Public reporting of black participation in anti-hypertensive drug clinical trials

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Background Non-Hispanic Black people in the United States have the highest prevalence of essential hypertension. Unfortunately, clinical trials often underrepresent Black patients. We aim to understand whether trial sponsorship type is associated with representation of Black participants in anti-hypertensive drug clinical trials. Then, we contextualize our findings amongst current efforts to improve diversity in clinical research populations.

Methods We searched ClinicalTrials.gov in May 2022 for antihypertensive drug trials. Of $n = 408$ trials in our initial search, $n = 97$ (23.77%) met inclusion criteria and were stratified by sponsorship type (industry vs non-industry). Standardized tests of difference were employed to compare characteristics of these trials, and linear regression was used to model change over time.

Results Of 97 trials reporting results from 2010 to 2020, there were minimal differences in the percent of Black patients enrolled in anti-hypertensive clinical trials by sponsorship type. Both industry and non-industry sponsored studies had high rates of non-reporting, with slightly more non-reporting for industry (73.2%) vs non-industry (66.67%) studies. Industry funded studies reported results to ClinicalTrials.gov within 23.3 ± 15.0 months from completing studies, while non-industry funded trials reported within 18.9 ± 10.8 months.

Conclusions Despite Black Americans carrying the highest burden of disease for essential hypertension, they are underrepresented in anti-hypertension clinical trials and their overall participation has decreased between 2010 and 2020. In addition, there is major underreporting of trial participant race. We implore researchers and funders to establish clear, meaningful targets for anti-hypertensive drug trial diversity, and improve transparency in reporting of study characteristics. (Am Heart J 2023;258:129–139.)

The prevalence of hypertension among Black people living in the United States (U.S.) is among the highest of any population worldwide.[1-4] While interest in understanding the drivers of this disparity has grown with time, there are persistent knowledge gaps regarding the role of environmental, behavioral, and psychosocial factors that impact the use of and adherence to medications for Black patients.[5] In parallel, there is growing acknowledgement that, as a socially constructed variable, race impacts health outcomes not via biophysical pathways but through a complex set of factors that operate at both the individual (provider bias) and system (systemic racism) levels. A major barrier to better understanding drivers of hypertension disparities is low racial/ethnic diversity in clinical trials, which is often exacerbated by underreporting of racial demographics in trial results, preventing full exploration of the impact of race on cardiovascular outcomes. Given the greater population health burden and unique factors that exacerbate adverse hypertension-related outcomes among Black patients, it is critical to understand the current landscape of enrollment of racial minority populations in clinical trials and what factors influence diversity of trial populations.

As of 2020, Black people accounted for 14.2% of the U.S. population, but only made up 8% of 32,000 individuals that participated in new drug trials in the U.S. during 2020.[6] While the relative overall underrepresentation of Black patients in U.S. clinical trials is alarming, it is especially problematic in the case of cardio protective drug trials given the higher cardiovascular disease

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burden of Black populations compared with white populations and the corresponding greater potential benefit. Recognition of the multiple benefits of more diverse trials – improved generalizability, more precise estimates of subgroup effectiveness and better evidence to support policy interventions – is not new.

While underrepresentation of Black patients in clinical trials is due to a combination of historical, social, system, and study-level factors, sponsors have been identified as a key stakeholder in the diversity of clinical trial populations, because they articulate and guide the study goals, including those related to the moral and scientific value of diversity.[7] Additionally, the relationship between sponsors and the community from which potential participants are drawn must be trustworthy if recruitment efforts are to succeed. Due to the high burden of hypertension among Black patients and corresponding impacts on chronic disease, it is critical to understand whether public and private funders prioritize racial diversity within their studies, a priority that can be viewed through the lens of enrolled participant characteristics. The majority of clinical trials in hypertension are funded by either public (National Institute of Health [NIH], Agency for Healthcare Research and Quality [AHRQ]) or industry (eg, for-profit pharmaceutical or device companies) sources. While government-based funding from the NIH has declined, there has been a call for more industry funded clinical trials.[13,14] To date, there has been little research on differences in racial diversity in trials funded by public vs private research sponsors. In the United States, organizational structure, and the method of compensation for research determines the status of a funder as either industry or public. While the goal of any clinical trial, regardless of funder, is to generate knowledge, the mission of public entities, like the NIH, centers on population health and may therefore motivate a greater focus on diversity and producing generalizable knowledge opposed to the underlying motivation of profits for industry. Major revenue streams for pharmaceutical companies include drug sales and asset appreciation, while public entities budget allocate tax dollars for research intended to serve the public good. Ultimately, both industry-initiated and public clinical trials have individual motivators for pursuing clinical research projects. Unlike publicly funded studies, privately funded clinical trials may be affected by changing business interests.[8] One example of this are prematurely terminated trials for financial rather than for scientific or ethical reasons.[9] Given the broadly different motives of the 2 entities, trials may differentially prioritize racial diversity depending on how or whether it can support their specific goals. All these factors cumulatively affect who is recruited in a clinical trial, and the priorities of the recruitment plan.[7]

Prior work has demonstrated differences in reporting by funding source.[15,16] Overall results of industry-sponsored trials are reported at a lower rate than NIH funded clinical research, while simultaneously reporting meaningfully higher positive effect estimates.[15] When comparing industry-sponsored and NIH-sponsored studies on ClinicalTrials.gov, 20.6% of NIH-sponsored trials on ClinicalTrials.gov report a positive outcome while 50.6% of industry-sponsored trials report a positive outcome.[10] These patterns are especially pronounced in cardiovascular trials, where 12% of NIH-funded trials report favorable outcomes, compared with 50.7% of industry-funded trials.[10] Hypothesized drivers of these differences include publication bias in industry-funded work (the "file drawer problem"), which is presumably less common in NIH-funded studies which are often required to publish results on ClinicalTrials.gov even when main effect estimates are null.[11] Despite improvements in reporting transparency for publicly funded studies, the persistent lack of population diversity, particularly with respect to Black patients, raises important concerns about generalizability of the results regardless of funding source.

