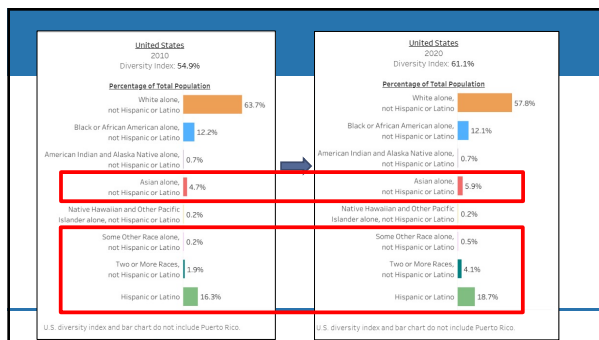
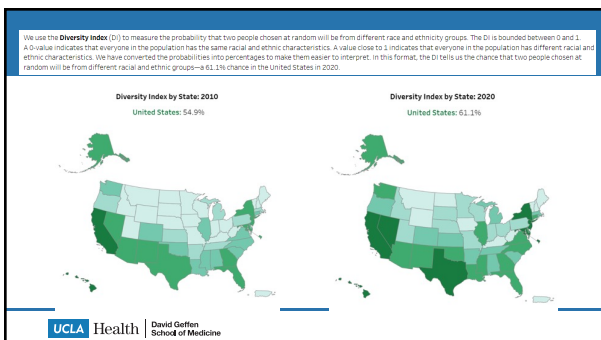


Racial And Ethnic Disparities In Clinical Trials And The Treatment Of CLTI: What Are The Causes And What Can Be Done About Them

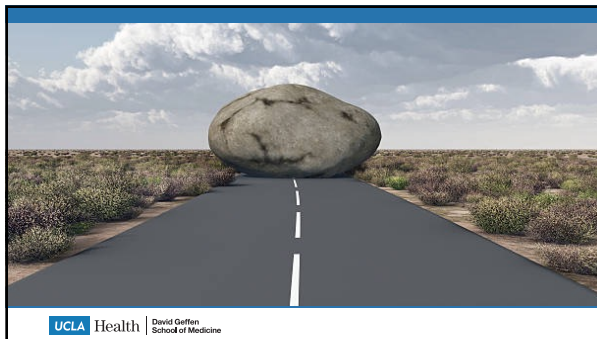
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No Financial Disclosures



Clinical Trials

- Critical to advancement of medicine
- Changes or reactions different with each group?
- Results applicable to the population?
- Reduce disparities in outcomes?
- **Need a diverse patient cohort!!!**



Systematic Review

Diversity in randomized clinical trials for peripheral artery disease: a systematic review

Chandler Long, Amanda S. Williams, Alyssa M. McGovern, Caroline M. Jackson, Lindi M. Hargrett, Sue Davis, and Michael R. Griffin

Abstract: Significant race and sex disparities exist in the prevalence, diagnosis, and outcomes of peripheral artery disease (PAD). However, clinical trial sub-analyzing outcomes for PAD often lack representative patient populations. This systematic review aims to summarize the demographic representation and enrollment strategies in clinical trials of lower extremity endovascular interventions for PAD.

Methods: Following the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we searched the MEDLINE, Embase, Cochrane, and Scopus databases from 1980 until 2022 for randomized controlled trials (RCTs) of PAD patients, and peer-reviewed journal publications of RCTs conducted between January 2017 and December 2022. Descriptive analysis was used to summarize the characteristics of patients for or not included in trials, and the reporting of demographic characteristics. Meta-analysis was used to compare outcomes between demographic characteristics and outcomes for characteristics.

Results: A total of 20 RCTs were identified. 17 trials included the enrollment characteristics of patients, including patients' race/ethnicity, sex, age, and socioeconomic status. Information regarding demographic representation was frequently missing. While 4 of 17 trials published enrollment and sex, only 1 reported race/ethnicity, and none reported socioeconomic or marital status. Additionally, only 4 publications reported clinical outcomes by demographic characteristics. Meta-analysis analysis revealed that the mean number of enrolled racial/ethnic groups from 1000 to 1000000 was 0.06.

