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Systematic Review and Meta-analysis

Is Our Science Representative? A Systematic Review of Racial and Ethnic Diversity in Orthopaedic Clinical Trials from 2000 to 2020

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Abstract

Background A lack of racial and ethnic representation in clinical trials may limit the generalizability of the orthopaedic evidence base as it applies to patients in underrepresented minority populations and perpetuate existing disparities in use, complications, or functional outcomes. Although some commentators have implied the need for mandatory race or ethnicity reporting across all orthopaedic trials, the usefulness of race or ethnic reporting likely depends on the specific topic, prior evidence of disparities, and individualized study hypotheses.

Questions/purposes In a systematic review, we asked: (1) What proportion of orthopaedic clinical trials report race or ethnicity data, and of studies that do, how many report data regarding social covariates or genomic testing? (2) What trends and associations exist for racial and ethnic reporting among these trials between 2000 and 2020? (3) What is the racial or ethnic representation of United States trial participants compared with that reported in the United States Census?

Methods We performed a systematic review of randomized controlled trials with human participants published in three leading general-interest orthopaedic journals that focus on clinical research: *The Journal of Bone and Joint Surgery, American Volume*; *Clinical Orthopaedics and Related Research*; and *Osteoarthritis and Cartilage*. We searched the PubMed and Embase databases using the following inclusion criteria: English-language studies, human studies, randomized controlled trials, publication date from 2000 to 2020, and published in *Clinical Orthopaedics and Related Research*; *The Journal of Bone and Joint Surgery, American Volume*; or *Osteoarthritis and Cartilage*. Primary outcome measures included whether studies reported participant race or ethnicity, other social covariates (insurance status, housing or homelessness, education and literacy, transportation, income and employment, and food security and nutrition), and genomic testing. The secondary outcome measure was the racial and ethnic categorical distribution of the trial participants included in the studies reporting race or ethnicity. From our search, 1043 randomized controlled trials with 184,643 enrolled patients met the inclusion criteria. Among these studies, 21% (223 of 1043) had a small (< 50) sample size, 56% (581 of 1043) had a medium (50 to 200) sample size, and 23% (239 of 1043) had a large (> 200) sample size. Fourteen percent (141 of 1043) were based in the Northeast United States, 9.2% (96 of 1043) were in the Midwest, 4.7% (49 of 1043) were in the West, 7.2% (75 of 1043) were in the South, and 65% (682 of 1043) were outside the United States. We calculated the overall proportion of studies meeting the inclusion criteria that reported race or ethnicity. Then among the subset of studies reporting race

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Ethical approval was not sought for the present study.

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or ethnicity, we determined the overall rate and distribution of social covariates and genomic testing reporting. We calculated the proportion of studies reporting race or ethnicity that also reported a difference in outcome by race or ethnicity. We calculated the proportion of studies reporting race or ethnicity by each year in the study period. We also calculated the proportions and 95% CIs of individual patients in each racial or ethnic category of the studies meeting the inclusion criteria.

Results During the study period (2000 to 2020), 8.5% (89 of 1043) of studies reported race or ethnicity. Of the trials reporting this factor, 4.5% (four of 89) reported insurance status, 15% (13 of 89) reported income, 4.5% (four of 89) reported housing or homelessness, 18% (16 of 89) reported education and literacy, 0% (0 of 89) reported transportation, and 2.2% (two of 89) reported food security or nutrition of trial participants. Seventy-eight percent (69 of 89) of trials reported no social covariates, while 22% (20 of 89) reported at least one. However, 0% (0 of 89) of trials reported genomic testing. Additionally, 5.6% (five of 89) of these trials reported a difference in outcomes by race or ethnicity. The proportion of studies reporting race or ethnicity increased, on average, by 0.6% annually (95% CI 0.2% to 1.0%; $p = 0.02$). After controlling for potentially confounding variables such as funding source, we found that studies with an increased sample size were more likely to report data by race or ethnicity; location in North America overall, Europe, Asia, and Australia or New Zealand (compared with the Northeast United States) were less likely to; and specialty-topic studies (compared with general orthopaedics research) were less likely to. Our sample of United States trials contained 18.9% more white participants than that reported in the United States Census (95% CI 18.4% to 19.4%; $p < 0.001$), 5.0% fewer Black participants (95% CI 4.6% to 5.3%; $p < 0.001$), 17.0% fewer Hispanic participants (95% CI 16.8% to 17.1%; $p < 0.001$), 5.3% fewer Asian participants (95% CI 5.2% to 5.4%; $p < 0.001$), and 7.5% more participants from other groups (95% CI 7.2% to 7.9%; $p < 0.001$).

Conclusion Reporting of race or ethnicity data in orthopaedic clinical trials is low compared with other medical fields, although the proportion of diseases warranting this reporting might be lower in orthopaedics.

