et al., 2008). PIs and/or owners of a research site initiated individual efforts to educate colleagues. This finding provides an opportunity by leveraging the finding that social relationships affect behavior (McLeroy, Bibeau, Stecker, & Glanz, 1988). Clinical trial stakeholders, such as sponsors, clinical research organizations and federal agencies, may want to consider attempting to influence social norms by launching education programs targeted toward the healthcare provider community to raise awareness of the critical need to improve access to clinical trials among minority populations and to enhance the belief in the research process among potential referring physicians.

Policy themes interpreted with literature. There was a strong sense of obligation within participants' organizations to meet their committed enrollment goals. Participants discussed minority enrollment expectations only in the context of study-specific racial or ethnic subgroup enrollment numbers required by either the study sponsor or the FDA. In this study, the intermittent minority enrollment requirements discussed by participants is to be expected because of the focus on expediting trial recruitment and lack of policy mandating enrollment of clinically relevant populations in industry-funded trials (USHHS, FDA, 2014; USHHS, FDA, 2016; USHHS, OIG, 2000). These findings result in a reduced focus on inclusion of diverse populations that for some trickles down to the site's activities where striving to meet enrollment targets on a study level becomes a top priority. Rather than enact federal policy, pharmaceutical sponsors could start to hold research sites accountable or incorporate minority enrollment targets into site contracts that are based on disease prevalence in those populations. This may encourage

research sites to focus more on minority recruitment, especially since participants in this study discussed the need to meet established enrollment goals as motivation behind fulfilling this commitment. In addition, the pressure to meet enrollment goals shifts priorities within participating organizations. Although they still engage in actively pursuing efforts to increase access to clinical trials among minorities, at a study level, they may need to shift focus to fulfill the study requirements. This may also be partly due to the paradigm described by study participants in that they take broader efforts to provide education and build trust to encourage minority participation, while their goals on a study level are to fulfill the need for enrollment in the trial. A shortage of educational campaigns nationwide also may contribute to the efforts taken by participants in this study to raise general awareness of clinical trials within minority communities. Various resources are available, such as the free “AWARE for All” clinical research educational programs held by the non-profit organization “The Center for Information and Study on Clinical Research Participation (CISCRP)” (CISCRP, 2020). It is apparent there is a need to increase these efforts since lack of awareness of clinical research is a known barrier to minority participation in clinical trials (Ejiogu et al., 2011; Ford et al., 2008; Leiter, Diefenbach, Doucette, Oh, & Galsky, 2015; Ramirez et al., 2008; Roberson, 1994; Simon et al., 2004).

On an ad hoc level, expectations and requirements set forth by the trial sponsor or FDA to recruit a certain proportion of diverse participants for specific studies influenced minority recruitment practices within the participants’ research organizations in this study. If trial sponsors expand these expectations beyond select protocols, it may motivate more research sites to enhance their capabilities and efforts in recruiting diverse participants. Participants discussed a recent shift in the trial landscape with more emphasis being placed on diversity in areas such as site selection and expanding the number of protocols with minority enrollment requirements, for

example. However, the fact that the participants in this study actively recruit minorities already could partially explain the increased focus they reported seeing with trial sponsors.

Participants discussed barriers to access related to location of research sites and lack of diverse healthcare professionals conducting research. Efforts to promote a diverse workforce with the skills and interest in conducting clinical research may improve minority participation, as a known barrier to minority recruitment is a disparity of minority physicians involved in clinical research (Ramirez et al., 2008). This also may contribute towards the availability of known research sites with patient demographic populations that represent the prevalence of a disease.

In spite of strides the NIH has taken to enhance the diversity of clinical trial populations, it is evident that more work is required, since disparities in trial participation still exist for NIH-funded studies (National Academies of Sciences, Engineering, and Medicine, 2016). While the sample size was small, participants in this study working for research organizations that also receive NIH funding provided examples that support this. Surprisingly, for example, informed consent forms are not always translated into Spanish, despite conducting a trial in locations with a large Spanish-speaking population. The literature supports that there is still a lack of focus in that recruitment goals for individual minority groups are not always set, consent forms and recruitment materials often are not translated and cultural competency training is not often required for site staff conducting NIH-funded studies (Boden-Albala et al., 2015; Durant et al., 2007; Durant et al., 2014). It is evident that the NIH may need to provide additional funding and support to research sites to enable adherence to and accountability for their policy on achieving proportionate trial representation (USHHS, NIH, 2001).

Unfortunately, the participants discussed that some of the attempts made by trial sponsors to stipulate demographic cohort requirements failed. For example, several participants discussed

trials with mandated minority cohort enrollment requirements that were canceled because none of the sites could recruit the needed numbers. One participant mentioned minority lack of trust and a need for education as barriers to recruitment, while another participant discussed study design barriers. These examples demonstrate that a concerted effort is needed to enhance understanding of successful minority recruitment practices that can be shared with research stakeholders across the nation. Pharmaceutical sponsors and contract research organizations need to plan for diversity upfront in considering the target demographic representative of the disease prevalence and then design the protocol and select research sites in accordance with the target patient population. They then need to develop a diversity recruitment strategy and provide funding to support these initiatives. Research sites implement minority recruitment practices at a local level, and it is critical that they are equipped with the skills and resources to be able to do so effectively.