The primary objective of this study is to understand trajectories in racial diversity in hypertension treatment clinical trials in the United States, and how funding source relates to diversity. The diversity deficit in clinical trials promotes research that is not necessarily generalizable.[12] We used publicly available data from ClincalTrials.gov to characterize differences in racial diversity in between NIH-funded and industry-sponsored hypertension clinical trials, and whether patterns have changed with time. We analyzed the publicly available results in ClinicalTrials.gov to make claims on the reporting of racial diversity in United States antihypertensive drug clinical research.

Methods

Eligibility criteria

We searched for U.S.-based clinical trials of adult antihypertensive medications, defined as medications whose target is to lower blood pressure for essential hypertension. Studies were excluded if they targeted treatment for secondary hypertension, pregnancy-induced/gestational hypertension, ocular hypertension, intracranial hypertension, portal hypertension, hypertensive retinopathy, pre-hypertensive populations, or pediatric hypertension. Additionally, studies examining dietary or behavioral interventions or those evaluating medication adherence rather than treatment effectiveness were excluded.

Search methods for identification of studies

An experienced medical librarian (L.S.) conducted a comprehensive search of the clinical trials registry, ⟨13:italic⟩ClinicalTrials.gov⟨/13:italic⟩ (NIH U.S. National Library of Medicine) on June 2, 2022 to find com-

pleted drug intervention trials with results for hypertension. The search was developed and conducted in consultation with the author team and utilized the Advanced Search function of clinitrials.gov. Keywords searched in the "Condition or disease" field included "Hypertension" OR "Blood Pressure" OR "Hypertensive" with "Study type" selected as "Interventional Studies (Clinical Trials)," "Study Results" limited to "Studies with Results," and "Status: Recruitment" selected as "Completed." The "Eligibility Criteria" of participants was limited to adults by selecting "Adult (18-64)" and "Older Adult (65+)" in the "Age Group" field. To limit trial results to drug intervention studies, the term "drug" was searched in the "Intervention/treatment" field. Intervention/treatment option tags in ClinicalTrials.gov include drug, biological, procedure, device, behavioral, dietary supplement, and other. Trials were limited to studies in the United States, and those with results first posted from January 01, 2010 through January 01, 2020. Trials were not limited by "Funder Type." The full, reproducible list of database variables searched is located in the Appendix/Supplementary Materials.

Results were exported from ClinicalTrials.gov as an XML file and then imported into Covidence, a systematic review screening software [Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.Covidence.org.

Selection process

The initial search yielded 408 studies, and the screening process to reach the analytical sample is displayed in Figure 1.

Covidence automatically identified duplicate studies initially, and 1 reviewer manually identified duplicate studies Covidence failed to detect. Two reviewers (M.G. and M.D.) independently screened references by title and study description in the Covidence systematic review screening software. A third arbitrator (J.L.) resolved conflicts. Next, the included articles were independently screened by 2 reviewers at the full-text level. Conflicts at this stage were once again resolved by a third arbitrator (J.L.).

Data collection process

Two reviewers independently extracted data from study records in ClinicalTrials.gov (M.G. and M.D.), then were compared with differences resolved through communication. A third reviewer (E.O.) reconciled questions and conflicts that arose from the initial data collection process.

Data items

The data items extracted from these studies from ClinicalTrials.gov were defined as follows:

- Study Name: Full title of study as listed
- Study Start Date: Month and year listed as study start date
- Actual Study Completion Date: Month and year listed as actual completion date for study
- Results First Posted Date: Month and year listed as date that results for study first posted
- Funder Name: Sponsor named on study record
- Collaborator Name: Collaborator named on study record
- Phase Drug Trial: Stage of drug trial
- Intervention Model: Trial design
- Total Enrollment: Total number of enrolled participants listed on study results page
- Total Randomized and Received Treatment: Total number of individuals listed as randomized and received treatment under the study results page of study record
- Number of Black Participants Analyzed: If applicable, number of Black Participants analyzed, listed under study results page. Race only listed under analyzed patients, not enrolled.
- Total Participants Analyzed with "Not Reported" Race: If applicable, number of participants with a not reported racial category for a study under the study results section