Clinical Relevance Investigators should initiate discussions about race and ethnicity reporting in the early stages of clinical trial development by surveying available published evidence for relevant health disparities, social determinants, and, when warranted, genomic risk factors. The decision to include or exclude race and ethnicity data in study protocols should be based on specific hypotheses, necessary statistical power, and an appreciation for unmeasured confounding. Future studies should evaluate cost-efficient mechanisms for obtaining baseline social covariate data and investigate researcher perspectives on current administrative workflows and decision-making algorithms for race and ethnicity reporting.

Introduction

Despite rising awareness of orthopaedic healthcare disparities and efforts to mitigate differences in patient outcomes based on race and ethnicity, previous investigations of the orthopaedic evidence base have demonstrated limited diversity among study participants [40, 47]. A systematic review of 158 United States orthopaedic randomized controlled trials (RCTs) that were published between 2008 and 2011 found that only 20.3% (32) of trials reported at least one race or ethnicity variable. Among this subset, the representation of Black and Hispanic patients was 3.5-fold and 2-fold lower than estimates from the United States Census [47]. A similar review of 482 orthopaedic RCTs published from 2015 to 2019 found that 7.3% (35) of trials reported race and 3.1% (15) of trials reported ethnicity [40].

Previous research has suggested that a lack of minority representation in the orthopaedic evidence base may perpetuate disparities in metrics such as utilization [3, 41], postoperative complications [7, 20, 38, 48], and functional outcomes [21, 27, 44]. Likewise, others have suggested that increased reporting of racial and ethnic data may be an avenue to identify targets for policy intervention and to improve health equity [40, 47]. Racial differences in tumor pathophysiology and the incidence of important genetic loci, for example, have been studied for soft tissue sarcomas and osteosarcomas [1, 33–35]. Research into these diseases often involves testing of genome-wide associations but has historically relied on datasets of patients with predominantly European ancestry [28, 37]. A recent retrospective study of *The Cancer Genome Atlas*, a collection of comprehensive genomic studies for more than 11,000 individuals, found insufficient samples of patients with cancer from minority groups to detect even common genomic alterations [49]. For these types of studies, however, categorization based on self-reported race holds little explanatory power, especially where heterogeneity in racial groups has been shown to exceed that between groups [6, 12]. Furthermore, compared with fields such as cardiology and oncology, the biology of most orthopaedic conditions does not vary substantially based on patient race or ethnicity alone [30]. From a sociologic standpoint, differences in orthopaedic outcomes are similarly unlikely to be explained by race or ethnicity alone [29]. Rather, a combination of socioeconomic, psychologic, and cultural factors must be investigated and carefully parsed to determine whether there is a relationship between race or ethnicity and clinical findings [22, 29]. For instance, research has demonstrated there are longer wait times to radiographic

evaluation and surgical fixation for patients from underrepresented racial or ethnic groups who have hip fractures, and studies might benefit from including covariates such as economic incentives, cultural preferences, and unconscious bias [2].

Previous investigations of race and ethnicity reporting in orthopaedic studies have suggested the need for all clinical trials to engage in the reporting of those parameters in all instances [4, 40, 47]. However, these approaches do not consider the wide variations in the usefulness of race and ethnicity reporting, depending on the subject area, prior evidence of disparities, and individualized study objectives [30]. Although self-reported race and ethnicity may have explanatory value for many sociologic issues, there are many orthopaedic subjects in which these data may be unhelpful [29]. Unlike demographic variables such as age and sex, which are rooted in physiologic differences, racial and ethnic identities are socially constructed and historically fluid phenomena, with little to no basis in biology [4, 22, 45]. Conversely, ancestry and genomic sequencing have demonstrated clear utility in the evaluation of genetic risk, epidemiology, and treatment prognosis [34, 35]. Prior reviews of race and ethnicity reporting have not included genomic testing data, which may be a more precise analysis of biologic explanations for orthopaedic outcome disparities. Similarly, no prior review that we know of has investigated the reporting of social covariates such as income, housing, transportation, and literacy alongside race and ethnicity in orthopaedic clinical trials. The reporting of race and ethnicity alone, without the inclusion of appropriate social or biologic covariates, may prove counterproductive to the goal of reducing disparities [29]. The practice of superficial, isolated racial and ethnic reporting may lead to the generation of misleading inferences or the reinforcement of harmful stereotypes regarding the inevitability of poorer outcomes among minority patients [30]. Furthermore, previous systematic reviews have limited their searches to clinical trials in the United States and have yet to address the need for differing approaches to race and ethnicity reporting in multinational, multicenter trials [40, 47]. Finally, existing reviews of race and ethnicity reporting are limited to periods of 5 years at the most, and therefore are unable to assess for temporal trends across multiple decades [40, 47].

Therefore, we performed a systematic review of three leading orthopaedic journals to ask: (1) What proportion of orthopaedic clinical trials report race or ethnicity data, and of studies that do, how many report data regarding social covariates or genomic testing? (2) What trends and associations exist for racial and ethnic reporting among these trials between 2000 and 2020? (3) What is the racial or ethnic representation of United States trial participants compared with that reported in the United States Census?