Conclusions: The majority of clinical trial reports do not report the race/ethnicity, sex, age, and socioeconomic status of study findings in lower extremity PAD, which equated to the real-world population. Addressing these issues is critical to improve the generalizability and impact of clinical trial results in the real world, primarily leading to improved clinical outcomes for patients in underserved populations.

Keywords: Peripheral artery disease, Health disparities, Demographic representation, Systematic review, Enrollment strategies, Endovascular interventions, Clinical trials.

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- 59 Manuscripts (35 trials, 14 publications, 10 protocols)
- 4 reported race/ethnicity
- Zero socioeconomic factors
- 4 demographic related outcomes

Table 3 Characteristics of the included clinical trial study protocols for lower extremity endovascular interventions for the treatment of PAD.

Trial Name and Clinical Trial ID No.	Protocol accessible	Year of protocol publication	Method of recruitment	Information on barriers to transportation available	How transportation barriers were addressed?	Patient navigation coaching strategies adopted	Cultural competency training for clinical research associates	Relationship building/ social marketing	Strategies for follow-up
EMMAN2 NCT02012120	Yes	2019	Clinical/Pharmaceutical	Yes	Travel expenses	NR	NR	NR	Telephone, Office clinic visits
LINES NCT04772320	Yes	2022	NR	No	NR	NR	NR	NR	NR
SARNA NCT04457183	Yes	2021	Clinical/Pharmaceutical	No	NR	NR	NR	NR	Telephone, Office clinic visits, letter
SHRO NCT04385645	Yes	2022	Other Academic, Clinical/Pretrial	Yes	NR	NR	NR	NR	Telephone, Office clinic visits
LUKIN/STK/16f NCT01870401	Yes	2017	NR	No	NR	NR	NR	NR	Telephone, Office clinic visits
STAR3 NCT02692022	Yes	2016	Clinical/Pharmaceutical	No	NR	NR	NR	NR	Telephone, Office clinic visits
BEACON/BEAT NCT02881217	Yes	2022	NR	No	NR	NR	NR	NR	Unknown
RANGER I/IIa NCT03041416	Yes	2018	Clinical/Pharmaceutical	Yes	Stipend	NR	NR	NR	Telephone, Office clinic visits
AMORAL NCT02614481	Yes	2016	Clinical/Pharmaceutical	Yes	Travel expenses	NR	NR	NR	Telephone, Office clinic visits
FRANCISCO NCT02424019	Yes	2019	Clinical/Pharmaceutical	No	NR	NR	NR	NR	NR

Int J Equity Health 2024 Feb 13;23(1):29

Obstacles

Increasing Diversity in Clinical Trials: Overcoming Critical Barriers

Luther T. Clark, MD, Laurence Watkins, MD, Ileneo L. Pino, MD, Mary Elmer, MSN, CRNP, Ola Akinboboye, MD, Millicent Gorham, PhD (Hon), Brendo Jorneran, PharmD, Cassandra McCullough, MBA, Christine Pierre, RN, Adam B. Polis, MA, Gary Puckrein, PhD, and Jeanne M. Regnier

Abstract: Clinical trial results provide the critical evidence base for evaluating the safety and efficacy of new medicines and medical products. Efficacy and safety may differ among population subgroups depending on intrinsic/extrinsic factors, including sex, age, race, ethnicity, lifestyle, and genetic background. Racial and ethnic minorities continue to be underrepresented in cardiovascular and other clinical trials. Although barriers to diversity in trials are well recognized, sustainable solutions for overcoming them have proved elusive. We investigated barriers impacting minority patients' willingness to participate in trials and—based on literature, review, and evaluation—


- Patients were 35-80 years old with a cardiometabolic condition
 - Participated in at least 1 cardiometabolic clinical trial
 - Were asked to participate but declined
 - Were eligible for clinical trial participation but were not asked to participate
- Referring physicians who referred patients to participate in cardiometabolic trials
- Investigators were minority-serving physicians who led cardiometabolic trials
- Trial coordinators

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Problems

- Mistrust
- Lack of comfort with the process
- Lack of information
- Time and resource constraints
- Lack of awareness

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J. Marion Sims M.D.