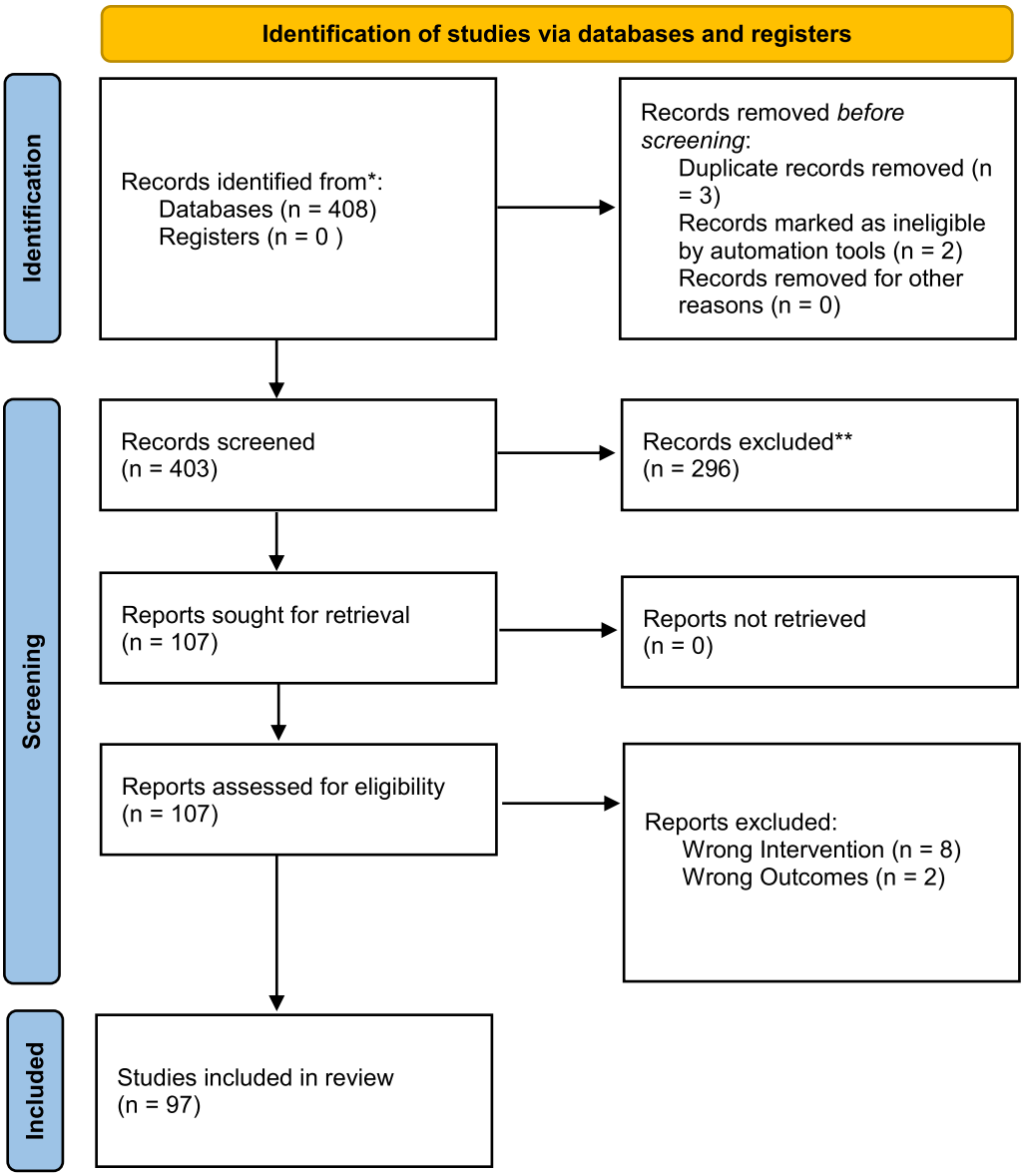
Additionally, during data collection each reviewer determined:

- Is the study industry-funded? Yes, or no response for primary sponsoring of study being industry-funded
- Second collaborator reported? (y/n) Yes or no response for a collaborator being reported
- Is there an industry collaborator? (y/n) Yes or no response for collaborator being an industry collaborator
- Is this a multicenter trial? (y/n) Yes or no response for clinical research being conducted at more than one site, determined based on number of locations listed under study overview section of study record
- Drug Class. Determined by clinician-scientist on author team (J.L.)
- Total participants that did not complete trial. Total number of enrolled participants who did not complete the intervention/trial. Reported on study results page
- Number of racial categories reported. If applicable, total number of racial categories reported by study sponsor

Statistical analysis

Industry-funded and non-industry funded trials were compared with standardized differences calculated for all variables, with differences of greater than 10% considered meaningful. Pearson χ^2 test were used to compare categorical variables and Kruskal-Wallis tests were used

Figure 1



PRISMA 2020 flow diagram, Antihypertensive Drug Trials reporting results to ClinicalTrials.gov, 2010-2020 *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj.n71 For more information, visit: http://www.prisma-statement.org/.

to compare continuous variables. Linear regression was employed to model change over time, with trial year as the independent variables and the mean percentage of Black participants as the dependent variable. Weighted averages were calculated accounting for all participants in the denominator of the equation. Statistical analysis was conducted in the analytical software StataSE 17 (*StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.*

Results

Antihypertensive drug trials reporting results to ClinicalTrials.gov, 2010 to 2020

Table I provides an overview of study characteristics for non-industry vs industry antihypertensive drug trials that were registered to ClinicalTrials.gov and reported results from 2010 to 2020. Of the 97 trials meeting inclusion criteria, the majority were industry-

