UNDERSTANDING AND IMPROVING DIVERSITY IN CLINICAL RESEARCH FOR BLACK PATIENTS: A QUALITATIVE META-ANALYSIS STUDY

by

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Abstract

Black patients remain underrepresented in clinical research, representing 5% of patients enrolled United States clinical trials (Alegria et al., 2021). Lack of diversity in clinical research creates blind spots about the effectiveness of treatments in underrepresented populations, resulting in substandard downstream care. Through analysis of available literature on Black patient engagement in clinical trials, proposals can be made to increase trial enrollment and equity.

A qualitative meta-analysis was conducted to interpret research completed to date on increasing clinical research diversity for Black patients. A PubMed literature search yielded 720 possible articles, 35 were used for meta-analysis. Each article underwent multiphasic review to identify research characteristics; generate enrollment promotors and barriers, identify themes; identify significant findings across multiple articles; identify under-investigation and contradictory findings; and review solutions applicable for future research.

Enrollment promotors included thorough explanation and information provision on study design, possible downstream beneficiaries; strong/longitudinal researcher-participant relationships and researcher-participant racial concordance; higher income and socioeconomic status of participants; research institution accessibility; compensation and increased study funding; community outreach and personal contact; and personal connections to research for both participants and researchers. Enrollment barriers included low income/socioeconomic status, low education, unfeasible time commitments, lack of transportation; lack of trust in medicine and clinical research teams; inadequate information on clinical research; studies
requiring medical record review, blood samples, novel pharmaceutical interventions, and invasive procedures; and studies with comorbidities as exclusion criteria.

Themes in research conducted to date include cancer research, investigations into Black women, and historical, structural, and personal factors. Historical factors that affect enrollment for Black patients include mistrust of the medical establishment, research institutions, and researchers. Structural barriers include income, socioeconomic status, time commitment and lack of transportation as well as exclusionary study designs and lack of resources for better clinical research engagement. Personal factors showcase the need for nuanced engagement around personal connections to research subjects, and benefits and pitfalls of utilizing religious institutions as partners depending on the research study subject. Solutions from current literature included better research explanation, improving diversity of clinical research teams, increasing interactive instruction, and using unique methods of increasing community around clinical research.

**Primary Reader and Advisor:** Jeffrey E. Kantor, Ph.D.
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Background

Race is one of the fundamental determinants of health which influences “process of care, quality of care, and outcomes” in many fields (Alegria et al., 2021). In the United States, Black patients are disproportionately affected by the major causes of morbidity and mortality (Harris et al., 1996). They also have disproportionately low access to care throughout the continuum of preventative, diagnostic, treatment and palliative services (Harris et al., 1996). Clinical research is a mainstay in the development of efficacious and safe treatments to minimize the burden of disease.

The National Institutes of Health Revitalization Act of 1993 mandated all federal grants for clinical trials to include statement son the inclusion of women and minorities (Freedman et al., 1995). However, Black patients remain extremely underrepresented in reported clinical trials in the United States. When reported, Black patients represent only 5% of patients enrolled in reported US clinical trials (Alegria et al., 2021). Data resulting from clinical trials are meant to be representative of and applied to large populations meaning that a lack of racial diversity in clinical research can lead to the wrongful generalization of research data to large scale populations. Racial inclusivity is crucial for preventing blind spots about the effectiveness of treatments in underrepresented populations, resulting in substandard downstream care.