- "Father of Gynecology"
- Numerous atrocities to enslaved women

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Havasupai Tribe

Had diabetes blood samples tested for other diseases without consent



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Tuskegee Experiment

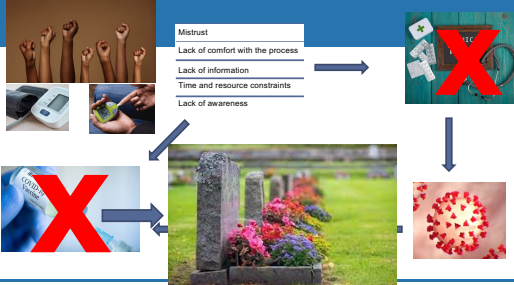


- Untreated for syphilis and allowed to progress to tertiary symptoms
- Men suffered blindness, cognitive disorders and death
- Investigators told local physicians not to treat study participants

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Mistrust
Lack of comfort with the process
Lack of information
Time and resource constraints
Lack of awareness

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Solutions

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NIH Grants & Funding

NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research

I. LEGISLATIVE BACKGROUND

The NIH Revitalization Act of 1993, PL 103-43, signed into law on June 10, 1993, directed the NIH to establish guidelines for inclusion of women and minorities in clinical research. The statute states that:

In conducting or supporting clinical research for the purposes of this title, the Director of NIH shall ... ensure that (a) women are included as subjects in each project of such research; and (b) members of minority groups are included in such research. 492B(a)(1)

The statute further directed the NIH to establish guidelines to specify:

- (a) the circumstances under which the inclusion of women and minorities as subjects in projects of clinical research is inappropriate ...;
- (b) the manner in which clinical trials are required to be designed and carried out; and
- (c) the operation of outreach programs. 492B(d)(1)

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TABLE B-1 Demographics of Participants in Trials Supported by NIH Centers and Institutes

	2013 (%)	2014 (%)	2016 (%)	2017 (%)	2018 (%)
Female	44.3	47.2	54.1	47.9	52.4
American Indian	2.1	1.3	0.8	0.7	1.0
Asian	15.1	17.2	8.4	26.4	7.8
Black/African American	12.2	14.3	10.0	10.8	13.5
Native Hawaiian/Pacific Islander	0.3	0.3	0.6	0.1	0.2
White	52.9	49.5	49.6	49.9	60.0
More than 1 race	1.1	1.1	2.0	1.9	2.3
Unknown race	1.1	1.1	2.0	1.9	2.3
Hispanic	9.8	8.1	10.8	6.7	8.5
Non-Hispanic	86.1	89.6	62.6	81.8	76.2
Unknown ethnicity	4.1	2.3	22.4	9.8	12.0
Sum of all races	84.7	84.8	73.5	91.8	87.2
Sum of all ethnicities	100.0	100.0	95.8	98.3	96.7

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National Academies of Sciences, Engineering, and Medicine, Committee on Improving the Representation of Women and Underrepresented Minorities in Clinical Trials and Research; Bibbins-Domingo, K., Heston, A., editors. Washington, DC: National Academies Press; 2016.

UNITE's Four Focus Areas

- FOCUS AREA 1: Elevating health disparities and minority health research** across clinical and community research.
- FOCUS AREA 2: Promoting equity in the NIH-supported biomedical research ecosystem.**
- FOCUS AREA 3: Promoting equity in the internal NIH workplace.**
- FOCUS AREA 4: Improving the accuracy and transparency of racial and ethnic equity data.**

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Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry

- Broaden eligibility criteria
- Make retention less burdensome
- Increase information availability
 - Webinars
 - Multi-lingual documents
 - Leverage social media
- Include varied geographic locations

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 2018
Consultation

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BEST-CLI

Best Endovascular vs. Best Surgical Therapy in Patients with Critical Limb Ischemia