Consideration of the Socio-Ecological Model

As discussed, the socio-ecological model guided this study and themes emerged at each level of the model that provided explanation for elements involved in the active implementation of minority recruitment practices. When reviewing the findings that represent each level of the model, more themes emerged for the intrapersonal and organizational levels of the model. A substantial number of findings emerged for the community level of the model. Fewer findings emerged that relate to the interpersonal and policy levels of the model. There are two points to note in relation to the model and its utility for providing a lens to answer the research questions. First, participants in this study represented the intrapersonal level of the model and spoke mainly to intrapersonal and organizational components. That is to be expected given the design of the study and the interview guide. Had other stakeholders, such as minority patients, participants'

co-workers and pharmaceutical sponsor representatives, also been included in this study, then it is anticipated that a substantial amount of additional information would have emerged at the community, interpersonal and policy levels. The information shared by participants offered unique contributions to the literature at each level of the socio-ecological model, even though data were collected from an intrapersonal perspective. Second, while looking at the findings that emerged at each level of the socio-ecological model individually offers unique insights, this approach also provides a fragmented view of elements involved in active minority recruitment practices. Instead, a comprehensive and holistic view facilitating the understanding of effective minority recruitment practices is offered when considering the findings at multiple levels in relation to one another. This is further explained in the next section discussing the theoretical implications for the utilization of the socio-ecological model for this study.

Theoretical Implication: Interaction of Socio-Ecological Elements Explain the Active Implementation of Minority Recruitment Practices

The socio-ecological model was used as a conceptual framework guiding this study. Themes emerged at each level of the model that helped to identify and explain the components contributing to the active implementation of minority recruitment practices. The premise of the model is environmental change based on interactions between individuals and their environment (Bronfenbrenner, 1977; McLeroy, Bibeau, Stecker, & Glanz, 1988). The model further supports this study's findings in that the environment plays a role in influencing behavior and vice versa, behavior influences the environment as it relates to minority recruitment. For example, participants in this study feel satisfied with their work and rewarded by the positive impact they make on patients, indicative of a reciprocal relationship with their environment. At an interpersonal level there is a sense of team spirit. They work for organizations that have an

inclusive culture. There is a scarcity of efforts at a sponsor or national policy level to educate minority communities on clinical trials, and study participants recognize a need to overcome barriers such as mistrust. All of these factors play a role in the commitment and actions participants take to provide minority patients with access to clinical trials. These results also suggest that we need to consider the interaction of components at all levels of the socio-ecological model for minority recruitment. Although more findings emerged for some levels of the model over others due to the nature of obtaining information from an individual perspective, it was evident that findings at all levels of the model in combination with each other offer a more comprehensive explanation of the elements involved in active minority recruitment practices. Thus, these multi-faceted findings reveal that an ecological perspective offers insight into improving access to clinical trials and the socio-ecological model provides an opportunity for improving minority recruitment practices in the future. This is illustrated graphically in Figure 3.

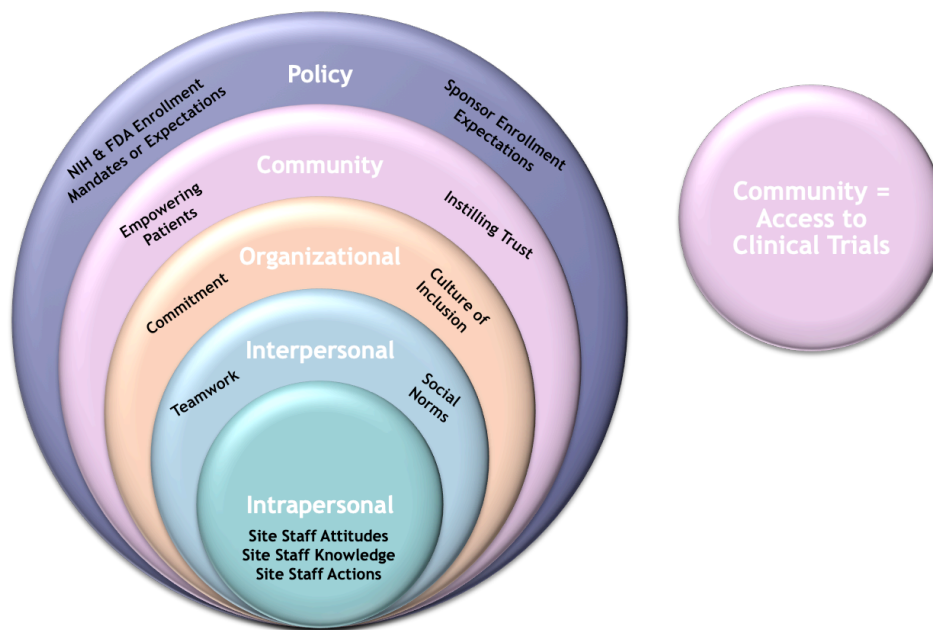


Figure 3. This figure illustrates the interaction of socio-ecological elements in explaining the active implementation of minority recruitment practices for improving access to clinical trials. Adapted from McLeroy, K., Bibeau, D., Steckler, A., & Glanz, K. (1988). An ecological perspective on health promotion programs. *Health Education Quarterly*, 15(4), 351-377.