Review of Literature

There have been prior investigations into the lack of representation for Black patients in clinical research. This includes studies to understand the perspectives of potential research
enrollees, and identification of medical community distrust, inadequate effort to engage Black patients specifically, and a historic alienation of Black health professionals from academic research (Shavers-Hornaday et al., 1997). There are also multiple epidemiologic studies that describe the demographics of patients who participate in major clinical studies, identifying the disparities in representation for Black patients in research on diseases that disproportionately affect Black populations, such as heart failure (Azam & Colvin, 2021). To date, the field of medical practice research that has done the most comprehensive work of identifying and addressing representation for Black patients is cancer research, including research that generates solutions at the patient, health system and clinical trial level going for future trials (Awidi & Al Hadidi, 2021). However, no studies have reviewed literature on increasing Black patient participation in clinical trials across all medical specialties. Despite growing efforts to identify and address this shortcoming in the past decades, there are ongoing demonstrations of this, including failure of a five-year action plan to improve diversity in drug research initiated by the Food and Drug Administration in 2015 (Green et al., 2022). More comprehensive review of literature is in Table 1.

The use of the qualitative meta-analysis has been growing since the 2000s, and builds upon the quantitative meta-analysis study ability to built a new integrative interpretation of prior findings, while incorporating more diverse study designs that purely quantitative outcomes studies. This has most been used in field of psychology and psychiatry where many studies utilize outcomes of patient perspectives and insight (Timulak, 2009). However additional medical specialties have been using them including a study in pediatrics on family-centered rounds and humanistic impact (Fernandes et al., 2021).
Problem Statement

To date, substantial research has been conducted in which measures have been taken to promote the inclusion of Black patients. In addition, research conducted to date includes investigation on the barriers to improved enrollment for Black patients. A qualitative meta-analysis allows understanding, synthesizing, and expanding upon this body of literature, creating opportunity to improve equitable enrollment of Black patients in clinical research in an effort to improve subsequent health outcomes.

Rationale

The qualitative meta-analysis is a unique means of reviewing and interpreting a vast body of literature to generate novel solutions (Levitt, 2018). While a more traditional meta-analysis of quantitative work enables stronger power through the combination of like studies, a qualitative meta-analysis expands the nature of studies that can be assessed. The inclusion of qualitative, descriptive, and mixed method studies enables understanding a dimension of research that is often not addressed in the context of like studies.

Moreover, the meta-analysis can provide additional insight by identifying the gaps in the current literature for future research, elucidating contradictory findings across research conducted to date, and generate novel solutions for the issue of suboptimal diversity in clinical research.
Methods

Literature Assembly

Literature on the research conducted to date on Black patient recruitment in clinical trials was acquired through the PubMed service of the National Library of Medicine. The literature review search utilized Boolean combinations of the terms: “Black”, “African American”, “Clinical Trial”, “Research”, “Participation”, “Enrollment”, “Barriers”. The resultant searched revealed 720 articles. Title review reduced the corresponding appropriate article count to 73. Abstract review reduced the article count to 47. Subsequently, the Critical Appraisal Skills Program (CASP) checklists were applied as a means of using a standardized rubric to assess quality of studies and fit to the meta-analysis inquiry (CASP Studies Checklist, 2023). Unique study designs (qualitative, randomized controlled trials, other quantitative studies) have corresponding checklists made available and utilized. Elements of the CASP checklists include evaluation for results validity, justification of research intention and design, and applicability of research findings to novel inquiry. The resultant list of articles included in the ultimate meta-analysis was 35. Literature assembly and screening is depicted in Figure 1.
Figure 1 Literature Review Flowchart

Meta-Analysis

Review of the literature was conducted in a multi-phasic approach. The initial review was the utilization of the CASP checklists, which also allowed for identification of the journal of publishing, the year of publishing, the study design and the study population.

A secondary review was completed to generate units of primary findings; categorization into themes; and produce labels of individual notes in the articles. The primary findings units were subdivided into enrollment promotors and enrollment barriers. The identification and categorization into themes were conducted both for the pattern of articles that were most
represented in the literature, and the overlapping themes most commonly seen amongst individual article results or discussion. The labels of individual notes in the articles were primarily produced as a means of rapid further search and review of articles as needed.

After creation of these units, the meta-analysis was completed initially through the identification of frequency and weight of findings. Tertiary review of articles with overlapping units enabled finding connections of like results, areas of under-investigation, and areas of contradictory findings.