Materials and Methods

Search Strategy, Study Selection, and Eligibility Criteria

We performed a systematic review of RCTs with human participants published in three leading general-interest orthopaedic journals that focus on clinical research: *The Journal of Bone and Joint Surgery, American Volume; Clinical Orthopaedics and Related Research; and Osteoarthritis and Cartilage*. RCTs were selected as the focus of the study because they represent a high level of evidence used to direct clinical practice and they involve the recruitment of various participants. We searched both the PubMed and Embase databases using the following inclusion criteria: English-language studies, human studies, RCTs, publication date from 2000 to 2020, and published in *Clinical Orthopaedics and Related Research*; *The Journal of Bone and Joint Surgery, American Volume*; or *Osteoarthritis and Cartilage*. This search was performed on September 4, 2021. Duplicates between databases were removed through an automated process by which we compared reference lists through Mendeley. Bibliographies were manually searched for additional studies meeting the inclusion criteria; however, none were found. All results that were not full-text articles, not RCTs, and did not have patients were excluded (Fig. 1).

Data Collection

Two investigators (GAM and AK) independently evaluated the title and abstracts of studies to see whether they met the inclusion criteria. Disagreements were resolved by a third investigator (TKJ). The following data were extracted for each study: publication year, sample size, funding source, location, single center versus multicenter, and subspecialty. Funding sources were categorized as government, industry, other, or none. Study location was categorized by United States Census region if located in the United States or by country if located outside the United States. Studies were classified by orthopaedic subspecialty according to the American Academy of Orthopaedic Surgeons (adult reconstruction, foot and ankle, hand and wrist, oncology, pediatric, shoulder and elbow, spine, sports, and trauma) [15]. Studies pertaining to multiple specialties or that were difficult to categorize into an individual specialty were listed as general.

Data Items

Primary outcome measures included whether studies reported the following: race or ethnicity, other social covariates (insurance status, housing or homelessness, education or

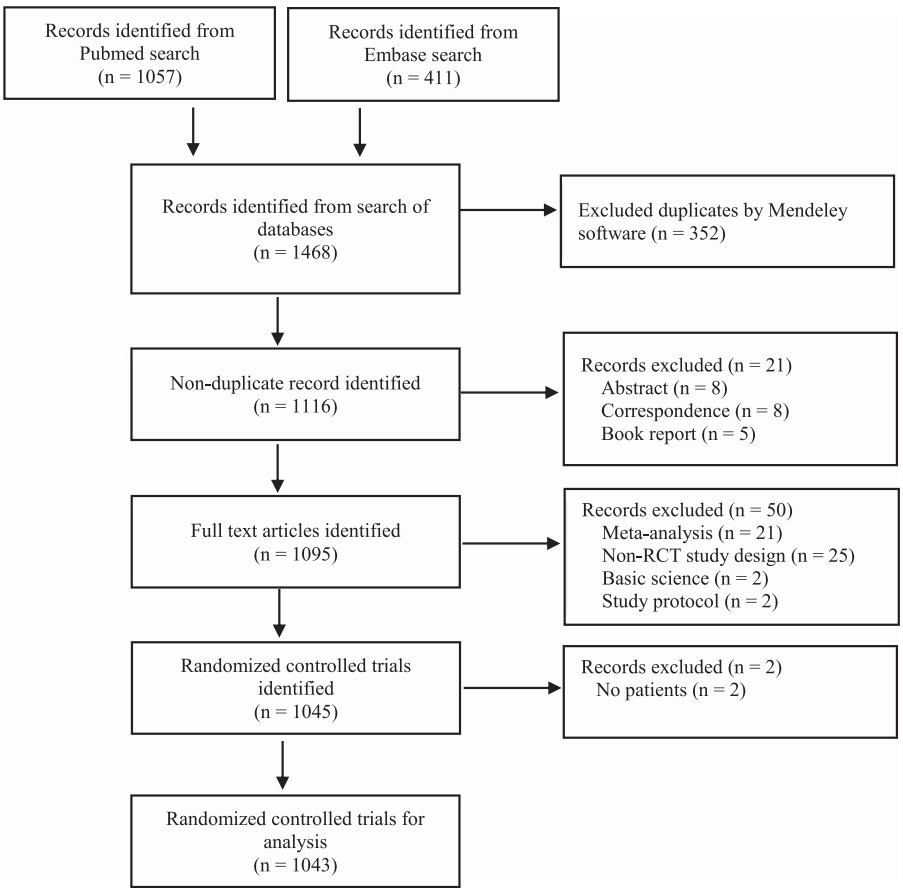

Fig. 1 This flow diagram demonstrates the search strategy and inclusion criteria. Criteria included English-language studies, human studies, RCTs, publication date from 2000 to 2020, and studies published in *Clinical Orthopaedics and Related Research*; *The Journal of Bone and Joint Surgery, American Volume*; or *Osteoarthritis and Cartilage*. All results that were not full-text articles, not RCTs, and without patients were excluded.