Similar to other health promotion interventions, the socio-ecological model only works when put into practice. As a means to help facilitate application of findings derived from the execution of a socio-ecological model, solutions emerged for improving minority recruitment practices that were guided by the implementation of an ecological perspective. Specifically, a model for research sites to use to inform the application of minority recruitment practices emerged from this study's findings, which demonstrates how a combination of recommendations interacting at multiple levels of the socio-ecological model can be applied practically.

Practice Implications: Site Action Plan for Making Minority Recruitment a Core Competency

The model that emerged from this study may provide a more comprehensive guide to help organizations that conduct clinical research improve their capabilities by creating an environment effective for recruiting minority study participants. This model was derived from an ecological perspective, and thus by making minority recruitment a site's core competency, the focus is on environmental system change with the ultimate goal of improving minority access to clinical trials. This model, the "E³ Model", consists of three components:

- Establish: Commit to prepare the foundation
- Engage: Invest in partnering with the community
- Execute: Prepare to deliver, refine, repeat

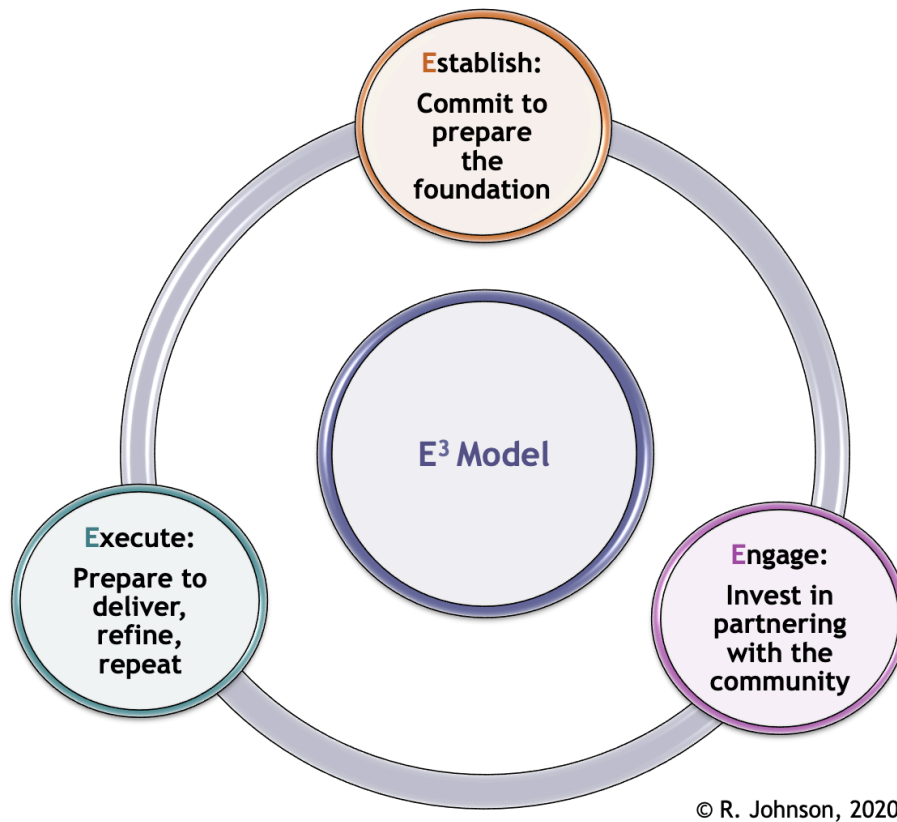
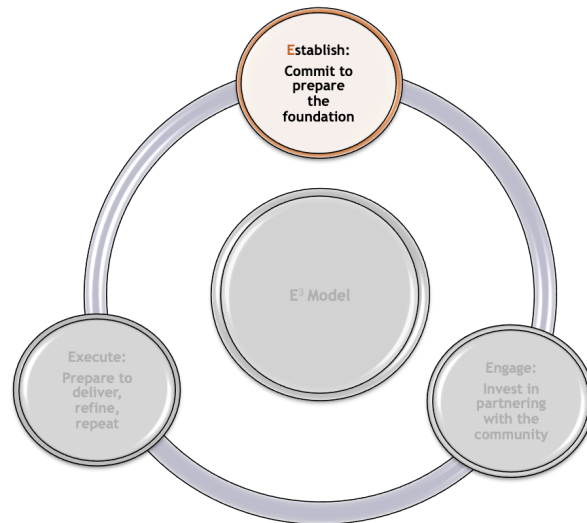


Figure 4. This figure illustrates the E³ Model site action plan for making minority recruitment a core competency.

Establish: Commit to prepare the foundation.