A quaternary review was also conducted to specifically assess solutions tested or suggested for the improvement of diversity in clinical research for future research.

**Results**

35 articles were included in the meta-analysis after review with the CASP checklists. All included articles had Black patients as at least one of if not the sole demographic group within the study population. Literature from 1994 to 2023 were represented in the meta-analysis literature set. Study designs included qualitative-only studies (12 articles), quantitative-only studies (9 articles), mixed-methods studies (7 articles), descriptive studies (2 articles), randomized control trials (3 articles), and non-randomized controlled trial experiments (2 articles). Amongst the non-qualitative-only studies included, many studies applied quantitative evaluations to data that could otherwise be interpreted as qualitative (e.g. Questionnaires
administered with Likert scale scoring). Details in brief of the studies included for the qualitative meta-analysis are included in Table 1.

**Primary Findings**

Most of the articles reviewed presented both enrollment promotors and enrollment barriers amongst their study findings. Consistently identified enrollment promotors included thorough explanation and information provision on study design, components, and possible downstream research beneficiaries (Fouad et al., 2001; Gooden et al., 2005; Linden et al., 2007; Millon-Underwood et al., 1993; Owens et al., 2013; Trauth et al., 2005; Unson et al., 2001). Another promotor identified across multiple studies was strong and/or longitudinal researcher-participant relationship (BeLue et al., 2006; Farmer et al., 2007; Hughes et al., 2017; McClary et al., 2023; Robinson et al., 1996) with additional emphasis placed on researcher-participant racial concordance (Frierson et al., 2019; Mouton et al., 1997; Smith et al., 2007). Higher income/socioeconomic status was also found to be associated with increased enrollment (Brown & Topcu, 2003; Robinson et al., 1996). Both research institution accessibility and treatment specifically at a university clinic were also noted to be enrollment promotors (Advani et al., 2003; Germino et al., 2011; Unson et al., 2001). Both study participant compensation and additional funding to enrollment sites were noted as enrollment promotors (Cook et al., 2010; Owens et al., 2013; Smith et al., 2007). Successful study recruitment strategies included community outreach, word of mouth/snowballing recruitment, personal contact (Ahaghotu et al., 2016; Brown et al., 2014; Germino et al., 2011; Haynes-Maslow et al., 2014; Jones et al., 2009; Otado et al., 2015; Smith et al., 2007). A personal connection to the research cause, whether
present in the participant or shared from the research team also promoted enrollment (Hughes et al., 2017; Linden et al., 2007; Smith et al., 2007; Trauth et al., 2005).

Enrollment barriers demonstrated throughout the literature include low income/socioeconomic status, low education, unfeasible time commitments, and lack of transportation (Advani et al., 2003; Ahaghotu et al., 2016; Brown & Topcu, 2003; Fouad et al., 2001; Linden et al., 2007; Martin et al., 2013; McClary et al., 2023; Otado et al., 2015; Pugh et al., 2022; Robinson et al., 1996; Smith et al., 2007; Woods et al., 2002). Lack of trust in medicine as an establishment as well as the research team was noted throughout multiple studies (Harris et al., 1996; Haynes-Maslow et al., 2014; Linden et al., 2007; Mouton et al., 1997; Otado et al., 2015; Owens et al., 2013; Pugh et al., 2022; Roberson, 1994; Robinson et al., 1996). A lack of information about the study under consideration and about clinical research as a practice was also a noted enrollment barrier (Harris et al., 1996; Hughes et al., 2017; Millon-Underwood et al., 1993; Owens et al., 2013; Rivers et al., 2019; Smith et al., 2007). Certain study designs were seen to be enrollment barriers, including those that reviewed medical records, required blood samples, involved pharmaceutical interventions with unknown side effects or invasive procedures (Brewer et al., 2014; Fouad et al., 2001; McClary et al., 2023; Pugh et al., 2022; Robinson et al., 1996; Unson et al., 2001). Studies that had exclusion criteria of comorbidities found that Black patients were disproportionately excluded accordingly (Adams-Campbell et al., 2004; Ahaghotu et al., 2016).

