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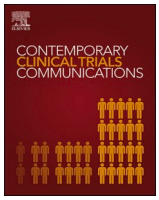

An evaluation of race-based representation among men participating in clinical trials for prostate cancer and erectile dysfunction

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ABSTRACT

Background: Inclusion of ethnic/racial minorities in clinical trials is essential to fully assess therapeutic efficacy. It is well-known that populations respond dissimilarly to interventions. Our objective is to analyze the inclusion of minority men in clinical trials for erectile dysfunction (ED).

Methods: We searched ClinicalTrials.gov for the disease keyword: "Erectile Dysfunction" and used "Prostate Cancer" for comparison. Completed trials which reported demographic data were included for analysis. Literature was reviewed to determine the prevalence of ED and prostate cancer (PC) among Hispanic, Black, White, and Asian men. The proportion of individuals of each group that participated in trials is divided by the proportion of each group in the disease population to calculate the "Participation to Prevalence Ratio" (PPR). PPRs between 0.8 and 1.2 indicates adequate representation, <0.8 is under-representation and >1.2 is over-representation.

Results: A total of 312 trials were assessed: 289 for prostate cancer and 23 for ED. Hispanic men comprised 11.8% of ED trial participants and 4.6% of prostate cancer trial participants, yet represented 18% of ED patients and 7.3% of PC patients. Black/African-American (AA) men accounted for 10.2% of ED trial participants and 9.4% of PC trial participants, but comprise 16% of ED patients, and 16.3% of PC patients. Hispanic and AA men are under-represented in trials for ED and Prostate Cancer (Hispanic ED PPR = 0.66; Hispanic PC PPR = 0.63; AA ED PPR = 0.64; AA PC PPR = 0.58).

Conclusion: Our analysis shows that both Hispanic and AA men are underrepresented in both ED and PC clinical trials.

1. Introduction

Erectile dysfunction is the most common form of male sexual dysfunction, which affects about 30 million men in the United States [1] and is expected to impact over 300 million men worldwide by the year 2025 [2]. Prostate Cancer is one of the leading causes of cancer death in men in the US. It accounts for nearly 20% of all male cancers and 9% of male cancer-related deaths [3], and is more common among African-American men [4]. Previous research has shown that clinical interventions and therapies can have varying success based upon racial and ethnic characteristics in the US population. While race has long been regarded to be a social construct [5], race and ethnicity have been shown to serve as indicators of ancestral heritage which impacts in internal factors (e.g. genetic polymorphisms, metabolism, pharmacokinetics) and external factors (e.g. diet, environment, sociocultural) across racial and ethnic lineages [6,7]. These variations lead to distinct and

Abbreviations: AA, Black/African American; CBPR, Community Based Participatory Research; ED, Erectile Dysfunction; FDA, United States Food and Drug Administration; ICD 10, International Classification of Disease, Tenth Revision; NCI, National Cancer Institute; NIH, United States National Institutes of Health; PC, Prostate Cancer; PPR, Participation to Prevalence Ratio; RQ, Representation Quotients; URM, Under-represented Minority.

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clinically relevant effects which influence treatment recommendations and dosage guidelines for their patients. Therefore, it is necessary to consider a patient's racial and ethnic background when prescribing a treatment regimen since the variability in treatment uptake and responses can differ, based on genetic susceptibility, environmental influences, and socio-cultural factors [8].

When designing a clinical trial, it is imperative to define the study population of interest in order to produce meaningful results which can be generalized and applied to a broader target population. Without a representative study population it becomes nearly impossible, in most circumstances, to achieve sufficient external validity which is necessary to accurately translate the research findings to the broader population [9]. Thus, having a diverse cohort of study participants is essential to fully assess the therapeutic efficacy across the full spectrum of the population.

In 2020, the US Food and Drug Administration (FDA) issued guidance for clinical trials to follow in order to increase participation rates among members of historically underrepresented groups [10]. These strategies include: (1) reducing the number of visits to external sites required by participants, (2) use of electronic communication instead of physical visits when possible, and (3) use of bi-directional communication strategies with community stakeholders at all levels of research design, implementation, and dissemination of results. However, despite these concerted efforts to promote diversity in clinical trial participation, there are still significant disparities in trial participation among historically underrepresented minorities (URMs) [11,12]. One recent review of recruitment of minorities and women in oncology trials found a decrease in recruitment of URMs in comparison to historical data [13]. Despite racial and ethnic minorities having a greater likelihood to develop certain chronic diseases, a recent systematic review found that they still remain underrepresented in clinical trials for such diseases/conditions [14]. A recent meta-analysis of trial participation among AA patients concluded that the main reasons for unwillingness to participate in trials is caused by: (1) mistrust of the healthcare system, (2) healthcare provider-related barriers, (3) familial influence, (4) socioeconomic status, (5) health literacy limitations, and (6) spirituality. Some of the proposed solutions to combat this are engagement in community based participatory research (CBPR), and use of educational tools and patient navigators [15]. While these studies have been helpful in identifying gaps and trends in clinical trial participation, such a study has not been conducted to evaluate trials for men with ED.