Commitment. First, it became evident that sites need to establish themselves internally. They need to make the commitment to prepare a foundation for minority recruitment within their organizations. For example, they need to articulate and gain buy-in for the value proposition across the board from leadership to front-line staff. It cannot just be the top executives who believe that minority recruitment is important. Research and diversity need to be incorporated into the organization's mission and the ways of working need to support that mission, including recruiting people who believe in and can help foster a culture of inclusivity. Appropriate training measures need to be in place to promote effective communication with patients, as well as with

other staff members internally. An illustration depicting the required measures for establishing the foundation is represented in Figure 5.



Commitment

- Articulate and gain buy-in for value proposition from leadership to front-line staff
- Incorporate research and diversity in organization's mission
- Align daily work, SOPs, KPIs and incentives to support mission
- Demonstrate commitment by fostering inclusivity and teamwork and eliminating barriers
- Recruit people who support mission and reflect diversity of community
- Incorporate cultural sensitivity and communication skills in staff training
- Create a platform for knowledge and results sharing

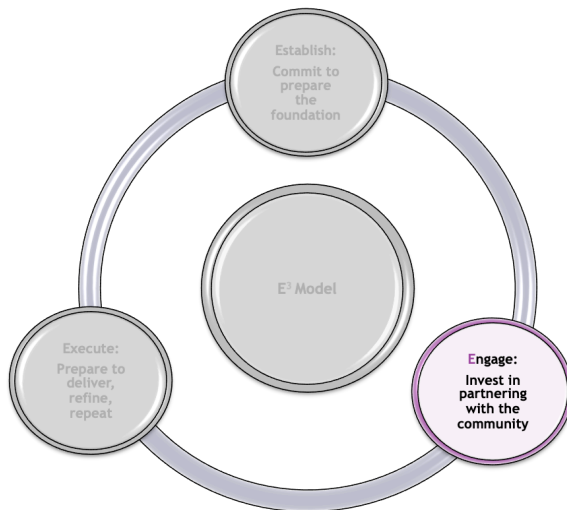
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Figure 5. This figure illustrates the “Establish” component of the E³ Model site action plan for making minority recruitment a core competency.

Only after the foundation is established will sites be ready to engage with the community.

Engage: Invest in partnering with the community.

Long-term investment with developing community relationships. The next component of the E³ Model is to engage in investing in partnerships with the community. This requires two main actions. First, listen and understand and second, educate and build trust. Figure 6 illustrates the engagement component of the E³ Model.



Long-term investment with developing community relationships

Listen and understand

- Immerse in community to understand culture and beliefs
- Solicit patient input (preferences, trusted sources for health-related information)

Educate and build trust

- Identify community-trusted sources, build relationships and create shared goals
- Provide culturally appropriate disease education and services (e.g., health screenings)
 - What does it mean to them?
- Empower patients and their families with enduring tools to manage disease
- Build understanding of treatment options, including clinical trials

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Figure 6. This figure illustrates the “Engage” component of the E³ Model site action plan for making minority recruitment a core competency.

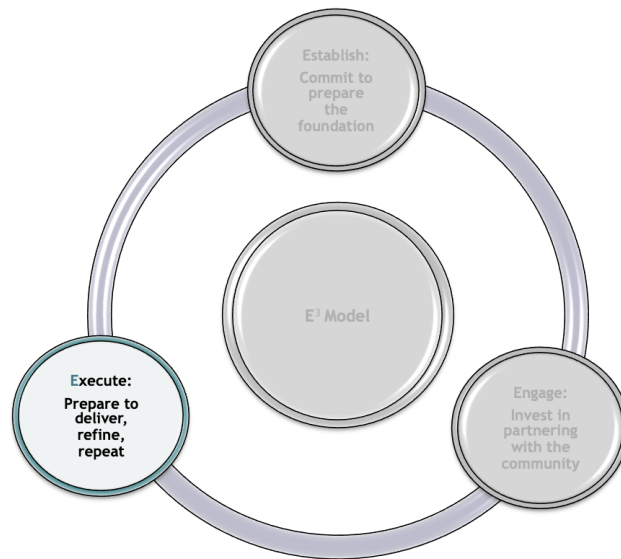
Listen and understand. The first step in partnering with the community to develop long-term relationships is to obtain an understanding of the preferences and culture of the local community. This is done by being immersed in an attempt to appreciate and learn other cultures, as well as by soliciting input directly from community members.

Educate and build trust. Once an understanding has been established, the second step in partnering with the community to develop long-term relationships is to start building trust and forming relationships by providing education, leveraging existing trusted sources as a catalyst for

delivery. This education needs to be personalized. For example, high blood pressure and diabetes are asymptomatic diseases and people with these conditions may be asymptomatic. The first step should be to educate people on the importance of screening and what each individual's results mean and tie it back to the importance of why that should matter to each individual. One critical success factor for this component is that recruitment is not the primary focus at this stage. The primary focus is empowering patients and their families with the knowledge and self-efficacy to understand and manage their disease and treatment options, including clinical trials as a potential option.

Execute: Prepare to deliver, refine, repeat.

