bmjmedicine

Check for updates

Fostering diversity in clinical trials: need for evidence and implementation to improve representation

David Collister,[1] Claire Song,[2] Shannon M Ruzycki [3]

For numbered affiliations see end of article.
Correspondence to: Dr Shannon M Ruzycki, Department of Medicine, Room 1422, Health Sciences Center, University of Calgary Cumming School of Medicine, 3330 Hospital Drive NW, Calgary, AB, Canada T2N 2T9;
shannon.ruzycki@ucalgary.ca

Cite this as: *BMJMED* 2024;3:e000984. doi:10.1136/bmjmed-2024-000984

Received: 5 June 2024
Accepted: 25 June 2024

Linked

► http://dx.doi.org/10.1136/bmjmed-2024-000920

The clinical trials community needs better guidance to translate ambitious diversity commitments into actual inclusion and diversity in clinical trials

The lack of diversity in clinical trials undermines the generalisability, quality, and external validity of medical research.[1] Depending on the area of study, women, older adults, and people with disabilities are typically under-represented.[2] Representation cannot be assessed for many groups, because important personal characteristics, such as racial and gender identity, are not consistently collected or reported in many trials.[3–5]

The reference standard of diversity commitments[6] created by Miller and colleagues is an important first step to deal with under-representation in clinical trials. The 14 commitments provide a framework for trial teams in both industry and academia to consider how elements of the design, conduct, and analysis of the study, reporting, and knowledge translation facilitate inclusive trial recruitment. However, operationalising these commitments will be challenging for sponsors who already have constrained resources, difficulties with recruitment and retention of participants, and pressured time lines. A thoughtful approach and systems level support in designing clinical trials that are inclusive is required to achieve these critical goals.

An implementation science approach to diverse trial recruitment is needed

As well as pharmaceutical companies, the focus of the work by Miller and colleagues,[6] diversity commitments have been adopted by many funding bodies, regulatory agencies, and journals. Also, numerous toolkits[7] are available to guide trial teams to build equity, diversity, and inclusion into their research programmes. Subsequent evaluations, however, suggest that this work has had limited effectiveness.

For example, some funding agencies require an approach to sex and gender based analyses[8 9] as part of the grant process. Although this approach has increased the proportion of applications that claim to consider sex and gender, observational evidence suggests that these requirements have not resulted in a more thoughtful approach to recruitment, collection of data, or reporting of results for female participants, women, and under-represented sex and gender minority groups.[10] Similarly, efforts by the National Institutes for Health to increase the number of racial and ethnic minority participants in funded trials have not meaningfully dealt with this under-representation,[11] and race and ethnic group of participants was not reported in about 50% of contemporary clinical trials published in high impact medical journals.[3]

The reasons that these well intentioned commitments have not resulted in real world improvements in diversity in clinical trials are not known. This problem highlights a need for implementation science, an approach to understanding why and how interventions, such as diversity commitments, do or do not work in some settings. This discipline offers a much needed, evidence based roadmap to fulfil diversity commitments, particularly in complex systems, such as health and medical research. Implementation science directs teams to describe the state of the local context, understand barriers and facilitators of current behaviour, and develop strategies informed by theory to enable success.

Trial teams should proactively identify and manage barriers to representative trial recruitment and retention

Applying an implementation science approach starts with understanding the local context, as emphasised by Miller et al, who reported that describing barriers to inclusive recruitment and retention are an essential diversity commitment. Many studies have described barriers to participation from the perspective of under-represented groups[12] and proposed interventions for research teams to deal with these barriers.[13] Investigators should note that these barriers and solutions likely vary by the topic, population, intervention, and setting of the trial, however, emphasising the need for a local approach rather than one-size-fits-all practices. For example, female participants are typically under-represented in cardiology trials[14] but adequately represented in geriatric trials,[15] which under-recruit participants with medical comorbidities, disabilities, and cognitive impairment.[16]

Emerging reseach has examined systems level[16] and research team drivers[17 18] of under-representation in clinical trials. Although many barriers are related to perceived resource constraints to recruit and retain under-represented groups,[18] attitudes of researchers might be an overlooked barrier. For example, a qualitative study suggested that many trialists perceived barriers to more diverse trial participation as insurmountable rather than modifiable, despite generally agreeing that diversity was an important goal.[17] Without dealing with this perception, other interventions to improve inclusion in clinical trials are likely to be under supported and unsuccessful.