In the present study, we hypothesized that Hispanic, Black/African-American (AA), and Asian men are underrepresented in clinical trials for Erectile Dysfunction (ED) and Prostate Cancer (PC). Furthermore, we hypothesized that white/caucasian men are overrepresented in clinical trials for these urological conditions. Our objective was to summarize and systematically evaluate the demographic composition of trial cohorts using data gathered from ClinicalTrials.gov.

2. Methods

Trials were identified via the ClinicalTrials.gov database by searching for the keyword terms, Erectile Dysfunction" and "Prostate Cancer". We aggregated data from trials that were completed between the years of 2010–2020 that reported participant enrollment characteristics stratified by sex, race, and ethnicity. Information including the study title, study disease, intervention, and outcome measures, sample size, and age range was extracted from the database for analysis. Racial categories included American Indian, Asian, Pacific Islander, Black/African American (AA), White, Biracial, and Unknown Race. We conducted a literature review of epidemiological studies from 2006 to 2022 to estimate the proportion of patients from each racial/ethnic group present in their respective disease populations.

The participation to prevalence ratio (PPR) was calculated for each demographic subgroup using the formula: *PPR = Proportion among trial participants ÷ Proportion among disease population.* PPR is expressed as a ratio which is used to assess the level of inclusion in clinical trials relative to the corresponding disease population. As described by Eshera et al., a PPR value of 1.0 indicates that inclusion in trials is equal to the proportion found in disease population [16]. Similarly, a PPR between 0.8 and 1.2 is considered adequate representation, while a PPR of <0.8 indicates under-representation and while a PPR of >1.2 indicates over-representation of the demographic sub-group. Data analysis was completed using Microsoft Excel (Microsoft 365).

3. Results

Among the 312 clinical trials that fit the inclusion criteria for our study, 23 (7%) were for Erectile Dysfunction (ED) and 289 (93%) were for Prostate Cancer (PC). Based on aggregated data, the proportion of participants in clinical trials stratified by race/ethnicity is presented in Table 1. The prevalence of each ethnicity and race is the disease populations were estimated using data gathered from external sources [17–19]. For PC, the majority of participants with the disease are White, whereas the racial breakdown is more evenly distributed in ED (Table 2).

When comparing the proportion of participants in the trials (Table 1) to the proportion of patients with the disease (Table 2), the PPR was calculated for each race/ethnicity and disease, and is displayed in Table 3. The PPR for Hispanic participants in ED trials was 0.66, indicating underrepresentation of this group compared to the source population. Regarding other demographic groups in ED trials, AA men were underrepresented (0.64), White men were slightly overrepresented (1.21), and Asian men (5.94) were overrepresented (Table 3). White and Asian men were found to be accurately represented in PC trials (1.16 and 0.98, respectively), yet Hispanic men and AA men were underrepresented in PC trials having PPRs of 0.63 and 0.58, respectively (Table 3).

4. Discussion

Clinical trials are touted as the 'Gold-Standard' in efficacy research, as they are essential to the development of new therapies [20] and critical for measuring the applicability of scientific discoveries to the general population. However, previous research has emphasized how underrepresentation of minorities in clinical trials can be problematic to the generalizability of the findings. In this study, we assessed relative differences in race/ethnicity reporting in clinical trials for two common urological conditions, and we computed the participation to prevalence ratio (PPR) to assess over-representation, under-representation, or adequate representation of the various demographic sub-groups of interest. Our findings show that Hispanic and AA men are underrepresented in trials for ED and PC. Furthermore, White and Asian men were represented accurately in trials for PC but were overrepresented in trials for ED. These results highlight the demographic differences in enrollment for urological studies, which poses substantial constraints on the external validity of the research being conducted.

The disproportionate burden of certain diseases in minority groups further highlights the importance of addressing gaps in clinical trial enrollment. For example, recent data from the American Cancer Society suggests that AA men are 1.7 times more likely to be diagnosed with prostate cancer compared to white men in the US [21], yet these patients tend to have less access to cancer facilities and prostate cancer trials [22]. This is reflected in our study results wherein AA participants were underrepresented in PC trials. Previous studies examined potential barriers to trial enrollment for minorities. These barriers are multifactorial and multilevel in that these factors can be interpersonal, individual, and structural [23]. Structural and institutional barriers include a lack of outreach programs or dedicated clinical trial staff, lack of hospital infrastructure in underserved communities, lack of or inadequate insurance coverage, restrictive eligibility criteria and/or study designs, and lack of culturally-competent care [24,25]. Of note, the impact of restrictive criteria for clinical trials can disproportionately

Table 1
Proportion of male clinical trial participants by race and ethnicity.