literacy, transportation, income or employment, and food security or nutrition), and genomic testing. The secondary outcome measure was the racial or ethnic categorical breakdown of the trial participants in the studies reporting race or ethnicity. Given the complexity of categorizing race, ethnicity, and the delineation between them, we based data collection on the following information: Race is a socially constructed term categorizing individuals based on shared physical characteristics [30]. In the United States, racial categories typically include American Indian or Alaskan Native, Asian, Black, Native Hawaiian or other Pacific Islander, and white. Ethnicity, likewise, is used to group individuals but is based on a shared culture identity and expression [18, 36]. In the United States, ethnic categories typically include Hispanic or Latino or non-Hispanic or Latino. In some of the included articles, Hispanic identity was classified as a racial group, whereas others classified it as an ethnic group [18, 36]. To account for this discrepancy, any study participants listed with either Hispanic race or ethnicity were classified as Hispanic ethnicity as a separate category. Additionally, many trials reported race as White and non-White or other. All participants for whom a specific race could not be ascertained from the data reported were listed in the "other" category. The final categorization of overall racial and ethnic breakdown thus included White, Black, Hispanic, Asian, and other.

Risk of Bias Assessment

Given that our analysis was not focused on the outcomes from the RCTs, and we included only articles that were published in a select set of journals, we did not include an assessment of bias in our analysis.

Summary of Included Studies

From our search, 1043 RCTs with 184,643 enrolled patients met the inclusion criteria (Fig. 1). Among these

studies, 21% (223 of 1043) had a small (< 50 participants) sample size, 56% (581 of 1043) had a medium (50 to 200) sample size, and 23% (239 of 1043) had a large (> 200) sample size. Sixty-nine percent (717 of 1043) were single-center studies and 31% (326 of 1043) were multicenter. Focusing on location, 14% (141 of 1043) were based in the Northeastern United States, 9.2% (96 of 1043) were in the Midwest, 4.7% (49 of 1043) were in the West, and 7.2% (75 of 1043) were in the South. Internationally, 8.4% (88 of 1043) were in North America, 0.4% (four of 1043) were in South America, 37% (388 of 1043) were in Europe, 13% (136 of 1043) were in Asia, 5.1% (53 of 1043) were in Australia or New Zealand, 0.4% (four of 1043) were in Africa, and 0.8% (eight of 1043) were in the Middle East. For funding sources, 14% (142 of 1043) were government-funded, 19% (195 of 1043) were industry-funded, 13% (139 of 1043) were funded with other sources, 20% (204 of 1043) were not funded, and 35% (363 of 1043) did not report funding sources. Twenty-three percent (236 of 1043) were classified as general orthopaedic studies, while the three most common subspecialties were adult reconstruction (37%; 390 of 1043), trauma (15%; 159 of 1043), and sports (6.7%; 70 of 1043) (Table 1).

Table 1. Characteristics of orthopaedic clinical trials meeting the inclusion criteria from 2000 to 2020 (n = 1043 patients)

Parameter	% (n)
Sample size	
< 50	21 (223)
50-200	56 (581)
> 200	23 (239)
Center type	
Single center	69 (717)
Multicenter	31 (326)
Funding	
Government funding	14 (142)
Industry finding	19 (195)
Other funding	13 (139)
No funding	20 (204)
Not reported	35 (363)
Region	
Northeast United States	14 (141)
Midwest United States	9.2 (96)
Western United States	4.7 (49)
Southern United States	7.2 (75)
North America	8.4 (88)
South America	0.4 (4)
Europe	37 (388)
Asia	13 (136)
Australia and New Zealand	5.1 (53)
Africa	0.4 (4)
Middle East	0.8 (8)
Subspecialty	
General	23 (236)
Adult reconstruction	37 (390)
Foot and ankle	3.2 (33)
Hand and wrist	3.0 (31)
Oncology	0.6 (6)
Pediatric	1.3 (14)
Sports	6.7 (70)
Shoulder and elbow	4.8 (50)
Trauma	15 (159)

Ethical Approval

This study was considered exempt from review by the Cleveland Clinic Foundation ethical review board because of the public nature of all data included and the lack of protected health information, as defined by 45 CFR 46.102 of the Department of Health and Human Services' Code of Federal Regulations.

Statistical Analysis

To answer our first research question of various reporting measures, we calculated the overall proportion of studies meeting the inclusion criteria that reported race or ethnicity. Among the subset of studies reporting race or ethnicity, we determined the overall proportion and distribution of social covariates and genomic testing reporting. Lastly, we calculated the proportion of studies reporting race or ethnicity that also reported a difference in outcome by race or ethnicity.