Table I. Study characteristics of antihypertensive drug clinical trials which reported results to ClinicalTrials.gov, 2010-2020

	Non-industry trails ($N = 15$)	Industry trials ($N = 82$)	*P*-value	Overall ($N = 97$)
Percentage of Black Participants (%)				
Mean (SD)	42.7% (±31.3%)	36.5% (±34.8%)	.3781	37.7% (±33.7%)
Median (%) [Min (%), Max (%)]	30% [17%, 100%]	24% [0%, 100%]		26% [0%, 100%]
Missing (%)	8 (57.1%)	58 (70.7%)		67 (69.1%)
Study Reports Race (y/n)				
No (%)	10 (66.7%)	60 (73.2%)	.3569	70 (72.2%)
Yes (%)	5 (33.3%)	22 (26.8%)		27 (27.8%)
Total Study Enrollment				
Mean (SD)	894 (±2480)	640 (±633)	.0079	670 (±1090)
Median [Min, Max]	48.5 [12.0, 9360]	471 [1.00, 3000]		443 [1.00, 9360]
Total Randomized and Received Treatment				
Mean (SD)	824 (±2480)	587 (±537)	.0050	616 (±1040)
Median [Min, Max]	39.5 [12.0, 9360]	471 [1.00, 2690]		443 [1.00, 9360]
Percentage Incomplete (%)				
Mean (SD)	17.8% (±17.8%)	15.5% (±16.4%)	.7768	15.7% (±16.5%)
Median [Min, Max]	14% [0%, 62%]	11% [0%, 132%]		11% [0%, 132%]
Missing (%)	0 (0%)	1 (1.2%)		1 (1.0%)
Number of Racial Categories Reported				
0	1 (7.1%)	1 (1.2%)		2 (2.1%)
1	0 (0%)	2 (2.4%)		2 (2.1%)
3	0 (0%)	1 (1.2%)		1 (1.0%)
4	0 (0%)	1 (1.2%)		1 (1.0%)
5	1 (7.1%)	2 (2.4%)		3 (3.1%)
6	0 (0%)	1 (1.2%)		1 (1.0%)
7	4 (28.6%)	15 (18.3%)		19 (19.6%)
Not applicable (%)	0 (0%)	2 (2.4%)		2 (2.1%)
Missing (%)	8 (57.1%)	57 (69.5%)		66 (68.0%)
Total Participants Analyzed with race "Not Reported"				
Mean (SD)	1.25 (±2.50)	20.9 (±86.8)	.8077	17.5 (±78.9)
Median [Min, Max]	0 [0, 5.00]	0 [0, 379]		0 [0, 379]
Missing (%)	10 (71.4%)	63 (76.8%)		74 (76.3%)
Difference Between Study Completion and Results Posted (months)				
Mean (SD)	18.9 (±10.8)	23.3 (±15.0)	.395	22.7 (±14.5)
Median [Min, Max]	20.0 [0, 33.0]	20.5 [5.00, 93.0]		20.0 [0, 93.0]
Missing (%)	2 (14.3%)	0 (0%)		2 (2.1%)
Multicenter Trial (y/n)				
No (%)	10 (71.4%)	17 (20.7%)	<.0001	28 (28.9%)
Yes (%)	4 (28.6%)	62 (75.6%)		66 (68.0%)
Missing (%)	0 (0%)	3 (3.7%)		3 (3.1%)
Phase of Drug Trial				
1	0 (0%)	2 (2.4%)		2 (2.1%)
2	3 (21.4%)	8 (9.8%)		11 (11.3%)
2 and 3	0 (0%)	2 (2.4%)		2 (2.1%)
3	1 (7.1%)	33 (40.2%)		34 (35.1%)
4	6 (42.9%)	34 (41.5%)		41 (42.3%)
5	1 (7.1%)	0 (0%)		1 (1.0%)
N/A	3 (21.4%)	2 (2.4%)		5 (5.2%)
Missing (%)	0 (0%)	1 (1.2%)		1 (1.0%)
Intervention Model				
Crossover Assignment (%)	5 (35.7%)	7 (8.5%)		12 (12.4%)
Parallel Assignment (%)	6 (42.9%)	65 (79.3%)		72 (74.2%)
Single Group Assignment (%)	3 (21.4%)	6 (7.3%)		9 (9.3%)
Factorial Assignment (%)	0 (0%)	3 (3.7%)		3 (3.1%)
Not Applicable (%)	0 (0%)	1 (1.2%)		1 (1.0%)

sponsored ($n = 82$; 84.5%). Overall, non-industry trials reported higher percentages of Black study participants compared with industry trials (non-industry median = 30%, industry median = 23.9%), but this difference was not significant ($P = .3781$). Across both trial categories Black participant enrollment was higher than the national population percent of Black individuals in the United States but lower than the percent of Black individuals with prevalent hypertension (median Black participant enrollment = 25.6%). On average, industry trials enrolled substantially more participants overall than non-industry trials (Industry total enrollment = 471

median, non-industry total enrollment = 48.5 median, $P = .0079$).