Putting preparation to work. The next component of the E³ Model is to execute and prepare to deliver, refine and repeat. Once the foundational core has been established and research sites are actively engaged in developing relationships with the community, only at this point is it time to put preparations to work and focus on recruitment for a specific study. At this point, when research professionals are out in the community educating on management for a specific disease, the notion of a clinical trial has already been discussed as a potential option for consideration. For example, the assessments that are required have been discussed and community member feedback and questions have already been solicited and responded to. At this point, a relationship and basic understanding has been established and discussions about the potential for enrollment in a specific trial can be offered. It's also important that an ongoing communication across teams and with the community is maintained in order to refine and leverage learning for future success as an ongoing process. Figure 7 illustrates the components for the execution phase of the E³ Model.



Putting preparation to work

- Confirm diversity enrollment goals with study sponsor and reinforce with all site staff
- Develop recruitment plan inclusive of learnings from community
- Activate community relationships and plan events/outreach
- Ensure ongoing dialogue between community educators and internal site staff
- Ensure patient experience at site and trial information meets individual/cultural needs
- Report mid-way and post-trial results back to patients and community leaders
- Share learnings and best practices with internal staff and across site affiliates
- Refine and leverage learnings and expertise for future success

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Figure 7. This figure illustrates the “Execute” component of the E³ Model site action plan for making minority recruitment a core competency.

While future research is required to assess the impact of the E³ Model, the shared goals with successfully implementing the E³ Model into practice include site staff satisfaction and growth, improved sponsor success, improved community and population health, greater trial generalizability, business growth and future funding.

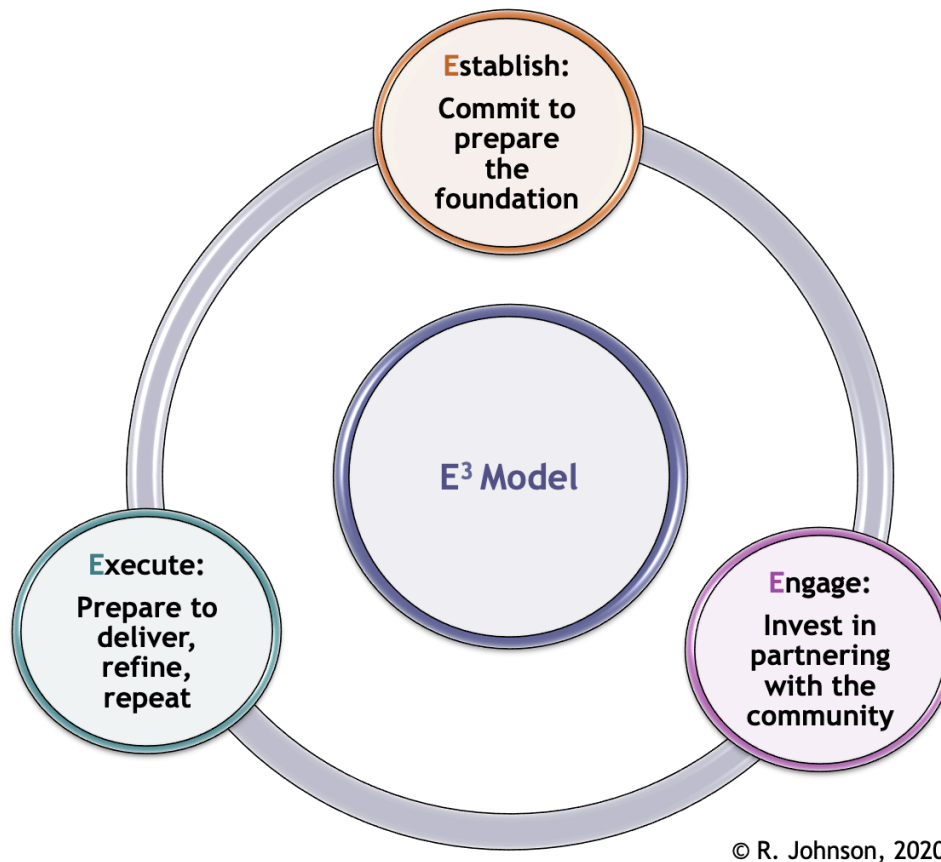


Figure 8. This figure illustrates the E³ Model site action plan for making minority recruitment a core competency.

Limitations

There are limitations to this study. First, the sample is a convenience sample, identified from publicly available data. For this reason, there is a potential for self-selection bias from participants interested in this topic. Also, data collected from the interviews reflect self-reported perceptions regarding organizational, community, interpersonal and policy elements. Finally, as this is a qualitative study, the results are not generalizable and an assumption was made that study participants honestly conveyed their experiences and perspectives. Participants did represent various roles across the full spectrum of clinical research organizational settings in both rural and urban areas, offered trials across a variety of therapeutic areas and had differing

historical performance in minority enrollment. This allowed for obtaining a broad range of perspectives from research stakeholders who were able to provide their first-hand experiences in recruiting minorities. However, the small sample size selected through purposeful sampling limits transferability of findings. Instead, readers will be able to apply findings to their own unique situations to make transferability judgments on their own.