Themes
Cancer research was notably the area of clinical research that had the most robust body of literature to date. In addition, many studies specifically looked into Black women as a population of interest.

Three themes into which the enrollment promotors and barriers were subdivided were historical, structural and personal. Historical factors included mistrust of the medical system and specific institutions or researchers. Structural factors included low income/socioeconomic status, time commitment, lack of transportation, lack of access to study information, and study design. Personal factors included lack of education on clinical trials as a practice, concerns about specific treatment/intervention format, a personal connection to study cause, and extent of participant and/or study integration with community.

**Novel Results Through Meta-Analysis**

One specific area of controversy that emerged from review of the literature was the use of churches for study enrollment and the impact of religious beliefs. Some studies identified that patients with religious beliefs were less likely to enroll in clinical research (Advani et al., 2003; Linden et al., 2007; McClary et al., 2023). There were also studies that found recruitment through churches to be an enrollment promotor (Fouad et al., 2001; Haynes-Maslow et al., 2014) and enrollment barrier (Brown et al., 2014).

A knowledge of the history of clinical research involving Black patients in the United States (typically the Tuskegee Syphilis Study) also had contradictory findings from the literature. Multiple studies noted knowledge/stigma in regards to clinical research as an enrollment barrier
(Haynes-Maslow et al., 2014; Hughes et al., 2017; Rivers et al., 2019; Shavers et al., 2001; Smith et al., 2007) however, one study noted no significant association in enrollment based on knowledge of the Tuskegee Syphilis Study (Brown & Topcu, 2003) and one specifically noted open discussion on historically problematic research as an enrollment promotor (Farmer et al., 2007).

Areas of lesser investigation in the current literature include health conditions of study outside of cancer. The use of novel, digital recruitment strategies for increasing diversity in clinical research for Black patients is also underreported in the current literature.