Sponsored by the National Heart Lung and Blood Institute

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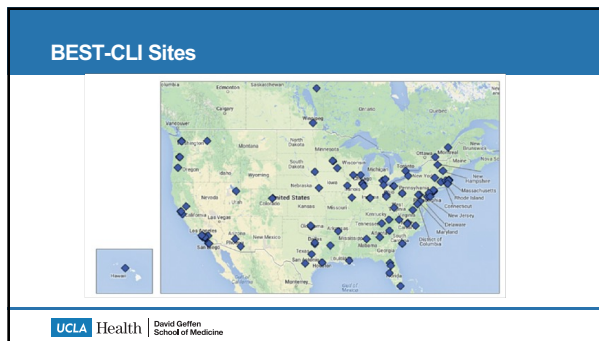
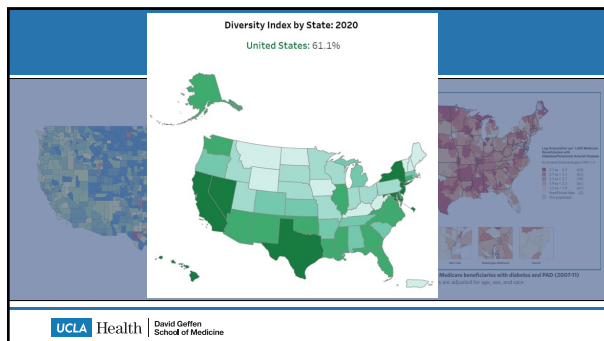
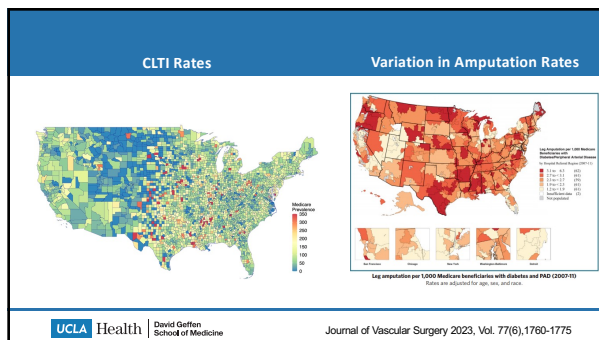


Table S4: Baseline Patient Characteristics

Characteristics	Cohort 1			Cohort 2		
	Overall (N=1434)	Surgery (N=718)	Endovascular (N=716)	Overall (N=396)	Surgery (N=197)	Endovascular (N=199)
Age — yr	66.9±9.9	66.9±9.8	67.0±10.0	68.6±9.2	68.4±8.8	68.8±9.6
Female Sex, no. (%)	408 (28.5)	201 (28.0)	207 (28.9)	111 (28.0)	56 (28.4)	55 (27.6)
Hispanic, no./total no. (%)	187/1433 (13.0)	82/717 (11.4)	105/716 (14.7)	53 (13.4)	28 (14.2)	25 (12.6)
Race, no./total no. (%)*						
White	1028/1423 (72.2)	500/711 (70.3)	528/712 (74.2)	275/390 (70.5)	143/194 (73.7)	132/196 (67.3)
Black	275/1423 (19.3)	156/711 (21.9)	119/712 (16.7)	96/390 (24.6)	40/194 (20.6)	56/196 (28.6)
Asian	20/1423 (1.4)	13/711 (1.8)	7/712 (1.0)	2/390 (0.5)	2/194 (1.0)	0 (0.0)
Other	100/1423 (7.0)	42/711 (5.9)	58/712 (8.1)	17/390 (4.4)	9/194 (4.6)	8/196 (4.1)

Implementing methods in the ELEGANCE registry to increase diversity in clinical research

