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Authors
Park, Christina K
Alhusayen, Raed

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Representation and treatment allocation of racial groups in dermatologic therapy trials: A 2-year review of the literature

Christina K Park[1] MD(c) MSc, Raed Alhusayen[1,2] MBBS MSCE FRCP

Affiliations: [1]Faculty of Medicine, University of Toronto, Toronto, Canada, [2]Sunnybrook Health Sciences Centre, Toronto, Canada

Corresponding Author: Raed Alhusayen, MBBS, MSCE, FRCPC, Associate Scientist, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue Toronto, Ontario M4N 3M5, Email: raed.alhusayen@sunnybrook.ca

Abstract

Although most investigators would agree that including minority races in clinical trials is important, recruitment and retention may differ among these populations. The objective of this review was to perform an audit of phase III dermatologic therapy trials to determine representation for minority groups and to explore the possibility of racial allocation bias. In this review of 11 dermatology or general medicine journals in 2015-16, we did not find evidence of systemic racial allocation bias. We did however note variation in the proportion of minority races included in studies; whereas some trials had high success in recruiting minorities, many did not. Furthermore, most studies did not provide information on individual racial groups and rather presented an 'other' category. This supports findings from previous reviews of dermatologic therapy trials that suggest that most participants are white, race data are not included for many studies, and there is underrepresentation of some racial groups. We conclude that although there is no evidence of racial allocation bias in the previous two years, there remains a need for standardization in the reporting of racial groups and for increased participant diversity in dermatologic therapy trials.

Keywords: Randomized controlled trials, dermatologic therapy trials, allocation bias, minority inclusion

Introduction

Most investigators would agree on the importance of including minority populations in clinical trials [1]. However, there are some perceived barriers in minority recruitment, including access to the study population, lack of experience in recruitment, and cultural differences between investigators and participants [1]. As for the participants, there may be lack of awareness of trials, financial or economic factors, cultural and language barriers, as well as mistrust of the medical community that may impact study enrollment [2-4]. These factors may lead to the perception that recruitment and retention of minority groups is difficult and result in lower enrollment rates [4]. Various studies conducted in the United States examining racial diversity in clinical trial recruitment, including those in dermatology, reported a poor rate of minority group inclusion [5-7].

However, there hasn't yet been a study to our knowledge that examines racial differences between intervention and control groups. It is possible that there is unintentional bias towards less allocation to the intervention group. Randomization inherently assumes the balance of participant characteristics between intervention and control groups, but ascertainment of the risk of allocation bias may not always be clear in practice [8].

In this review, we performed an audit of prominent dermatology and general medicine journals to explore representation and allocation of racial groups in phase III dermatologic therapy trials.

Body of Article

For this literature review, we examined trials published in 11 dermatology and general medicine journals between January 1, 2015 to December 31, 2016 (**Figure** 1). We chose to conduct the search over two years in case one of the years represented an outlier in patient recruitment pattern.

- Annals of Internal Medicine
- Archives of Dermatology
- British Journal of Dermatology
- JAMA Dermatology
- Journal of Investigative Dermatology
- Journal of the American Academy of Dermatology
- Journal of the American Medical Association (JAMA)
- Journal of the European Academy of Dermatology and Venereology
- Nature Medicine
- The British Medical Journal
- The Lancet
- The New England Journal of Medicine

Figure 1. *List of included journals.*

The journals were selected a priori based on relevance and impact, with consensus between the authors. Five clinical dermatology journals were selected based on impact factor ranking, after elimination of those that focus on basic science. In addition, five prominent general medicine journals and one internal medicine journal were selected for their propensity to publish high-impact randomized controlled trials (RCTs), including those of dermatology therapeutics.

The main inclusion criterion was phase III randomized controlled trials of systemic agents for any non-cancerous dermatologic indication in adults. Skin cancer drug trials were excluded as there is a significant difference in the prevalence of skin cancers between races. We excluded any other study designs, studies with inclusion/exclusion criteria based on race, studies that included < 30 patients, and duplicate data or secondary analysis of a primary study.

A search was conducted on Ovid MEDLINE in January 2017 for 11 journals (.jn) 'AND' RCT terms (MeSH and .mp), limited to years 2015-2016 (Appendix). The records were imported into Endnote X7 bibliographic software and duplicates were removed. One reviewer (CKP) screened the titles and abstracts for full-text review and selected the final trials for inclusion. A secondary reviewer (RA) performed an audit of the journals to identify any missing studies prior to data extraction.