Pilot and feasibility studies could incorporate an assessment of specific barriers to inclusive trial

recruitment and retention for individual trials and settings. Numerous validated instruments and tools to describe barriers to implementation exist that can be administered through field notes, surveys, or interviews, depending on the skills and resources of the trial team.[19 20] For example, surveys of acceptability and feasibility[21] of inclusive trial recruitment strategies among trial team members, before implementation, can identify if attitudes of researcher are a key barrier. All assessments should be informed by implementation frameworks and relevant critical approaches, such as critical race theory or critical race feminism.

After describing contextual barriers to selected diversity commitments, approaches of implementation science confirm the findings of Miller et al, suggesting that trial teams proactively work with relevant community members and other stakeholders to deal with barriers before enrolment. This work can use implementation theory[22] or mapping methods.[23] Investigators could test the effectiveness of these targeted strategies to improve representation of clinical trials with study-within-a trial methods,[24] thus contributing to the evidence base for inclusive trial design and improving the scientific productivity of the parent trial.

Diversity commitments are a shared responsibility between sponsors and institutions

Diversity commitments require coordinated, systems level support and accountability for both industry and investigators. Diversity in recruitment requires additional resources, time, and skills from trial teams, and this requirement for diversity needs to be balanced with the feasibility and generalisability of the trial. With decades of literature showing underrepresentation of trial participants for numerous acute and chronic diseases, new systems level approaches are necessary.

Firstly, the clinical trials community needs specific evidence on how to improve recruitment and retention across a diverse group of participants to match the epidemiology of the target disease, with input from patients, caregivers, and communities. Clinical trial networks are well placed to lead large study-within-a trial projects to generate this evidence, and funding agencies can incentivise this work with more resources for teams who include these protocols in their applications.

Secondly, this work should be mandated, monitored, and incentivised by an infrastructure for research and health services. For example, regulatory bodies could require protocol sections for each trial's specific diversity commitments. Guideline bodies, such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, should look at improving outdated recommendations for different ethnic group and geriatric participants, based on work on the eligibility criteria of pregnant and breastfeeding individuals as a precedent.[25] Research ethics boards could incorporate an assessment of risks to diverse recruitment as well as to existing assessments of participant risks. Funding bodies should require trial teams to define prespecified goals for diverse recruitment and allow budgetary items to support these goals, such as transportation for study participants or hiring experts in equity, diversity, and inclusion.

Most importantly, patients and their healthcare providers should be empowered to hold sponsors and investigators accountable. Through professional and patient organisations, these stakeholders should use their platforms to celebrate patient centred, inclusive trials by prioritising participation, committing to all study procedures, and ensuring adherence and follow-up.

AUTHOR AFFILIATIONS

[1]Department of Medicine, University of Alberta Faculty of Medicine and Dentistry, Edmonton, Alberta, Canada
[2]University of Calgary Cumming School of Medicine, Calgary, Alberta, Canada
[3]Department of Medicine, University of Calgary Cumming School of Medicine, Calgary, Alberta, Canada

Contributors SMR, CS, and DC wrote the first draft, provided edits, and compiled the final version.

Competing interests We have read and understood the BMJ policy on declaration of interests and declare the following interests: none.

Provenance and peer review Commissioned; internally peer reviewed.

ORCID iD

Shannon M Ruzycki http://orcid.org/0000-0002-8122-2910

REFERENCES

1 Schwartz AL, Alsan M, Morris AA, *et al*. Why diverse clinical trial participation matters. N Engl J Med 2023;388(14):1252–4. 10.1056/NEJMp2215609
2 Flores LE, Frontera WR, Andrasik MP, *et al*. Assessment of the inclusion of racial/ethnic minority, female, and older individuals in vaccine clinical trials. JAMA Netw Open 2021;4(2):e2037640. 10.1001/jamanetworkopen.2020.37640
3 Alegria M, Sud S, Steinberg BE, *et al*. Reporting of participant race, sex, and socioeconomic status in randomized clinical trials in general medical journals, 2015 vs 2019. JAMA Netw Open 2021;4(5):e2111516. 10.1001/jamanetworkopen.2021.11516
4 Soomro QH, McCarthy A, Varela D, *et al*. Representation of racial and ethnic minorities in nephrology clinical trials: a systematic review and meta-analysis. J Am Soc Nephrol 2023;34(7):1167–77. 10.1681/ASN.0000000000000134
5 Loree JM, Anand S, Dasari A, *et al*. Disparity of race reporting and representation in clinical trials leading to cancer drug approvals from 2008 to 2018. JAMA Oncol 2019;5(10):e191870. 10.1001/jamaoncol.2019.1870
6 Miller J, Pelletiers W, Suttiratana S, *et al*. Harnessing policy to promote inclusive representation in medicine development: reference standard and structured audit for clinical trial diversity policies. BMJ Med 2024. 10.1136/bmjmed-2024-000920
7 Kuaban A, Force ASoCTaHET. ASH DEI Toolkit for Clinical Trial Sponsors: Incorporating DEI Principles throughout the Clinical