To answer our second research question of trends of racial or ethnic reporting, we first calculated the proportion of studies reporting race or ethnicity by each year during the study period. A linear regression analysis of the proportion of studies reporting race or ethnicity by year was used to determine the average annual change in reporting, along with a 95% CI. Additionally, we performed a Mann-Kendall test to test the significance of the trend in the proportion over time. Furthermore, a multivariable logistic regression model was generated to determine which of the collected study variables were most associated with racial and ethnic reporting while controlling for confounding. Allowing for compatibility with the model, the subspecialty of each study was recategorized as either general or subspecialty-specific, and countries outside the United States were grouped by the following geographic regions: North America, Europe, Asia, Australia and New Zealand, and other. Variables were selected for inclusion in the

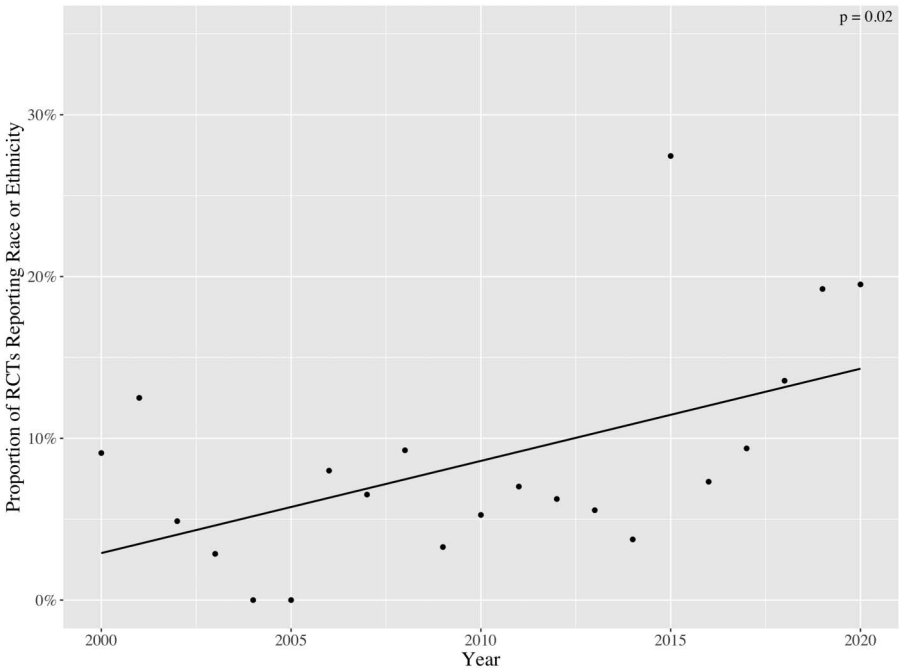

Fig. 2 This graph shows the annual trend in the proportion of orthopaedic clinical trials reporting race or ethnicity from 2000 to 2020.

model based on a threshold of $p < 0.2$ in an unadjusted analysis.

To answer our third research question about the racial and ethnic breakdown in the studies, we calculated the proportions and 95% CIs of individual patients in each racial and ethnic category of the studies meeting the inclusion criteria. We then subset for only United States–based studies and compared the proportion measured for each racial and ethnic category with that of the 2019 United States Census using one-proportion z tests. All analyses were conducted using R (version 4.0.2). All tests were two-tailed, with the significance threshold set to < 0.05.

Results

Reporting of Race or Ethnicity, Social Covariates, and Genomic Testing

During the study period (2000 to 2020), 8.5% (89 of 1043) of the studies reported race or ethnicity. Of the trials reporting race or ethnicity, 4.5% (four of 89) reported insurance status, 15% (13 of 89) reported income, 4.5% (four of 89) reported housing or homelessness, 18% (16 of 89) reported education or literacy, 0% (0 of 89) reported transportation, and 2.2% (two of 89) reported food security or nutrition of trial participants. Examining the distribution, we found that 78% (69 of 89) of trials reported no social covariates, 5.6% (five of 89) reported one social covariate, 12% (11 of 89) reported two social covariates, and 4.5% (four of 89) reported three or more social covariates. However, 0% (0 of 89) of trials reported genomic testing. Lastly, 5.6% (five of 89) of these trials reported a difference in outcomes by race or ethnicity.

Trends in Racial and Ethnic Reporting

During the study period, the proportion of studies reporting race or ethnicity increased, on average, by 0.6% annually (95% CI 0.2% to 1.0%; $p = 0.02$) (Fig. 2). An increasing trend in racial and ethnic reporting was further confirmed by the Mann-Kendall test (Kendall τ 0.36; $p = 0.03$). After controlling for potentially confounding variables such as funding source, we found that sample size, location, and specialty topic were associated with racial and ethnic reporting. We also found that large trials (> 200 participants) had an increased odds of reporting (adjusted odds ratio [OR] 6.43 [95% CI 2.51 to 16.46]; $p < 0.001$) compared with small trials (< 50 participants). Trials conducted in North America (adjusted OR 0.26 [95% CI 0.10 to 0.66]; $p = 0.004$), Europe (adjusted OR 0.05 [95% CI 0.02 to 0.11]; $p < 0.001$), Asia (adjusted OR 0.05 [95% CI 0.01 to 0.22]; $p < 0.001$), and Australia and New Zealand (adjusted OR 0.02 [95% CI 0.00 to 0.18]; $p < 0.001$) had decreased odds of reported race or ethnicity compared with the Northeast United States. However, there were no differences in the odds of reporting between the Midwest United

Table 2. Multivariable logistic regression analysis of associations of racial and ethnic reporting in orthopaedic clinical trials from 2000 to 2020

