ASPE ASSISTANT SECRETARY FOR PLANNING AND EVALUATION
OFFICE OF SCIENCE & DATA POLICY

ISSUE BRIEF
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HHS Actions to Enhance Diversity in Clinical Research

BACKGROUND

Clinical research forms the foundation for understanding and developing treatments for all types of medical conditions, but participants often do not reflect the diversity of the nation – in terms of sex, age, race, ethnicity, disability status, gender identity, socioeconomic status, geography, or other characteristics. When considering diversity in clinical research, HHS uses a broad definition of diversity including, but not limited to, underserved communities reflected in Executive Orders 13985[1] and 14091[2] such as Black, Latino, and Indigenous and Native American persons, Asian American, Native Hawaiian and Pacific Islanders and other persons of color; members of religious minorities; persons of all ages, including children and older adults; persons of all sexes and genders in all stages of reproductive aging, including pregnancy, postpartum and menopausal persons; lesbian, gay, bisexual, transgender, and queer (LGBTQ+) persons; persons with disabilities; persons who live in rural areas; and persons otherwise adversely affected by persistent poverty or inequality. Lack of diversity and representation in clinical research can impact trust in the medical community, results in inequitable access to cutting-edge therapies, and can even hinder scientific discovery. Each of these issues highlights the core goals in increasing diversity in clinical research: earning and building trust, promoting fairness, and generating biomedical knowledge.[3]

Distrust in the medical community is compounded when patients do not see themselves represented in research, and when participating in clinical research represents the only way to access promising new therapies, lack of diversity in clinical research also means inequitable access to care.[4] Even after a therapy becomes available outside of clinical research studies, without adequate representation in research, federal and private insurance many not recognize therapies as necessary or effective, thus denying coverage, and medical providers may be unsure of whether a therapy will work for a certain patient.[5] The lack of generalizability of new research findings can then further compound existing health disparities by undermining trust in clinical research and reducing access to promising therapies when clinical evidence is insufficient to

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[1] The White House (2021). Executive Order on Advancing Racial Equity and Support for Underserved Communities Through the Federal Government. Available at: https://www.whitehouse.gov/briefing-room/presidential-actions/2021/01/20/executive-order-advancing-racial-equity-and-support-for-underserved-communities-through-the-federal-government/, last accessed February 27, 2024.

[2] The White House (2023). Executive Order on Further Advancing Racial Equity and Support for Underserved Communities Through the Federal Government. Available at: https://www.whitehouse.gov/briefing-room/presidential-actions/2023/02/16/executive-order-on-further-advancing-racial-equity-and-support-for-underserved-communities-through-the-federal-government/, last accessed February 27, 2024.

[3] Schwartz AL, Alsan M, Morris AA, Halpern SD. Why Diverse Clinical Trial Participation Matters. N Engl J Med. 2023 Apr 6;388(14):1252-1254. doi: 10.1056/NEJMp2215609. Epub 2023 Apr 1. PMID: 37017480.

[4] *Ibid.*

[5] Corneli A, Hanlen-Rosado E, McKenna K, Araojo R, Corbett D, Vasisht K, Siddiqi B, Johnson T, Clark LT, Calvert SB. Enhancing Diversity and Inclusion in Clinical Trials. Clin Pharmacol Ther. 2023 Mar;113(3):489-499. doi: 10.1002/cpt.2819. Epub 2023 Jan 11. PMID: 36628990.

support use in diverse populations.[6] These are just a few of the ways in which the lack of diversity in clinical research can impact patient trust, healthcare, and health equity. In addition, many clinical research studies fail to fully enroll, potentially resulting in studies being unable to meet the needed sample size to conduct rigorous statistical analyses. Increasing diversity in clinical research, and thereby increasing the pool of potential participants, could assist in ameliorating this widespread issue.[7,8] Successful recruitment can also help contribute to shorter trial lengths and decreased long-term trial costs. Improving diversity in clinical research is therefore not only an ethical imperative, but also will benefit the clinical research enterprise and the healthcare system at large.

Improving diversity of participation in clinical research has been a policy priority for the U.S. Department of Health and Human Services (HHS) for many years. HHS policies to increase diversity in research have included grant requirements, regulations, and guidance, supported also by Congressional action such as provisions in the 21st Century Cures Act. Research offices such as the Office of Research on Women's Health and the National Institute on Minority Health and Health Disparities within the National Institutes of Health (NIH), the National Institute on Disability Research within the Administration for Community Living (ACL), and the Office of Women's Health and the Office of Minority Health and Health Equity (OMHHE) in the Food and Drug Administration (FDA) have supported clinical research on diverse populations for many years. These efforts have significantly increased inclusion of women in clinical trials; an analysis of recent FDA approvals found that women represented an average of 51 percent of participants between 2014 and 2021.[9] However, some research areas such as cardiovascular disease still suffer from a lack of women in clinical trials, and gaps remain for participation of women from racial and ethnic minority groups, and pregnant and lactating women. More broadly, racial and ethnic minority populations, older adults, persons with disabilities, and other populations remain underrepresented in research. New action is needed to ensure continued progress toward goals of increasing diversity in clinical research, including expanding diversity efforts beyond race, ethnicity, sex, or gender.