For trials that did report race, the most frequent number of racial categories reported were 7 and presented frequencies in the following categories: "American Indian or Alaska Native," "Asian," "Native Hawaiian or Other Pacific Islander," "Black or African American," "White," "More than one race," or "Unknown or Not Reported." Non-industry studies were predominantly single center trials (71.4%), while industry studies were predominantly multi-center studies (75.6%). The average time to report study results to ClinicalTrials.gov after the reported completion date for industry studies was higher than for non-industry studies (industry average months to report results ± Standard Deviation = 23.3 ±15.0, non-industry average months to report results ± Standard Deviation = 18.9 ± 10.8). Across both industry and non-industry sponsored trials, the most frequent trial phase was Phase 4 (Phase 4 Trials overall = 42.3%) and the most frequent interventional model was parallel assignment (industry = 79.3%, non-industry = 42.9%).

Cross-sectional diversity in antihypertensive clinical research

Temporal trends in average participation of Black participants in antihypertensive drug trials from 2010 to 2020 are displayed in Figure 2.

Notably, there is an overall negative trend in percentage of Black participants over time, mostly due to declining percentages of participation in non-industry sponsored clinical trials.

Longitudinal reporting of race in clinical trials

Unweighted averages of Black participants for non-industry sponsored studies which reported results to ClinicalTrials.gov between 2010 and 2020 appear in Figure 3 (industry unweighted average = 36.5%, non-industry unweighted average = 42.7%, $P = .3781$). This difference remained for weighted averages, but with lower overall average percentages for both industry and non-industry trials (Figure 3, industry weighted average = 21%, non-industry weighted average = 31%).

Reporting of race for clinical trials

For studies reporting results to ClinicalTrials.gov, both industry and non-industry trials largely failed to report the race of their participants overall (Figure 4, industry percent not reported = 73.2%, non-industry percent not reported = 66.6%). The difference between sponsor type is statistically insignificant ($P = .3569$).

Supplement Figure 2 displays the distribution of time to report results to ClinicalTrials.gov after the registered study completion date, comparing studies reporting race vs those not reporting race. For studies not reporting race, the median months to report was 20.5 months, [25th, 75th percentile = 13 months, 27 months]. For studies reporting race, the median was 16 months [25th, 75th percentile = 14 months, 29 months]. Supplement Figure 3 displays the distribution of the participants who received treatment for an antihypertensive drug trial that was reported to clincaltrials.gov, comparing studies which report race and those who do not. The median treated number is higher for studies reporting race (median treated for studies which report race = 568, median treated for studies which do not report race = 437.5). There is also a widespread in size for studies which have not reported race (minimum size study which does not report race = 1, maximum size study which does not report race = 2694).