Future Research

There are several opportunities for future research that emerged during data analysis. While not a dominant theme, participants discussed the importance of recruiters having certain personality characteristics in relation to minority recruitment. They also discussed being passionate about what they do and going “above and beyond.” Future research could be designed to better understand how personality characteristics contribute to recruitment efforts and job satisfaction as an implication for future hiring decisions.

As the findings in this study are based solely on the interview respondent’s perceptions, future research could involve additional stakeholders to represent direct perspectives at each of the socio-ecological model levels. For example, minority patient preferences were conveyed as experienced by the interview respondents. Although perspectives shared, such as mistrust of research and interest in learning about clinical trials, are similarly documented in the literature, obtaining direct input from minority community members would offer a more comprehensive view of community factors, for example.

The themes presented at the intrapersonal level were consistent across the participants that represented various roles within their organizations, except for several occurrences in which the responses from the participant in a non-patient role varied. However, there was also an apparent difference in responses between roles with regards to other information shared at the

intrapersonal level that was not considered an overarching theme. The PIs' and owners' responses were consistent with one another, yet varied with the recruitment leads' responses in some areas. This also occurred at the interpersonal level as it relates to peer influence regarding minority recruitment with the PIs and owners actively encouraging others. Future research could explore these differences in responses between roles.

This study was bound by recruitment practices and, therefore, retention of minority participants was not incorporated into the interview guide and thus not a main focus for the study. As these participants shared their gainful knowledge and perspectives related to minority recruitment, future research could be conducted to understand how these participants promote retention.

Finally, while many participants in this study recruit a high percentage of minority clinical trial participants, this was not a specification in the eligibility criteria for study participation. Participants representing organizations with lower historical minority recruitment performance still offered indistinguishable insights related to their minority recruitment commitment and practices. For this reason, future research could focus on success not by excluding individuals that have not historically recruited a high number of minority trial participants and instead conduct a focus group or survey with these same participants to establish the E³ Model as a model for success.

Conclusion

In conclusion, guided by the socio-ecological model, the results of this research demonstrate that environmental change can provide a premise for improving access to clinical trials among minority populations. This research also provides practical guidance for research sites to implement minority recruitment practices by implementing the E³ Model. To effectively

implement the E³ Model will require a shift in the standard approach to recruitment by moving from a study-level recruitment focus to empowering patients and developing trust as the core focus, which will require environmental change. The participants in this study demonstrated that it is possible, even with their current resources, to create an environment conducive for improving minority access to clinical trials.

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APPENDICES

APPENDIX A

INTERVIEW GUIDE

1. Tell me about yourself.
 - a. How did you get into clinical trials?

Transition: First, I want to get a general sense of the wider picture related to recruitment in terms of the societal and environmental landscape. Please answer this next question considering this broader aspect.

2. What do you see playing a role in your recruitment efforts?
 - a. How about with minority recruitment?
 - b. What concerns do you have with what is happening with healthcare in this country right now and how that could impact recruitment?
3. Talk to me about your organization's mission.
4. Walk me through your organization's approach to recruitment (in general).
 - a. What's working? Not working?
 - b. If your organization had unlimited resources, what would you do differently to make your organization the best it could possibly be with regards to minority recruitment?
 - c. How does your organization engage with the community?
 - i. How responsive do patients seem to be with your outreach efforts?
 - ii. How have you changed what you do based on what you've learned?
5. What types of discussions are happening amongst your colleagues with regards to minority recruitment?
 - a. Can you share an example of when one of your colleagues encouraged you to focus on minority recruitment?
6. When tasked with recruiting for a new study, what is it like for you?
 - a. How do you react personally?
 - b. What about others on the team – what's it like for them?
7. What are your perceptions with recruiting for clinical trials (in general)?
 - a. What about with minority recruitment?
8. What additional ideas do you have that we haven't discussed that will help me better understand what is involved when you specifically focus on minority recruitment?

Demographic Information

1. How many years of clinical research experience do you have?
2. How long have you been involved with promoting minority recruitment?
3. How long have you been with your current organization?
4. What is your current title?
 - a. In your role, do you speak directly with potential clinical trial participants?
5. [If answered 'yes' to question 4a only] Do you speak a language fluently other than English?
6. [If answered 'yes' to question 5 only] What other languages do you speak?
7. What is your gender?
8. From an ethnicity perspective, would you categorize yourself as Hispanic, Latino or Spanish origin?
9. Which of the following racial designations best describes you? You can select one or more:
 - a. White
 - b. Black or African American
 - c. Asian
 - d. Native Hawaiian or Other Pacific Islander
 - e. American Indian or Alaska Native
10. What type of organization do you currently work for:
 - a. Dedicated research institution
 - b. Academic medical center/University hospital
 - c. Community physician/medical practice
11. Which of the following best describes the geographical area of your clinical trial setting?
 - a. Urban [within city limits of a metropolitan area's central city]
 - b. Suburban [part of a metropolitan area that is not in that metropolitan area's central city]
 - c. Rural [not part of a metropolitan area]
12. What other funding outside of biopharmaceutical sponsors do you receive for conducting clinical trials?
13. What are the therapeutic areas of the trials that you typically conduct?
14. Are racial/ethnic minorities included on your research team, specifically in the following roles:


[Minority defined as a race and ethnicity other than non-Hispanic White]

 - a. Principal Investigator
 - b. Sub Investigator
 - c. Recruiter
 - d. Study coordinator
 - e. Study nurse
15. Is it common practice for minority recruitment goals to be set within your organization?
16. Are staff members required to take cultural competency training?
17. Approximately what percentage of your patients who participate in clinical trials are minorities?
18. Does this reflect the population demographics in your community?