Race data for the control and intervention group(s) were extracted for all races that were presented by a single reviewer (CKP). If there was more than one intervention group, the numerator and denominator for the race data were summed to a single proportion. An online calculator that performed the "N-1" Chi-squared test was used, with a $p<0.05$ considered to be a significant difference in the race proportion between groups [9]. All data were stored in Microsoft Excel.

The search yielded 1,687 articles for title and abstract screening. Thirty-one were selected for full-text screening, and 11 articles for 14 international, multicenter trials were included in the final analysis (Table 1 [10–20]). All trials were for chronic indications, including 7 for moderate-to-severe plaque psoriasis and one each for idiopathic/spontaneous urticaria, moderate-to-severe atopic dermatitis, and hidradenitis suppurativa.

All trials reported a balance of baseline characteristics across groups in the methods. The proportion of race groups except for those categorized as 'other' are shown in Table 2. All trials reported the white group as the majority, ranging from overall proportions of 67.1% to 95.1%. Seven trials reported data on blacks (2.5% to 20.2%) and 5 trials on Asians (5.2% to 24.0%).

Overall, all comparisons for the proportion of whites and Asians were not significant between intervention and control groups ($p\geq0.05$). One trial had a significantly larger proportion of blacks in the placebo group (12.3% vs 5.5%, $p=0.03$), although the proportion of whites were balanced [14].

Discussion

True randomization in a trial allows equal opportunity for all participants to be allocated to each of the study groups [21]. Allocation bias can occur even with randomization, for instance with inadequate concealment [21]. Of 26 analyses, we found one instance of an increased proportion of blacks in the placebo group. Therefore, we cannot conclude that there is evidence of allocation bias for racial groups to either the intervention or control groups in dermatologic trials published in 11 prominent dermatology and general medicine journals during 2015-2016.

We did note the variation in inclusion of nonwhite races across studies; whereas some trials had high success in recruiting nonwhites, many did not. Furthermore, most studies did not include data on specific race groups (e.g. black, Asian), and rather reported an 'other' category in which various races were grouped. The largest consumer of prescription drugs worldwide remains the United States [22]. In the United States, minorities are projected to total over 50% of the population by 2044 [23]. It is important to note the genetic variations underlying diseases among racial groups, as it could lead to differing drug responses [24]. For instance, angiotensin converting enzyme inhibitors, β blockers, and angiotensin receptor antagonists may be less effective as monotherapy in blacks [25]. Considering this, the shifting demographic towards an increasing minority population was not reflected in most of the clinical trials of dermatologic therapies, despite international collaborations.

A recent review of minority groups in dermatology trials conducted in the United States report that the gross majority of participants remain white [5]. In addition, two reviews examining trials for atopic dermatitis therapies in the United States found that race data are not included for many studies and there was underrepresentation of some racial/ethnic groups, particularly Hispanics [6, 7]. There is a distinct clinical presentation of atopic dermatitis for blacks [26], as well as a potentially increased demand for atopic dermatitis care among Asians/Pacific Islanders and blacks [27]. However, one of the reviews concluded that there is a "dearth of studies demonstrating efficacy of systemic therapy in different racial and ethnic subsets [7]."

A strength of this study is that it explored racial allocation bias in dermatological randomized trials, which has not yet been examined previously to our knowledge. This study presented a cross-sectional review of the previous two years in the case of the previous year being an outlier. However, this study is limited by including 11 journals in a short duration of time. We acknowledge that a review of the literature performed by a single reviewer is not as robust as a full systematic review with multiple reviewers. This review is not intended to be a thorough review of the literature, but rather a cross-section of the patient demographics of larger select trials. We also note that increasing the number of racial subgroups would decrease statistical power, which may discourage researchers from analyzing drug effects in multiple groups. In this regard, we encourage even greater effort to recruit members of different races to ensure adequate statistical power in all or most of the racial groups in the setting(s) of study.

Conclusion

There are some identified challenges of recruiting minority groups, including lack of access, investigator experience, and cultural differences [1]. Although there may be erroneous beliefs in the research community that retention rates may be lower in minority races, it has been reported that minority races have equal or greater trial completion rates as whites [4]. Additionally, investigators who believe more strongly in the importance of minority inclusion may be more successful at minority recruitment rates [1]. Therefore, several strategies to increase recruitment rates of nonwhites may be to encourage investigators to prioritize minority inclusion and to dispel the notion that minority groups are more difficult to retain in trials. Studies conducted outside of North America and Europe should also be encouraged to increase diversity in the literature. In conclusion, although it is reassuring that the existence of racial allocation bias is unlikely, there remains a need for standardization in the reporting of racial groups and for increased participant diversity in dermatologic therapy trials.

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