Trial Life Cycle. American Society for Hematology, 2023. Available: https://www.hematology.org/-/media/hematology/files/dei/ash-dei-toolkit-for-clinical-trial-sponsors.pdf
8 How to integrate sex and gender into research: Government of Canada. 2019 Available: https://cihr-irsc.gc.ca/e/50836.html
9 What are sex & gender office of research on women's health: National Institutes of Health, Available: https://orwh.od.nih.gov/sex-gender
10 Johnson J, Sharman Z, Vissandjée B, *et al*. Does a change in health research funding policy related to the integration of sex and gender have an impact PLoS One 2014;9(6):e99900. 10.1371/journal.pone.0099900
11 Chen MS, Lara PN, Dang JHT, *et al*. Twenty years post-NIH revitalization act: enhancing minority participation in clinical trials (Empact): laying the groundwork for improving minority clinical trial accrual: renewing the case for enhancing minority participation in cancer clinical trials. Cancer 2014;120 Suppl 7:1091–6. 10.1002/cncr.28575
12 Clark LT, Watkins L, Piña IL, *et al*. Increasing diversity in clinical trials: overcoming critical barriers. Curr Probl Cardiol 2019;44(5):148–72. 10.1016/j.cpcardiol.2018.11.002
13 Bodicoat DH, Routen AC, Willis A, *et al*. Promoting inclusion in clinical trials-a rapid review of the literature and recommendations for action. Trials 2021;22(1):880. 10.1186/s13063-021-05849-7
14 Tahhan AS, Vaduganathan M, Greene SJ, *et al*. Enrollment of older patients, women, and racial and ethnic minorities in contemporary heart failure clinical trials: a systematic review. JAMA Cardiol 2018;3(10):1011–9. 10.1001/jamacardio.2018.2559
15 Pinho-Gomes AC, Gong J, Harris K, *et al*. Dementia clinical trials over the past decade: are women fairly represented BMJ Neurol Open 2022;4(2):e000261. 10.1136/bmjno-2021-000261
16 Shepherd V. An under-represented and underserved population in trials: methodological, structural, and systemic barriers to the inclusion of adults lacking capacity to consent. Trials 2020;21(1):445. 10.1186/s13063-020-04406-y
17 Passmore SR, Kisicki A, Gilmore-Bykovskyi A, *et al*. There's not much we can do…" researcher-level barriers to the inclusion of underrepresented participants in translational research. J Clin Trans Sci 2022;6(1):e4. 10.1017/cts.2021.876
18 Kurt A, Semler L, Meyers M, *et al*. Research professionals' perspectives, barriers, and recommendations regarding minority participation in clinical trials. J Racial Ethn Health Disparities 2017;4:1166–74. 10.1007/s40615-016-0322-0
19 Pick a theory, model, or framework The UW implementation science resource hub: University of Washington, 2024. Available: https://impsciuw.org/implementation-science/research/frameworks
20 Lakusta B. Implementation Science: the best thing you've never heard of as an evaluator. Eval Academy 2024, Available: https://www.evalacademy.com/articles/implementation-science-the-best-thing-youve-never-heard-of-as-an-evaluator
21 Weiner BJ, Lewis CC, Stanick C, *et al*. Psychometric assessment of three newly developed implementation outcome measures. Implement Sci 2017;12(1):108. 10.1186/s13012-017-0635-3
22 Waltz TJ, Powell BJ, Fernández ME, *et al*. Choosing implementation strategies to address contextual barriers: diversity in recommendations and future directions. Implement Sci 2019;14(1):42. 10.1186/s13012-019-0892-4
23 Fernandez ME, Ten Hoor GA, van Lieshout S, *et al*. Implementation mapping: using intervention mapping to develop implementation strategies. Front Public Health 2019;7:158. 10.3389/fpubh.2019.00158
24 Forge T. Trial forge studies within a trial (SWAT) center University of York: health sciences. n.d. Available: https://www.york.ac.uk/healthsciences/research/trials/swats
25 health Ihfb. Efficacy guidelines ICH2024. n.d. Available: https://www.ich.org/page/efficacy-guidelines