Parameter	Adjusted OR (95% CI)	p value
Sample size		
< 50	1 [Reference]	
50-200	2.10 (0.85-5.18)	0.11
> 200	6.43 (2.51-16.46)	< 0.001
Center type		
Single-center	1 [Reference]	
Multi-center	1.67 (0.93-2.99)	0.09
Funding		
Government funding	1.17 (0.45-3.03)	0.74
Industry funding	0.91 (0.38-2.19)	0.85
Other funding	0.73 (0.26-2.05)	0.55
No funding	1 [Reference]	
Not reported	0.70 (0.30-1.65)	0.42
Region		
Northeast United States	1 [Reference]	
Midwest United States	0.43 (0.19-1.01)	0.05
Western United States	0.51 (0.18-1.47)	0.22
Southern United States	0.66 (0.29-1.48)	0.32
North America	0.26 (0.10-0.66)	0.004
Europe	0.05 (0.02-0.11)	< 0.001
Asia	0.05 (0.01-0.22)	< 0.001
Australia and New Zealand	0.02 (0.00-0.18)	< 0.001
Other	0.34 (0.04-2.82)	0.32
Subspecialty		
General	1 [Reference]	
Subspecialty-specific	0.13 (0.07-0.23)	< 0.001

States (adjusted OR 0.43 [95% CI 0.19 to 1.01]; p = 0.05), West (adjusted OR 0.51 [95% CI 0.18 to 1.47]; p = 0.22), and South (adjusted OR 0.66 [95% CI 0.29 to 1.48]; p = 0.32) compared with the Northeast. Lastly, trials conducted on an orthopaedic subspecialty-specific topic had decreased odds of reporting (adjusted OR 0.13 [95% CI 0.07 to 0.23]; p < 0.001) compared with trials on general topics (Table 2).

Racial and Ethnic Representation of Clinical Trial Participants

The overall distribution of the 37,798 participants included in the trials reporting race or ethnicity was 81.5% white (30,788 of 37,798; 95% CI 81.1% to 81.8%), 6.6% Black (2481 of 37,798; 95% CI 6.3% to 6.8%), 1.3% Hispanic (479 of 37,798; 95% CI 1.2% to 1.4%), 1.5% Asian (561 of 37,798; 95% CI 1.4% to 1.6%), and 9.2% other (3489 of 37,798; 95% CI 8.9% to 9.5%). Of the 26,554 patients in trials in the United States, the racial or ethnic distribution was 79% white (20,980 of 26,554; 95% CI 78.5% to 79.5%), 8.5% Black (2243 of 26,554; 95% CI 8.1% to 8.8%), 1.5% Hispanic (401 of 26,554; 95% CI 1.4% to 1.7%), 0.6% Asian (164 of 26,554; 95% CI 0.5% to 0.7%), and 10.4% other (2766 of 26,554; 95% CI 10.1% to 10.8%). According to data from the 2019 United States Census, the racial or ethnic distribution of the national population is approximately 60.1% white, 13.4% Black, 18.5% Hispanic, 5.9% Asian, and 2.1% other or unknown [54]. Compared with the distribution of race and ethnicity reported by the United States Census, our sample of United States trials contained 18.9% more white participants (95% CI 18.4% to 19.4%; p < 0.001), 5.0% fewer Black participants (95% CI 4.6% to 5.3%; p < 0.001), 17.0% fewer Hispanic participants (95% CI 16.8% to 17.1%; p < 0.001), 5.3% fewer Asian participants (95% CI 5.2% to 5.4%; p < 0.001), and 7.5% more participants from other groups (95% CI 7.2% to 7.9%; p < 0.001) (Fig. 3).

Discussion

Previous investigations of the orthopaedic evidence base have demonstrated limited diversity among clinical trial participants [4, 40, 47]. Increased reporting of race and ethnicity data has been discussed as a means to improve health equity and find opportunities for policy intervention [40, 47]. For studies investigating the biology of orthopaedic diseases, self-reported race and ethnicity identities have shown limited utility as a clinical covariate, although exceptions exist where genetic risk factors have been validated through rigorous genomic testing. Likewise, among studies exploring the sociology of orthopaedic conditions, self-reported race is insufficient to understand the path from social predisposition to differences in patient outcomes. Our findings suggest that approximately one in 12 orthopaedic clinical trials report racial or ethnic data, one in 18 report at least one social covariate, and essentially none report genomic testing data. The rate of race and ethnicity reporting has increased by approximately 0.6% annually between 2000 and 2020. Furthermore, after controlling for confounding, the factors associated with race and ethnicity reporting were large sample size, location, and subspecialty. Finally, comparing the demographics reported in the United States Census with the patient population of United States–based clinical trials reporting race or ethnicity, white patients were overrepresented while Black, Hispanic, and Asian patients were underrepresented. Based on these findings, researchers should consider the relevance of race and ethnicity data collection and reporting before beginning a clinical trial. Using the available evidence as a guide, investigators should strive to collect