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ABSTRACT
Objective: Women and underrepresented minorities (URMs) who are at an increased risk of presenting with severe peripheral artery disease (PAD) and have different responses to treatment compared with non-Hispanic White males yet are underrepresented in PAD research.
Methods: ELEGANCE is a global, prospective, multi-center, post-market registry of PAD patients treated with drug-eluting device that aims to enroll at least 40% women and 40% URMs. The study design incorporates strategies to increase enrollment of women and URMs. Inclusion criteria are age >60 years and treatment with any commercially available Boston Scientific Corporation drug-eluting device marketed for peripheral vasculature lesions, exclusion criteria is life expectancy <1 year.
Results: Of 750 patients currently enrolled (951 lesions) across 39 sites, 524 (44.2%) are female and 350 (47.3%) are URMs (2.6% Black, 11.2% Asian, 8.5% Hispanic/Latino, and 5.3% other). Rutherford classification is distributed differently between sexes (P = .028). Treatment indication differs among racial/ethnic groups (P < .005). Chronic limb-threatening ischemia was higher for Black (38.3%) and Hispanic/Latino (28.3%) patients compared with non-Hispanic White (21.8%) and Asian patients (21.4%). Diabetic ulcers were higher in Asian patients (62.3%) compared with Black non-Hispanic White and Hispanic/Latino patients (72.2%, 68.7%, and 77.6%, respectively, P < .001). Mean lesion length was longest for Black patients (62.7 mm) than non-Hispanic White (52.2 mm), Asian (54.8 mm), and Hispanic/Latino patients (52.1 mm), P = .006.
Conclusions: Analyses of data from the ELEGANCE registry show that differences exist in baseline disease characteristics by sex and race/ethnicity these may be the result of other underlying factors, including time to diagnosis, burden of underlying comorbidities, and access to care. (J Vasc Surg 2024;79(1):136-145.e3)
Keywords: Clinical trials, Health disparities, Health equity, Patient engagement, Patient recruitment, Peripheral artery disease

UCLA Health | David Geffen School of Medicine | J Vasc Surg 2024 Jan;79(1):136-145.e3

"global, prospective, multi-center, post-market registry of PAD patients treated with drug-eluting device that aims to enroll at least 40% women and 40% URMs"

Table II Baseline demographics, medical history, and disease characteristics by sex

Subject characteristic	Sex		P value*	Overall (N = 750 patients)
	Female (n = 324)	Male (n = 426)		
Age, years	70.7 (9.7)	68.7 (9.4)	.0059	69.6 (9.6)
Race/Ethnicity ^b			.0001	
Hispanic or Latino				64 (8.6)
Non-Hispanic White				360 (52.7)
Asian				84 (11.4)
Black, of African heritage				162 (21.9)
Other	16 (5.0)	24 (5.7)		40 (5.4)
Not disclosed	6	4		10

**43% Female
47% URMs**

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Solutions

- Sponsors
 - Look for sites with diverse populations
 - Diverse site investigators

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Concordance

- Interpersonal competence
- Technical competence
- Not always race
- Culturally understanding

Understanding African Americans' Views of the Trustworthiness of Physicians
 Elizabeth A. Alvarado, MD, MPH¹; Nancy Butler, MD, PhD²; Carol Shroyer, MD, PhD³; Eric E. Whitaker, MD, MPH⁴; Richard B. Woschek, PhD⁵
 1. Johns Hopkins University, Baltimore, MD; 2. University of Illinois at Chicago, Chicago, IL; 3. University of Illinois at Chicago, Chicago, IL; 4. University of Illinois at Chicago, Chicago, IL; 5. University of Illinois at Chicago, Chicago, IL

BACKGROUND: Many studies have written about the historical and ongoing mistrust of African Americans toward the health care system, and little research has been done to understand if and how this mistrust affects disease management across various of the common chronic diseases.
OBJECTIVE: To better understand what trust and distrust in physicians mean to African Americans.
DESIGN: Qualitative study using an open-ended interview guide.
SETTING: Large public hospital and community organization in Chicago, IL.
PARTICIPANTS: Community sample of African American adult men and women.
MEASUREMENTS AND MAIN RESULTS: Data from 16 interviews were analyzed using grounded theory analysis. The analysis was then validated through the community advisory board.
CONCLUSIONS: Large public hospital and community organization in Chicago, IL. The analysis was then validated through the community advisory board.

KEYWORDS: Trust, African Americans, Health equity, Patient engagement, Patient recruitment, Peripheral artery disease

J Gen Intern Med. 2006;21:642-7

Solutions

- Sponsors
 - Look for sites with diverse populations
 - Diverse site investigators
 - Whole team (Coordinator)
- Cultural Competency
 - Reinforce personal health and safety
 - Confirm clear information
 - Appreciate involvement
 - Include referring physician
 - Provide transportation, compensation
 - Make as patient centric as possible
 - Mobile app
- Demographic reporting
- Intangibles

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Conclusion

- Mistrust and lack of information leading causes
- Efforts to increase underrepresented minorities in clinical trials are underway
- Consider investigators and hospitals with diverse patient population
- Physician and team training to improve cultural awareness