**Solutions in Literature to Date**

The bulk of solutions suggested in the literature to date pertain to maximizing the enrollment promotors identified and minimizing the enrollment barriers. Mechanisms to improve the explanation of clinical research, including taking more time to assure safety and explain the desired outcome of benefitting future patients has been suggested (Owens et al., 2013). Improving the diversity of research teams to generate greater research team-subject concordance, and focusing on communication to maximize the perception of researcher competence and compassion are also among the suggested improvements (Robinson et al., 1996; Smith et al., 2007). One randomized controlled trial demonstrated that interactive-computer assisted instruction created greater adherence to mammography screening among Black women than passive media like pamphlets or videos (Champion et al., 2006). The use of novel interventions to produce improved community presence and optimize word-of-mouth dissemination was also discussed in the form of “Home Health Parties”, events hosted by participants for others that
generate discussion on subjects of health and clinical research through games and other engaging activities (Sadler et al., 2006).
<table>
<thead>
<tr>
<th>Author(s), Year</th>
<th>Study Design</th>
<th>Study Population</th>
<th>Enrollment Promotors</th>
<th>Enrollment Barriers</th>
<th>Other Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adams-Campbell, et al., 2004</td>
<td>Descriptive (Registry Review)</td>
<td>Cancer Patients</td>
<td>--</td>
<td>Comorbidities as exclusion criteria</td>
<td></td>
</tr>
<tr>
<td>Advani, et al., 2003</td>
<td>Quantitative</td>
<td>Cancer Patients</td>
<td>Treatment at University Clinic (over outreach clinic)</td>
<td>Religious belief, low education, low income</td>
<td></td>
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<tr>
<td>Ahaghotu, et al., 2016</td>
<td>Mixed Methods</td>
<td>Prostate Cancer Patients</td>
<td>Personal contact, contact via community groups</td>
<td>Comorbidities, socioeconomic status, education &amp; awareness, cultural barriers, institution of treatment</td>
<td></td>
</tr>
<tr>
<td>BeLue, et al., 2006</td>
<td>Qualitative</td>
<td>General Population Focus Group</td>
<td>Men: Understanding funding, financial stakeholders; Women: researcher-participant relationship</td>
<td>--</td>
<td>Study goal to understand differences in beliefs and attitudes by gender</td>
</tr>
<tr>
<td>Brewer, et al., 2014</td>
<td>Quantitative</td>
<td>African American women’s service organization</td>
<td>Study Design: interview studies. General research favorability for professional African American women</td>
<td>Study Design: clinical trials, medical record review</td>
<td></td>
</tr>
<tr>
<td>Brown &amp; Topcu 2003</td>
<td>Quantitative</td>
<td>General Population</td>
<td>Males, Younger, Higher Income, ‘Nonfatalistic’ Cancer beliefs</td>
<td>Older, Lower Income</td>
<td>No significant association found with knowledge of Tuskegee Study</td>
</tr>
<tr>
<td>Brown, et al., 2014</td>
<td>Mixed Methods</td>
<td>Rural, Florida Men</td>
<td>Community outreach, ethnographic mapping</td>
<td>Church-based recruitment</td>
<td>Specific investigation on HIV testing</td>
</tr>
<tr>
<td>Study Authors, Year</td>
<td>Study Design</td>
<td>Participant Characteristics</td>
<td>Intervention Details</td>
<td>Recruitment/Access Details</td>
<td>Outcomes</td>
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<tr>
<td>Champion, et al., 2006</td>
<td>Randomized Controlled Trial</td>
<td>Low-income women</td>
<td>Interactive computer-assisted instruction</td>
<td>Pamphlets, passive videos</td>
<td>Specific investigation on mammography screening</td>
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<tr>
<td>Cook, et al., 2010</td>
<td>Experimental, matched post hoc</td>
<td>Sites for clinical trial enrollment, seeking greater African American enrollees</td>
<td>Minority Recruitment Enhancement Grants (additional funding)</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Farmer, et al., 2007</td>
<td>Mixed Methods</td>
<td>Women</td>
<td>Longitudinal community relationships, Open discussion on historically problematic research</td>
<td>--</td>
<td>No differences in participation perspective between African American and low-socioeconomic status White women</td>
</tr>
<tr>
<td>Fouad, et al., 2001</td>
<td>Qualitative</td>
<td>Alabama residents</td>
<td>Adequate study information, presentation from pastor or physician</td>
<td>Time commitments, family obligations, blood required, poor past experiences</td>
<td></td>
</tr>
<tr>
<td>Frierson, et al., 2019</td>
<td>Mixed Methods</td>
<td>Women</td>
<td>Participant and researcher racial concordance; trust building</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Germino, et al., 2010</td>
<td>Randomized Controlled Trial</td>
<td>Young breast cancer survivors</td>
<td>Community outreach, study accessibility expansion, use of cultural brokers</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Type</td>
<td>Participants</td>
<td>Study focus</td>
<td>Barriers</td>
<td>Notes</td>
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<tr>
<td>Gooden, et al., 2005</td>
<td>Qualitative</td>
<td>Adults 41-65 in North Carolina</td>
<td>Comprehension of study process and progress</td>
<td>--</td>
<td>Study on participation in cancer observational epidemiologic study</td>
</tr>
<tr>
<td>Harris, et al., 1996</td>
<td>Quantitative</td>
<td>Adults or caregivers</td>
<td>--</td>
<td>Lack of trial awareness, economic factors, communication issues, mistrust</td>
<td></td>
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<tr>
<td>Haynes-Maslow, et al., 2014</td>
<td>Qualitative</td>
<td>Female cancer survivors and caregivers</td>