Study Disease	ICD 10 Code	Trials	Participants	Hispanic	White	AA	Asian
Erectile Dysfunction	N52.9	23	7,822	11.8%	77.7%	10.2%	10.4%
Prostate Cancer	C61	289	95,154	4.6%	85.2%	9.4%	2.2%

ICD 10 = International Classification of Disease, tenth revision; AA = Black/African-American.

Table 2
Population prevalence estimates among men with erectile dysfunction and prostate cancer by race and ethnicity.

Study Disease	Hispanic	White	AA	Asian	Source
Erectile Dysfunction	18.0%	64.2%	16.0%	1.8%	Laumann et al. (2007) [17] Ho CC et al. (2011) [18]
Prostate Cancer	7.3%	73.7%	16.3%	2.2%	Iyengar et al. (2020) [19]

AA = Black/African-American; Prevalence estimates may not sum to 100% due to rounding and other demographic groups not shown.

Table 3
Male participation in urology clinical trials by race and ethnicity: Prevalence corrected estimates.

Study Disease	Hispanic	White	AA	Asian
Erectile Dysfunction	▼ 0.66	▲ 1.21	▼ 0.64	▲ 5.94
Prostate Cancer	▼ 0.63	✓ 1.16	▼ 0.58	✓ 0.98

AA = Black/African-American; PPR interpretation: < 0.8 = under-representation (▼); 0.8 - 1.2 = adequate representation (✓); > 1.2 = over-representation (▲).

limit minority enrollment, as members of these populations are more likely to present with comorbidities that render them ineligible for important trials [26].

The results of this study highlight the ongoing gaps in race reporting in clinical trials – urological or otherwise. Despite a mandate by the National Institutes of Health (NIH) that requires sufficient representation of women and minority populations in clinical research, under-enrollment remains a documented challenge for researchers [27]. Twenty years after the 1993 NIH Revitalization Act, Chen et al. reviewed racial enrollment in trials funded by the National Cancer Institute (NCI) and reported that just 2% of 10,000 NCI trials demonstrated NIH-compliant minority enrollment [28]. In the field of urology, Owens-Walton et al. evaluated 341 interventional trials in prostate, kidney, and bladder cancers. Only 49.7% of the trials reported race and ethnicity, and aggregated representation quotients (RQs) showed a persistent overrepresentation of White participants [29]. In 2019, Paul et al. noted that non-urological trials were significantly more likely to mention race data than urological trials [30].

The main strength of this study is the relevance to public health and the focus on diversity, equity, and inclusion in research. Although widely used in evaluation of trial recruitment metrics in other medical fields, to our knowledge PPR has not been used to estimate representation in urology trials. Moreover, previous studies on this topic have typically focused on oncology trials, leaving gaps in assessing minority representation in clinical trials for ED or other disease fields within urology. However our study is not without limitations, such as the estimations of population prevalence that were used to assess PPRs. We scoured previous literature to estimate the proportion of each race in the disease populations which could lead to inaccurate PPR calculations. Data on Asian male sexual dysfunction is also relatively scarce compared to the other populations, possibly leading to under-estimations of prevalence. In addition, many of the studies in ClinicalTrials.gov did not include complete datasets, requiring some trials to be removed from the final calculations for PPR. Our study expands the question of minority enrollment to non-oncological diseases affecting urological patients. The results from this study highlight the importance of thoughtful and culturally competent study design and recruitment strategies, as well as the diversification of the urology workforce in order to better serve minority populations. To ensure the applicability and generalizability of clinical trials, it is essential that racial minorities are included.

5. Conclusion

Overall, our study highlights a gap in participation rates among men in Hispanic and AA communities with respect to urology clinical research. As a result, there must be an amplified effort to develop culturally relevant recruitment strategies to engage with underrepresented communities to improve the conduct of clinical research. Future efforts are needed to see if the establishment of recruitment targets for new clinical trials can increase community engagement and participation among minorities.

Author contributions

RS conceived of the research question that led to the submission, acquired data, helped interpret the results, and helped draft and revise the manuscript. IZ conceived of the research question, acquired data, helped interpret the results, and helped draft and revise the manuscript. KC, DG, KO, and AW acquired data and helped draft the manuscript. TM and RR contributed to interpretation of the results and revised the manuscript. All authors approved of the final version of the manuscript and agreed to be accountable for all aspects of the work to ensure that questions related to accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data availability statement

The data that support the findings of this study are available from https://clinicaltrials.gov/

Conflict of interest

All authors indicated no potential conflicts of interest.

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