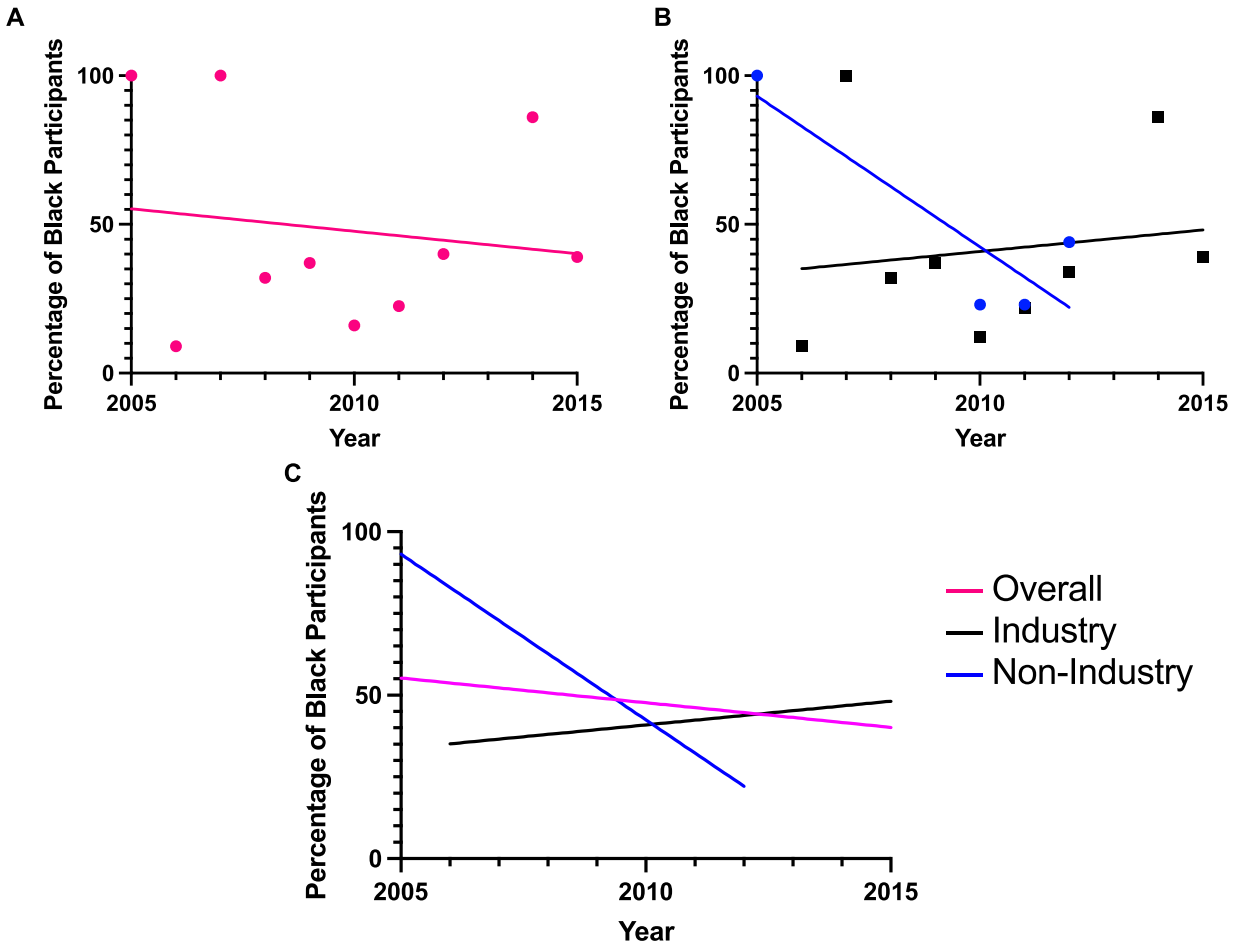
Discussion

We examined trends in Black enrollment in antihypertension drug clinical trials reported to ClinicalTrials.gov between 2010 and 2020. Our main findings were as follows: (1) non-industry sponsored studies reported higher percentages of Black participants enrolled than their industry counterparts; (2) across both industry and non-industry studies Black participants were overrepresented relative to their percentage of the U.S. population, but underrepresented relative to their burden of disease; (3) both industry and non-industry studies had high rates of not reporting racial demographics of participants; and (4) over time, there was a negative trend in participation of Black participants in antihypertension drug clinical trials.

We found minimal change in the percentage of Black participants enrolled in antihypertensive drug trials over a 10-year time period. This is notable, because neither industry nor non-industry study sponsorship was associated with increased Black participation despite this group being the most afflicted by uncontrolled hypertension. The large proportion of both types of trials that failed to report the race of study participants is alarming. Among trials reporting racial distribution, the % of Black participants was comparable to that in the general population. However, this was a small subset of all antihypertensive drug trials from 2010 to 2020, the majority of which did not report racial distributions on ClinicalTrials.gov at all. Whether the overall percent of Black participants in our study was impacted by reporting bias – with preferential reporting by studies enrolling more diverse study populations – is unknown.

Lack of diversity in clinical trials raises concerns about generalizability, which may adversely affect the care experiences of populations who are already at risk for suboptimal treatment due to their racial identities. Prior work suggests there are 5 critical barriers to trial participation for racially diverse participants: mistrust, lack of comfort with clinical trial process, lack of information, time and resource constraints based on

Figure 2



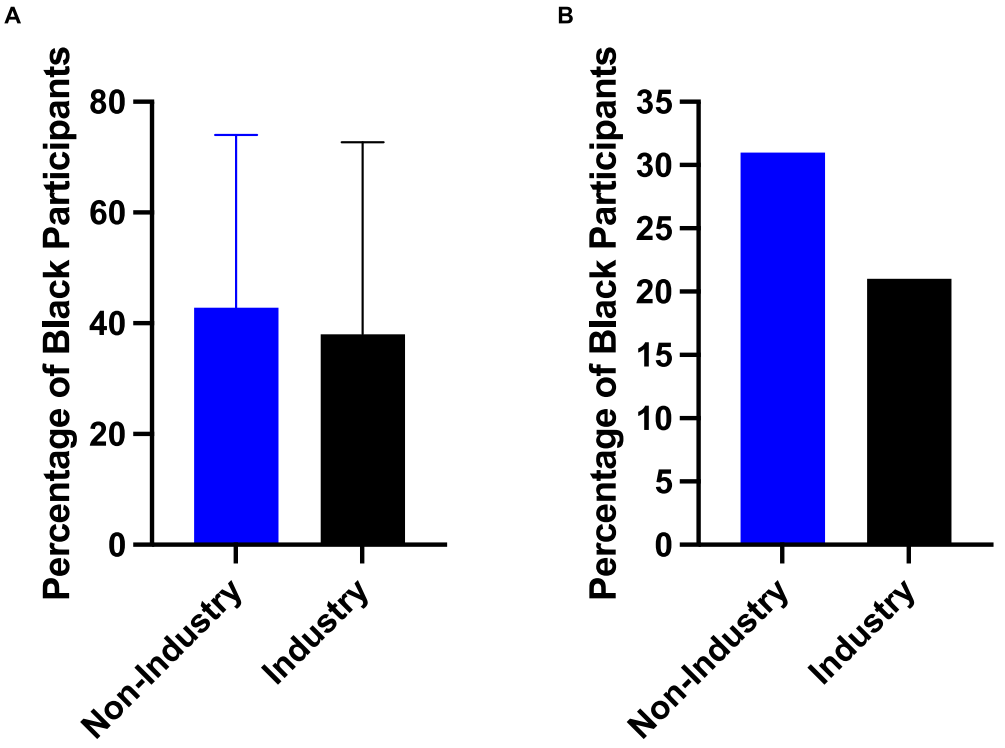
Average percentage of black participants in antihypertensive drug clinical trials, based on study start dates. A, overall percentage of Black participants between 2010 and 2020. B, percentage of Black participants in industry studies and non-industry studies between 2010 and 2020. C, linear regression of overall percentage, industry percentage, and non-industry percentage of Black participants.