<td>Increased community knowledge, use of churches for education, community members with past trial experience</td>
<td>Lack of trust, historical stigma on research and healthcare</td>
<td></td>
</tr>
<tr>
<td>Hughes, et al., 2015</td>
<td>Qualitative</td>
<td>Community members and community leaders (clergy, healthcare and service providers)</td>
<td>Providing personal stories on potential benefits of research, familiarity with recruiter</td>
<td>Lack of information about research, knowledge about historical occurrences</td>
<td></td>
</tr>
<tr>
<td>Jones, et al., 2009</td>
<td>Descriptive</td>
<td>Rural Central Virginia Men</td>
<td>Word of mouth recruitment, usage of community sites</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Linden, et al., 2007</td>
<td>Qualitative</td>
<td>Women</td>
<td>Significance of research topic to individual/community; Understanding trial elements; Openness to Risk</td>
<td>Mistrust in system; preference for natural treatments or religious intervention; cost</td>
<td></td>
</tr>
<tr>
<td>Study Authors, Year</td>
<td>Study Type</td>
<td>Study Population</td>
<td>Study Design/Method</td>
<td>Main Findings</td>
<td></td>
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<tr>
<td>Martin, et al., 2013</td>
<td>Randomized Controlled Trial</td>
<td>Postpartum women</td>
<td>--</td>
<td>Lack of interest; time commitment; fatigue/pain; relocating; feeling overwhelmed; issues of confidentiality</td>
<td></td>
</tr>
<tr>
<td>McClary, et al., 2023</td>
<td>Quantitative</td>
<td>Multiple Myeloma Patients</td>
<td>High trust; human connection</td>
<td>Strong religious beliefs, side effects concern, costs, travel distance</td>
<td></td>
</tr>
<tr>
<td>Millon-Underwood, et al., 1993</td>
<td>Quantitative</td>
<td>Adults</td>
<td>Information on increased risk, explanation on nature of screening/detection</td>
<td>Lack of knowledge on research beneficiaries</td>
<td></td>
</tr>
<tr>
<td>Mouton, et al., 1997</td>
<td>Quantitative</td>
<td>Women who rejected initial RCT enrollment</td>
<td>Preference for racial concordance with researchers</td>
<td>Lack of trust, perceived lack of care in researchers</td>
<td></td>
</tr>
<tr>
<td>Otado, et al., 2015</td>
<td>Mixed Methods</td>
<td>Prior studies review, study coordinators</td>
<td>Field based strategy, snowballing recruitment strategies</td>
<td>Distrust, poor compensation, education disadvantage, lack of interest</td>
<td></td>
</tr>
<tr>
<td>Owens, et al., 2013</td>
<td>Mixed Methods</td>
<td>Adults</td>
<td>Incentives, assurance of safety, knowledge and awareness, benefitting others</td>
<td>Poor knowledge of trials and informed consent process, limited prior experience in trial participation, fear and mistrust of cancer research</td>
<td></td>
</tr>
<tr>
<td>Pugh et al., 2022</td>
<td>Qualitative</td>
<td>Adults 51+ in Louisiana</td>
<td>--</td>
<td>Invasive procedures, pharmaceutical interventions, mistrust of investigators, inadequate</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Study Type</td>
<td>Population</td>
<td>Location</td>
<td>Issues</td>
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<tr>
<td>Rivers, et al., 2019</td>
<td>Qualitative</td>
<td>Women</td>
<td></td>
<td>Knowledge of historic research abuses, lack of information, lack of cultural relevance of education and outreach materials</td>
<td></td>
</tr>
<tr>
<td>Roberson, 1994</td>
<td>Qualitative</td>
<td>Buffalo, New York Adults</td>
<td></td>
<td>Mistrust of white researchers, feeling of “guinea pig” treatment</td>
<td></td>
</tr>
<tr>
<td>Robinson, et al., 1996</td>
<td>Qualitative</td>
<td>Men 40+ in South Central Los Angeles, California</td>
<td></td>
<td>Low socioeconomic status, drug toxicity concerns, medical experimentation and distrust of medical establishment</td>
<td></td>
</tr>
<tr>
<td>Sadler, et al., 2006</td>
<td>Experiment</td>
<td>Women in San Diego County, California</td>
<td>Home Health Parties</td>
<td>High importance placed on race of physician in seeking medical care, belief that poor bear most risk in medical research, knowledge of Tuskegee Study</td>
<td></td>
</tr>
<tr>
<td>Shavers, et al., 2001</td>
<td>Quantitative</td>
<td>Adults in Detroit, Michigan</td>
<td></td>
<td>High importance placed on race of physician in seeking medical care, belief that poor bear most risk in medical research, knowledge of Tuskegee Study</td>
<td></td>
</tr>
<tr>
<td>Smith, et al., 2007</td>
<td>Qualitative</td>
<td>Women</td>
<td>Community involvement, relevance to African Americans or their community, use of existing networks for</td>
<td>Lack of information reaching individuals and community, perception that benefits biased to</td>
<td></td>
</tr>
<tr>
<td>Study (2005)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Key Findings</td>
<td>Notes</td>
<td></td>
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<tr>
<td>Trauth, et al.</td>
<td>Quantitative</td>
<td>Women 55-74</td>
<td>Importance placed on cancer prevention and detection, experience of having loved one with cancer, knowledge and experience with clinical trials, beliefs regarding benefits and risks of trial participation</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Unson, et al. (2001)</td>
<td>Qualitative</td>
<td>Older Women</td>
<td>Research institution accessibility, assurance of full disclosure of test procedures and results</td>
<td>Lack of benefit perceived from participation, risks associated with drug intervention</td>
<td></td>
</tr>
<tr>
<td>Woods, et al. (2001)</td>
<td>Mixed Methods</td>
<td>Adults</td>
<td>--</td>
<td>Transportation, lack of readiness to quit, inadequate reminders, employment conflicts</td>
<td>Specific study on smoking cessation intervention</td>
</tr>
</tbody>
</table>
Discussion