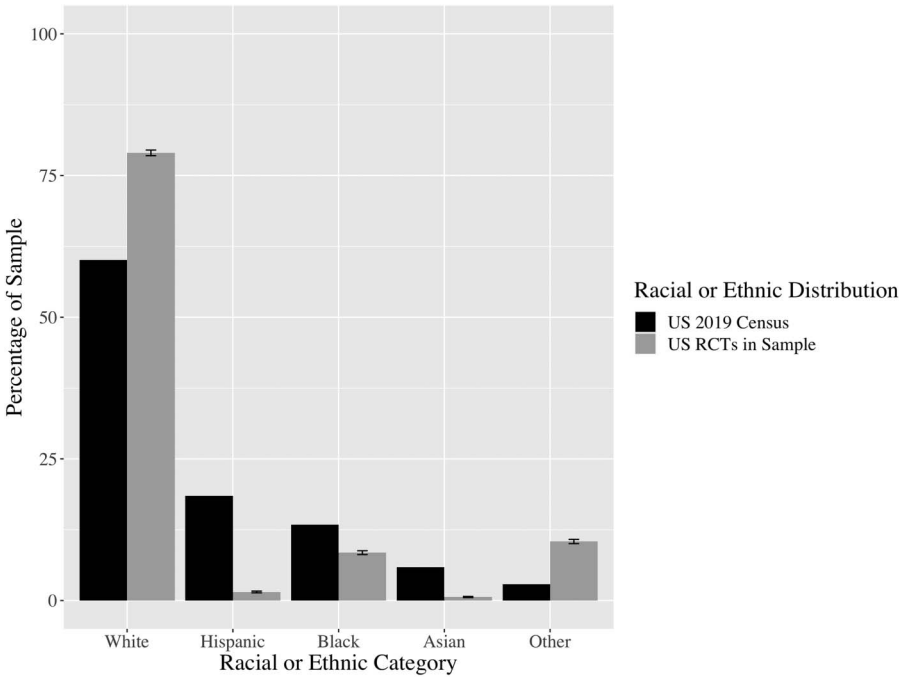

Fig. 3 This graph shows the sample's racial or ethnic representation of RCTs in the United State compared with the racial and ethnic representation reported in the 2019 United States Census.

relevant social or biologic covariates that may help explain observed variance in clinical outcomes by race or ethnicity [18, 36].

Limitations

Our study has several limitations. We restricted our investigation to three prominent orthopaedic journals that may not represent all orthopaedic journals with respect to diversity in published clinical trials. However, the three chosen journals are among the most selective in the field and apply rigorous editorial standards. Therefore, it is reasonable to suspect that the sample of clinical trials included in the present study may have engaged in a higher quality of scientific reporting than what might be found in all orthopaedic journals. A similar strategy has been used by several previous systematic reviews investigating clinical trial quality [5, 10, 46], industry bias [13, 31, 32], and data reporting [11, 19, 42] in a sample of studies from a few prominent journals. Our analysis only measured racial and ethnic representation in studies reporting this information. The complete orthopaedic clinical trial population may have a different level of minority representation depending on the true racial or ethnic distribution of participants in non-reporting trials. Even among reporting trials, there is substantial heterogeneity in the definition of racial and ethnic categories and varying levels of specificity. Because a large proportion of United States–based trials reported race as either white or non-white, many minority patients could not be further classified nor incorporated into our analyses of representation compared with the United States Census. If nonreporting studies took fewer measures to ensure the recruitment of minority populations, it is reasonable to suspect that the racial and ethnic distribution of clinical trial participants calculated for our analysis would be an overestimate.

Reporting of Race or Ethnicity, Social Covariates, and Genomic Testing

In the sample of clinical trials analyzed, approximately 8.5% (89 of 1043) reported racial or ethnic data, of which 22% (20 of 89) reported at least one social covariate and 0.0% (0 of 89) reported genomic testing. Although the proportion of articles that reported race or ethnicity appears relatively low in orthopaedic surgery, it is equally concerning that most studies reporting race did not include any other covariates, either social or genomic. Furthermore, 5.6% (five of 89) of reporting trials claimed an association between race or ethnicity and clinical outcomes. Such claims of an independent association should be interpreted with skepticism, and inferences regarding the predictive

value of race should be tempered by an appreciation for unmeasured confounding variables. These findings support the work of previous studies estimating the rate of race and ethnicity reporting among orthopaedic clinical trials, between approximately 7% and 20% [40, 47]. The present findings also document the limited reporting of social and biologic covariates. The absence of these data is noteworthy because they may explain variance in patient outcomes through biologically plausible mechanisms such as reduced access to multidisciplinary care [3, 41], increased time to surgery [25], or implicit biases affecting treatment decision-making [23, 24, 50]. Orthopaedic trialists should collect meaningful social and biological covariates based on evidence and hypothesize about precise mechanisms for race and ethnicity disparities in need of investigation [30]. Furthermore, inferences of an association between any given social factor (race or otherwise) and clinical outcomes should be kept modest and discussed in the context of potential unmeasured confounding [29]. Currently, social covariate data are not routinely collected for most patients and may impose a substantial measurement burden on existing clinical workflows [8, 51]. Future studies should therefore investigate cost-efficient strategies to expand existing information technology infrastructure in order to improve the accessibility of social covariate data [9, 52]. The inclusion of socially focused z-codes in the *International Classifications of Diseases, Tenth Edition,* presents an opportunity for administrative standardization; however, lack of reimbursement for these codes has led to gross underuse [26, 53]. The Centers for Medicare and Medicaid Services, however, has begun moving toward using these codes in the adjustment of various value-based payment systems to prevent inappropriate penalization for physicians caring for socially complex patients [14].