participation, and lack of awareness of existence or the relevance.[7] Addressing the multiple cultural, historical, and social drivers of mistrust in clinical research and corresponding impacts on trial recruitment requires intentional effort from a variety of stakeholders. Recent calls for regulators and investigators to prioritize community engagement hold promise for implementation of practical tools and concrete metrics to meet these goals.[13]

Diversity in clinical research for other cardiovascular therapeutics

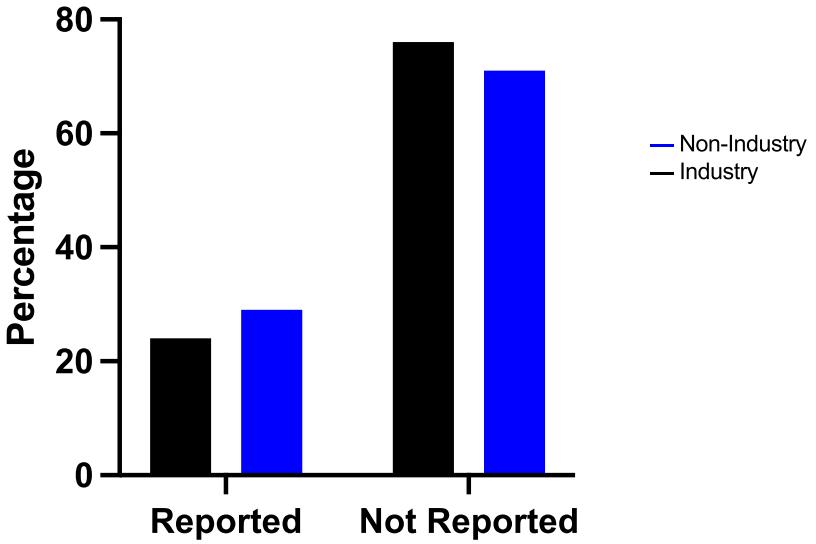
Success in achieving clinical trial diversity varies by both therapeutic area and by drug class. A global study evaluating trials of treatments for heart disease, cancer, and disorders of the central nervous system found that, in 2014, 86% of clinical trial participants identified as white, 3% as Black, 6% as Asian, and 5% as another race or ethnicity.[13] A prior study of trials used to support eventual FDA approval of 24 cardiovascular drugs found the highest participation to prevalence ratio (where a range between 0.8 and 1.2 indicates that the proportion represented in the trial is roughly equal to the proportion in the disease population) was for hypertension at 0.52, and the lowest was for hypercholesterolemia at 0.072.[14] Other conditions, such as acute coronary syndrome, atrial fibrillation, coronary artery disease, heart failure, and pulmonary arterial hypertension all had participation to prevalence ratios between 0 and 0.4, suggesting that trials enrolled substantially fewer Black par-

Figure 3



Average Percentage of Black Participants in Antihypertensive Drug Clinical Trials Industry vs Non-Industry Funding. A, Weighted averages of Black participation in industry vs non-industry studies between 2010 and 2020. B, Unweighted averages of Black participation in industry vs non-industry studies between 2010 and 2020.

Figure 4



Percentage of Studies Reporting Race between 2010 and 2020.

ticipants than expected in the relevant population of individuals affected with each disease.[14] Similarly, Black adults are underrepresented in NIH-funded cardiovascular trials, and the majority of trials in our study did not specify a Black enrollment target, did not meet targets, and/or did not report specific plans to enroll Black adults in their studies.[15]

Our finding of underreporting of race/ethnicity is consistent with prior work. A systematic review of trials for acute coronary syndrome found that, across both drug and procedural interventions, the distribution of racial or ethnic groups was only reported in 21.5% of trials, and of those trials that reported distributions of racial or ethnic groups, only 15.0% of participants were nonwhite, with Black patients representing 3.7%, Asian patients representing 9.6%, and Hispanic patients representing 7.8% of all patients.[16] Similar trends were seen in a systematic review of heart failure clinical trials, where between 2000 and 2020 only 37.9% of trials reported race and ethnicity data, and 18.7% of trial participants identified as Black, Indigenous, or people of color.[17] While the literature on enrollment in clinical trials specifically for hypertension is sparse, our study adds to the literature in cardiovascular disease by showing that hypertension clinical trials appear to report race more frequently than other areas of cardiovascular, and tended to enroll greater percentages of Black patients relative to other areas of cardiovascular medicine.

Failure to report race of study participants has both proximal and distal negative impacts on health equity. In the short term, it calls into question applicability of results to minority patient populations and as a result, may exacerbate persistent treatment disparities. Over time, lack of transparency about minority underrepresentation prevents researchers, policymakers, and patient stakeholders from understanding the full extent of the problem and proposing and testing solutions. Even when the problem is fully appreciated, efforts to enhance diversity often face high levels of mistrust of the medical system in racial/ethnic minority populations due to historical injustices (eg, the Tuskegee Syphilis experiment), as well as economic and logistical barriers.