APPENDIX B

INFORMED CONSENT FORM

<p>Seton Hall University Institutional Review Board</p> <p>OCT 08 2018</p> <p>Approval Date</p>	<p>Expiration Date</p> <p>OCT 08 2019</p>
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Informed Consent Form

Study Title: *Understanding Elements Involved in Active Racial and Ethnic Minority Recruitment Practices for Biopharmaceutical-Sponsored Clinical Trials: A Socio-Ecological Qualitative Inquiry*

(STUDY #2)

Affiliation

The researcher of this study is Rebecca Johnson, a doctoral student at Seton Hall University in the Department of Interprofessional Health Sciences and Health Administration, School of Health and Medical Sciences.

Purpose

The purpose of this study is to understand elements involved in active racial and ethnic minority recruitment practices for biopharmaceutical-sponsored clinical trials. Approximately 20 individuals will participate in the data collection for this research study as an opportunity to share their thoughts and practices specific to clinical trial recruitment, as well as specifically focusing on recruiting minority participants.

Procedure

You will be asked to participate in a telephone interview. In general, you will be asked questions on clinical trial recruitment with regard to:

- a. Personal knowledge and practices
- b. Communication within your research center
- c. Your organization's approach
- d. The surrounding community
- e. Environmental elements that may play a role in your recruitment efforts

The interview could take approximately 1 hour to complete and will be conducted over the phone. During the last 5 minutes of the interview, demographic information will be collected.

Approach and provide answers during the interview from your individual point of view candidly, expressing your thoughts regarding the above-mentioned topic. The telephone interview will be recorded, if you permit. The recording will then be saved on to a USB and accessed only by the Principal Investigator. If you prefer that the interview not be recorded, the Principal Investigator will be capturing ideas by hand-written notes.

Voluntary Participation

Your participation in this research study is voluntary. You may decide at any time not to participate in this study. If you decide not to participate or withdraw, the Principal Investigator will not reveal your decision to any other individual.

School of Health and Medical Sciences
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Tel: 973.275.2076 • Fax: 973.275.2171
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A H O U S E F O R T H E S I N D T H E H E A R T A N D T H E S P I R I T

Anonymity

Through the conduct of the telephone interview, the Principal Investigator will know your identity. However, your participation and responses will remain confidential. For purposes of confidentiality, a participant number and pseudonym will be assigned to you. When your interview is transcribed, your participant number will be utilized. You will not be identified by name or your contact information in any reports or publications about this study.

Privacy and Confidentiality

Protection and confidentiality will be maintained throughout the duration of the research project. Upon completion of the study, all data collected will be kept in a locked filing cabinet in the Principal Investigator's home office. Similarly, all electronic data will be stored on a USB memory key in that secured filing cabinet. The Principal Investigator will have access to all of the data for a period of up to three years after the end of the study. After three years, all data will be destroyed.

Risk

There is no foreseeable risk factor or discomfort that is anticipated by participating in this research study.

Benefit of Participation

There will be no monetary compensation or any kind of compensation for participating in this study. However, participants will be providing valuable information to better understand minority recruitment for biopharmaceutical-sponsored clinical trials.

Ways to Participate

A telephone interview will be scheduled. This consent form must be signed prior to the interview. Once this signed consent form is returned to the Principal Investigator, the interview may take place at your earliest convenience.

Contact Information

You have the right to ask questions concerning this study at any time. If you have any questions concerning this study or your rights as a study participant, please feel free to contact the Principal Investigator, Rebecca Johnson, through the offices of Dr. Terrence Cahill, Dissertation Chair and Department Chair in the Department of Interprofessional Health Sciences and Health Administration, School of Health and Medical Sciences, at Seton Hall University at (973) 275-2449 or terrence.cahill@shu.edu. Additionally, for information concerning the rights of research participants you can contact Dr. Mary Ruzicka, Chair of the Institutional Review Board, in the office of IRB at Seton Hall University at (973) 313-6314.

**Seton Hall University
Institutional Review Board**

OCT 08 2018

Approval Date

Expiration Date

OCT 08 2019

Thank you for your consideration in participating and contributing to this research. Your time and contribution are greatly appreciated. If you consent to participate in this study, please provide your signature below.

Consent

I consent voluntarily to participate in this study, as described in the Informed Consent Form.

I consent to audio recording of the telephone interview. If I check no to audio recording, please understand that for purposes of the study the Principal Investigator will be capturing ideas by hand-written notes.