Trends in Racial and Ethnic Reporting

From 2000 to 2020, reporting of race or ethnicity increased at a rate of roughly 0.6% per year. After controlling for confounding, the variables associated with reporting were sample size, location, and subspecialty focus. The observed gradual increase in race or ethnicity reporting in published orthopaedic studies in the journals we evaluated may represent a steady shift toward a greater awareness of health disparities [16, 39]. The sample of clinical trials evaluated in this study might fall into one of two distinct categories. In the first category are trials focusing on subjects where prior evidence suggested race and ethnicity are relevant risk factors, whereas the second group involves trials on subjects where no such evidence exists. The extent to which trials in the former group are reporting racial and ethnic data remains unclear, although this represents an important area of investigation. Rather than mandate that all orthopaedic clinical trials collect and report race and ethnicity information, it may be more prudent to interrogate relevant prior evidence on a case-by-case basis [17, 36]. This strategy would promote reporting targeted where it is most useful for the understanding and mitigation of race and ethnicity health disparities, while also avoiding extraneous material with no obvious connections to disease pathophysiology or social determinants of health [29]. The present findings regarding modest increases in racial and ethnic reporting may be explained, in part, by the recent issuance of reporting guidelines by funding and regulatory agencies such as the National Institutes of Health and FDA [18, 36]. Both organizations suggest minimum criteria for race and ethnicity categories and emphasize that decisions regarding the necessity, utility, and practicality of reporting should be a part of early RCT planning discussions, institutional review board protocols, and grant submissions. In cases where prior research neither supports nor negates differences in a given intervention based on racial or ethnic identity, the National Institutes of Health specifically encourages reporting where possible but acknowledges that many trials may lack the statistical power necessary for subgroup comparisons [36]. In orthopaedics, researchers should remain wary of race and ethnicity reporting for its own sake, because this phenomenon may result in the overuse of underpowered, post hoc testing approaches and suggestions of spurious associations [29, 30].

Racial and Ethnic Representation of Clinical Trial Participants

Among reporting clinical trials in the United States, the proportion of minority patients was substantially lower than that of the general United States population, as estimated by the Census. These findings align with those of a prior review on the subject [4] and support concerns that the current orthopaedic evidence base may not be generalizable to minority patient populations; however, the implications must be interpreted modestly**.** Because the epidemiology of orthopaedic conditions may vary across demographic subgroups and the racial and ethnic diversity of available study participants will vary by region, it is unwise to impose a universal benchmark for racial and ethnic representation among RCTs. Such mandates are unlikely to be practical for studies with smaller sample sizes or for those in demographically homogeneous regions. As orthopaedic clinical trials increase in scale and unite institutions in multiple countries, it would be inappropriate to impose racial and ethnic benchmarks from any one country on others [41, 46]. It would similarly be impractical to expect each trial to reflect the shifting demographics of the global population [43]. Goals for racial and ethnic diversity and representativeness should be well-

reasoned based on the available evidence, determined a priori, and made explicit at each stage of the research process. When these goals are not achieved, the reasons should be outlined within a study's limitations section and accompanied by a discussion of future study directions to enhance generalizability and mitigate health disparities wherever they exist.

Conclusion

Race and ethnicity data are less commonly reported in orthopaedic clinical trials than in other medical fields, although the proportion of diseases warranting this reporting might be lower in orthopaedics. We found that studies rarely reported on social covariates such as education, income, housing, and transportation; however, these data may help clarify the causal pathways by which racial or ethnic disparities are produced. We also found that studies rarely reported on biological covariates such as genomic testing. In the future, this information may help elucidate mechanisms between race, ancestry, and physiologic predispositions and severe disease or robust treatment response. Investigators should initiate discussions about whether and how to report race and ethnicity in the early stages of clinical trial development by surveying available publications for relevant health disparities, social determinants, and, when warranted, genomic risk factors. The decision to include or exclude race and ethnicity data in study protocols should be based on the specific hypotheses being tested, the necessary statistical power, and an appreciation for unmeasured confounding. Furthermore, these deliberations should be tailored to the relevant demographic contexts of the regions, countries, or continents in which the trials are performed. Goals for race and ethnicity representation should be selected and justified a priori. If, at the end of the study period, these targets are not met, the implications of that fact on the validity and generalizability should be discussed in a study's limitations section. Future studies should evaluate cost-efficient mechanisms for obtaining baseline social covariate data and investigate researcher perspectives on barriers to race and ethnicity reporting in cases where it is indicated.

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