Improving diversity in clinical research over time

Improving diversity of participants enrolled in clinical trials has been a major goal for the clinical research community for several decades. However, while modest progress has been made, creation of equitable access to clinical trial participation has been slow. Clark et al. developed an improvement roadmap to improve participant trust and help provide potential trial participants with high-quality information about clinical trial participation.[7] However, structural barriers also limit equitable participation in clinical trials: eg, structural racism leading to neighborhood segregation can make transportation to physically access clinical trials difficult.[18,19] A focus on robust community engagement that centers the voices of trial participants from underrepresented backgrounds, as well as strong effort to develop institutional capacities to engage communities often not well-represented in clinical trials effectively are essential.[18] An alternative approach to promote the participation from underrepresented populations in clinical trials has been the development of targeted trials enrolling only underrepresented minority participants, such as the African American Heart Failure Trial and the PLATINUM diversity study.[20,21] While these trials are highly effective in enrolling participants from targeted backgrounds, this is not a feasible trial design for trials that do not have a pre-specified hypothesis pertaining to a particular race or ethnicity.[22] Aggregating data from multiple trials and registries is another potential solution to small numbers and corresponding imprecision in effect estimates. However, this is not possible for every condition and does not address the root cause of inequities in trial recruitment or the subsequent concerns about generalizability to a broad patient population.[22] Increasing use of pragmatic trial designs could be an effective strategy to reduce enrollment barriers and facilitate recruitment of patients from underrepresented communities in clinical trials.[23] Overall, it is clear that multiple strategies, such as financial incentives or penalties tied to trial recruitment, engagement of community leaders in research design and conduct, and a commitment to the inclusion of investigators from diverse backgrounds in clinical research are needed to improve equitable representation in clinical trials.[18,22]

Limitations

There are several limitations to our study worth noting. First, our review focused on using information from the public repository ClinicalTrials.gov to examine the landscape of the participation of Black patients in antihypertensive drug clinical research. ClinicalTrials.gov is a free tool for the public to use, which facilitates transparency relative to using manuscripts from subscription-based journals, which often have high cost and limited accessibility for the general public. The scope of studies represented on ClinicalTrials.gov has grown with time, with 412,667 total studies registered including 50,758 interventional trials.[24]

Our methodology is limited by exclusively evaluating studies registered with ClincalTrials.gov. However, since not all trials report their final data to ClinicalTrials.gov, results from our review could be over- or underestimates of the representation of Black patients in anti-hypertension clinical trials overall.[25] Additionally, results for all trial types over this time period took well over a year on average to be reported. Regardless of whether all studies report their final data, in 2017 under Section 801 of the Food and Drug Administration Act of 2007 (FDAA801),

all clinical trials are federally required to be registered to ClinicalTrials.gov.[26] We believe that this tool is an important one because it is a central repository where informed consumers can locate information on clinical research for drugs. Our results illustrate that these consumers would not be able to easily find information on the racial demographics of many studies registered to this tool, because that data was not reported. Additionally, while local demographics may impact Black representation in clinical trials, we did not have access to region of residence for trial participants or the specific location of enrolling sites; therefore, we were unable to examine how local demographics may have influenced racial representation or lack thereof. Future research testing strategies to support diverse trial enrollment in racially homogenous locations is needed

Future implications

The NIH Revitalization Act of 1993 was created to increase inclusion of minorities and women and to assure generalizability of trial results to these populations.[27] Despite limited progress over nearly 3 decades since the Act's passage, most studies still fail to set and meet appropriate diversity targets, with many failing to even publicly report participant race/ethnicity distributions. In a cross-sectional analysis of U.S. vaccine trials from 2011 to 2020, only 58% reported race despite countless policies mandating race reporting and improved representation.[28]

The growing field of health equity research is accelerating efforts to understand the mechanisms of racial disparities, rather than simply describing them. However, low racial diversity in hypertension clinical trials and suboptimal race-specific reporting have hampered investigational endeavors into the biopsychosocial and system-level factors that impact key health behaviors such as medication adherence. According to a meta-analysis of observational studies on adherence to drugs which address cardiometabolic disease, approximately half of patients do not adhere to their prescribed medications.[5] At the population level, key factors affecting adherence, like less coordinated care from their health teams and suboptimal education regarding their interventions disproportionally affect Black people.[5] However, future interventions to mitigate these drivers must be built on a foundation of evidence generated from diverse study populations.

For patient populations with a greater degree of mistrust of the medical system, it is important to be transparent about study diversity, particularly for medications in a common condition. As shown in our analysis, the lack of race reporting in many studies makes this impossible. We advocate that future clinical trials be required to report the racial and ethnic distributions of their study participants, and that they be required to rapidly report their final results rather than waiting for a year or longer Encouraging transparency in reporting can support both scientific rigor as well as transparency in reporting, with long-lasting potential benefits for both patients and the greater scientific community.

Conflict of Interest

Michael D. Green is a contractor for the healthcare startup company Zealcare Inc. (private company based in Cary, NC). Green does not hold an ownership stake in the company.

CRediT authorship contribution statement

Michael D. Green: Conceptualization, Investigation, Data curation, Writing – original draft, Project administration, Formal analysis. **Mahalia R. Dalmage:** Writing – original draft, Visualization, Data curation, Investigation, Formal analysis. **Jay B. Lusk:** Writing – original draft, Investigation, Data curation, Methodology. **Emilie F. Kadhim:** Writing – original draft, Visualization, Writing – review & editing. **Lesley A. Skalla:** Methodology, Software, Writing – original draft. **Emily C. O'Brien:** Writing – review & editing, Supervision, Data curation, Methodology, Investigation.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2023.01.001.

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