This qualitative meta-analysis provided a summative view of the research to date on understanding clinical research participation for Black patients, and generated novel findings through the practice of comparing, contrasting, and analyzing findings from the pre-existing literature. There are a myriad of enrollment promotors and enrollment barriers that affect how Black patients interact with clinical research, many of which can be acted upon in the short term and many of which are reflective of societal, longitudinal challenges that healthcare continues to combat.

With regards to historical factors that affect enrollment, mistrust of the medical establishment as well as individual institutions or researchers was the result of longstanding discrimination and racism rooted in the history of the United States. Interestingly, while the Tuskegee Syphilis Study is a sentinel event in mistreatment of Black patients by the medical establishment, it can serve both as a barrier and promotor based on the level of engagement on the subject. Potential research subjects expressing a desire to have open discussion on the study reflects an important opportunity for improved enrollment, but one that required investment of time and resources to effectively address. The nature of a study, specifically one that does involve novel drug investigations or procedures may specifically warrant increased engagement about historical harms.

Structural barriers likely provide the greatest hurdle to overcome in the gamut of factors that prevent Black patients from participating in clinical research. Factors like income or
socioeconomic status, time commitment, lack of transportation are all reflective of areas that require increased resource investment in order to create greater diversity, and there is evidence that financial backing for the explicit purpose of increasing enrollment diversity did work. Study design is largely planned in anticipation of the desired study result. While this may limit changes for a randomized controlled trial testing a novel drug or procedure, designing studies to promote inclusion is possible, including restriction of comorbidities as exclusion criteria and increasing resources and interactivity to build better understanding on the nature and importance of clinical research.