Yes ☐

No ☐

Printed Name

Signature

Date

Seton Hall University
Institutional Review Board
OCT 08 2018
Approval Date

Expiration Date
OCT 08 2019

APPENDIX C

RESEARCHER POSITIONING STATEMENT

Researchers recognize that their own background shapes their interpretation, and they “position themselves” in the research to acknowledge how their interpretation flows from their own personal, cultural, and historical experiences. Thus the researchers make an interpretation of what they find, an interpretation shaped by their own experiences and background. The researchers intent, then, is to make sense of the meanings others have about the world (Creswell, 2013, p. 25).

As a result of being responsible for providing strategic direction or implementation oversight of patient recruitment programs for pharmaceutical-sponsored clinical trials for more than 10 years, I have first-hand experience and understanding of the pressures related to meeting and exceeding recruitment timelines. These pressures are understandable, given the financial impact tied to recruitment performance for sponsors, contract research organizations and research sites. In my experience, considerations for inclusion of clinically relevant populations related to race or ethnicity have historically been limited to a handful of studies in which demographic-specific cohorts were the result of a mandate by the Food and Drug Administration.

The vast majority of trial participants are non-Hispanic white, even though industry stakeholders and governmental agencies have recognized a need for greater diversity in recruitment. More recently, I have engaged in discussions with diversity and inclusion leaders whose roles are to improve diversity in the pharmaceutical-sponsored clinical trials in which they participate. Unfortunately, they face some of the same barriers I have encountered when attempting to implement a diversity strategy plan on a trial level. While they are in alignment on the necessity of diversity inclusion, there is hesitation regarding the return on investment and the

potential impact of time and cost on a trial. While that can be frustrating, I have an appreciation for the difficulties of operationalizing diversity inclusion on a trial level.

I grew up in a non-diverse area and did not appreciate social injustice until becoming an adult. In addition, my first-hand experiences with people in my life who have different values and beliefs regarding utilization of the healthcare system from mine opened my eyes to recognizing cultural and socio-economic differences that may impact their beliefs and attitudes about healthcare. That is when I began developing a strong interest in how different cultures assimilate healthcare information, healthcare disparities among minority cultures, and how to address these disparities by providing culturally relevant education through multi-cultural marketing initiatives. My professional background in clinical trial recruitment led to combining my interest in multi-cultural marketing with opportunities for addressing inequalities by focusing on improving access to clinical trials within diverse populations.

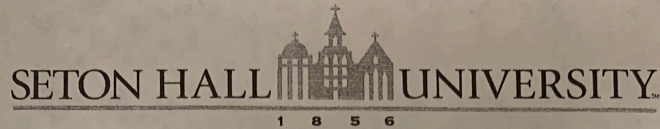
After reading the literature regarding minority recruitment in clinical trials, I was curious about what motivates researchers who conduct industry-sponsored trials and who actively focus on recruiting minority trial participants, since these researchers are not mandated to do so. I assumed that it is not just one reason, but that many different factors could be at play, and the socio-ecological model allowed for observing many elements in this regard. I did not want to incorporate my preconceived thoughts into the study as to what the motivation or other elements may be that are involved when researchers actively recruit minorities when not mandated to do so. Therefore, the interview guide was carefully designed to be very broad to allow participants to provide a wide view of their perceptions and experiences on this topic.

My professional background has afforded me experience with developing recruitment strategies, including strategies specific to recruiting minority populations. I do not have

experience working at a research site and hope that discussing the practical minority recruitment experiences of individuals who work at research sites will deepen my knowledge in this area and give me a better understanding of related activities that take place at a research site level. I would like to be able to be a part of moving the needle from recognizing the problem, to discussing and planning for change, to actually implementing a successful change initiative that will result in a more proportionate demographic representation in biopharmaceutical-sponsored research.

APPENDIX D

SETON HALL UNIVERSITY IRB APPROVAL



October 8, 2018

Dear Ms. Johnson,

The Seton Hall University Institutional Review Board has reviewed the information you have submitted addressing the concerns for your proposal entitled "Understanding Elements Involved in Active Racial and Ethnic Minority Recruitment Practices for Biopharmaceutical-Sponsored Clinical Trials: A Socio-Ecological Qualitative Inquiry (Study #2)". Your research protocol is hereby approved as revised through expedited review. The IRB reserves the right to recall the proposal at any time for full review.

Enclosed for your records are the signed Request for Approval form and the stamped original Consent Form. Make a copy only of this stamped form.

The Institutional Review Board approval of your research is valid for a one-year period from the date of this letter. During this time, any changes to the research protocol must be reviewed and approved by the IRB prior to their implementation.

According to federal regulations, continuing review of already approved research is mandated to take place at least 12 months after this initial approval. You will receive communication from the IRB Office for this several months before the anniversary date of your initial approval.

Thank you for your cooperation.

In harmony with federal regulations, none of the investigators or research staff involved in the study took part in the final decision.

Sincerely,

Mary F. Ruzicka, Ph.D.

Mary F. Ruzicka, Ph.D.
Professor
Director, Institutional Review Board

cc: Dr. Terrence Cahill

Office of Institutional Review Board
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