Personal factors that influence participation in clinical trials reflected the need for a nuanced approach to maximize clinical research diversity. For example, the use of churches and partnership with religious leaders has been demonstrated as a successful means of increasing Black patient enrollment in clinical research. However, on the subject of HIV testing, it becomes a barrier, potentially reflecting longstanding stigma associated with HIV. The ability to capitalize on personal connections to clinical research provides both opportunity and risk. While potential subjects are inherently more motivated to improve medical knowledge on diseases that have affected themselves, their family, or friends, it is important to approach conversations of informed consent while minimizing bias or possible coercion. If potential research enrollees have intrinsic motivation to contribute to clinical research, efforts should be taken to provide them the resources to participate in clinical research and to make any studies they participate in not onerous to limit future participation. In addition, longer term investments into improving the pipeline of physicians and other clinical research staff that represent Black communities will likely improve participant motivation.
A better future for diversity for Black patients in clinical research must build from and beyond findings from this analysis. There is a need for investment of time and resources in order to overcome the societal and structural disadvantages that many potential Black research participants face. This scales from individual research teams taking additional time as needed to explain how their study works and the intended benefits for future patients to significant funding provided across healthcare research specifically aimed at improving diversity. Recruitment strategies need to utilize approaches that capitalize on the impact of community and that ground the research outcomes in real-world impact. One pathway forward can utilize the principles of community-based participatory research, in which the community of interest is engaged from the earliest stage in study design to engage with Black patients are stakeholders instead of simply subjects. This strategy can also help bridge gaps where research teams do not reflect the diversity of their target subject community, and generate novel practices to enhance enrollment. The use of novel digital technologies, including mobile phone-based applications can increase both interactivity and education around clinical research and warrants further research.

It is also appreciable that many of the shortcomings in clinical research diversity for Black patients is reflected in healthcare, and even society in general. The barriers that Black patients with regards to clinical research are largely exacerbated by, but not unique to medical care. Social programs aimed at increasing the welfare and diversity of Black people in the United States will likely effect diversity in clinical research as well. Ultimately, participation in research can be viewed as a privilege of time, resources, and power.
In the same lens, many of the solutions generated from this meta-analysis are not unique to Black populations. Many articles that emerged from the literature review would jointly assess Black and other underprivileged United States populations, including low-income white patients. The efforts to increase Black patient representation in clinical research can therefore largely be applied to increase diversity in clinical research generally.

Limitations

The literature that is currently present on mechanisms to improve Black patient engagement with clinical research is robust but nevertheless limited. The extent of literature on cancer trials is a reflection of where national government funding for research has been directed, but also speaks to the importance of further research on increasing diversity in non-cancer clinical research with Black patients. The literature review conducted for this meta-analysis was comprehensive, but may be limited by multiple articles that utilize terminology such as “racial minority” or “underrepresented” populations in their titles and key terms.

Despite all that is captured in this qualitative meta-analysis, it is important to acknowledge that this investigation building from the research completed to date simply cannot be a comprehensive view of the factors affecting how Black patients interact with clinical research. It is important to understand first and foremost that Black Americans are not a monolithic group. There is immense diversity within Black community across the United States, and each community and individual likely has unique factors that impact how they approach clinical research. Some of this is reflected in the controversial findings in conducting this meta-
analysis, but some of it inherently means that future clinical research must be designed in partnership and with the unique target population in mind to optimize enrollment.

The significant amount of research to date that is focused on Black women specifically speaks to the importance of understanding how intersectionality affects Black populations. The unique challenges that Black women and Black LGBTQ+ community members face in interfacing with healthcare and clinical research in general presents more unique barriers to participation, not all of which are adequately captured in literature completed to date.

Conclusion

Increasing Black patient enrollment in clinical research is a crucial for equitable healthcare in the United States, and a shortcoming in the efforts of the medical establishment to date. This qualitative meta-analysis has identified promotors and barriers to clinical research participation, including historical, structural and personal factors affecting how Black patients approach clinical research. It has also elucidated areas for ongoing research and intervention to improve future clinical research diversity.
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