Factors influencing research participation are complex. Historical abuses by medical professionals, such as the U.S. Public Health Service Study of Untreated Syphilis[10] and the forced sterilization of institutionalized or incarcerated people[11] – as well as past and current personal experiences – may contribute to a distrust in science and medical professionals, emphasizing the importance of building and sustaining relationships with underserved populations. However, some research has shown that underserved populations such as racial and ethnic minorities express equal likelihood to participate in clinical research as other groups but are less

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[6] Clark LT, Watkins L, Piña IL, Elmer M, Akinboboye O, Gorham M, Jamerson B, McCullough C, Pierre C, Polis AB, Puckrein G, Regnante JM. Increasing Diversity in Clinical Trials: Overcoming Critical Barriers. Curr Probl Cardiol. 2019 May;44(5):148-172. doi: 10.1016/j.cpcardiol.2018.11.002. Epub 2018 Nov 9. Erratum in: Curr Probl Cardiol. 2021 Mar;46(3):100647. PMID: 30545650.

[7] National Academies of Sciences, Engineering, and Medicine. 2022. Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups. Washington, DC: The National Academies Press. https://doi.org/10.17226/26479.

[8] Desai M. Recruitment and retention of participants in clinical studies: Critical issues and challenges. Perspect Clin Res. 2020 Apr-Jun;11(2):51-53. doi: 10.4103/picr.PICR_6_20. Epub 2020 May 6. PMID: 32670827; PMCID: PMC7342339.

[9] *Ibid.*

[10] Brandt AM. Racism and research: the case of the Tuskegee Syphilis Study. Hastings Cent Rep. 1978 Dec;8(6):21-9. PMID: 721302.

[11] Minna Stern A (2016). That Time the United States Sterilized 60,000 Of Its Citizens. Available at: https://www.huffpost.com/entry/sterilization-united-states_n_568f35f2e4b0c8beacf68713, last accessed February 28, 2024.

likely to be asked to participate.[12,13] Other underserved populations such as older adults or persons with disabilities may also be excluded from clinical research due to inclusion or exclusion criteria, such as the presence of multiple comorbidities, or a failure to take into account the availability of accommodations that can facilitate participation.[14] Other barriers, such as transportation, missed work, childcare, and direct out-of-pocket costs associated with participation, also hinder participation in research by underserved populations.[15]

In 2022, the National Academies of Science, Engineering, and Medicine (NASEM) released a report entitled "Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups" (hereafter referred to as "NASEM Report").[16] This report explores barriers to clinical research participation, analysis of historical policies, and identifies strategies to include diverse populations in research.

Although the NASEM report was focused more narrowly on increasing participation by women and racial and ethnic minority populations, HHS considers these issues and challenges in the context of a broader definition of diversity – as noted at the beginning of this report, including disability status, gender identity, socioeconomic status, geography, and other factors in addition to age, sex, and race/ethnicity. This report highlights a subset of activities and policies being implemented by the Biden-Harris Administration to increase diversity in clinical research. This is not intended to provide a comprehensive overview of all clinical diversity related activities at HHS. Finally, we discuss gaps and opportunities for continued work on this important issue.

HHS ACTIONS ON CLINICAL RESEARCH DIVERSITY

Identifying and reducing barriers to participation

As discussed briefly above, there is large body of work examining barriers that may reduce participation in clinical research. These may include a wide range of factors including financial burden, distrust of the research community, geographic distribution of study sites, study protocols, researcher and provider bias, and more. HHS continues to work toward better understanding barriers to participate in clinical research, as well as ways to reduce these barriers to participation.

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[12] Unger JM, Hershman DL, Till C, Minasian LM, Osarogiagbon RU, Fleury ME, Vaidya R. "When Offered to Participate": A Systematic Review and Meta-Analysis of Patient Agreement to Participate in Cancer Clinical Trials. J Natl Cancer Inst. 2021 Mar 1;113(3):244-257. doi: 10.1093/jnci/djaa155. PMID: 33022716; PMCID: PMC7936064.

[13] Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S, Gibbons MC, Tilburt J, Baffi C, Tanpitukpongse TP, Wilson RF, Powe NR, Bass EB. Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. Cancer. 2008 Jan 15;112(2):228-42. doi: 10.1002/cncr.23157. PMID: 18008363.

[14] Bodicoat DH, Routen AC, Willis A, Ekezie W, Gillies C, Lawson C, Yates T, Zaccardi F, Davies MJ, Khunti K. Promoting inclusion in clinical trials-a rapid review of the literature and recommendations for action. Trials. 2021 Dec 4;22(1):880. doi: 10.1186/s13063-021-05849-7. PMID: 34863265; PMCID: PMC8643184.

[15] Sheridan R, Martin-Kerry J, Hudson J, Parker A, Bower P, Knapp P. Why do patients take part in research? An overview of systematic reviews of psychosocial barriers and facilitators. Trials. 2020 Mar 12;21(1):259. doi: 10.1186/s13063-020-4197-3. Erratum in: Trials. 2020 Oct 8;21(1):840. PMID: 32164790; PMCID: PMC7069042.

[16] National Academies of Sciences, Engineering, and Medicine. 2022. Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups. Washington, DC: The National Academies Press. https://doi.org/10.17226/26479.

The expansion of clinical trial strategies implemented during the COVID-19 pandemic such as decentralized clinical trials[17] (DCTs), in which some or all trial-related activities occur at locations other than traditional trial sites, has the potential to expand the reach of many clinical trials to underserved populations and reduce some barriers to participation. In order to better understand the impact of these strategies on costs to patients, the Office of the Assistant Secretary for Planning and Evaluation (ASPE) is currently conducting a research study on patient costs for clinical trial participation, which will include a survey of oncology clinical trial participants to capture real-world data on out-of-pocket costs.

HHS is also taking action to support the implementation of DCTs and expand their reach. For example, FDA published draft guidance on DCTs in 2023[18] and also created a framework for the use of digital health technologies, which may be used in DCTs.[19] The Biomedical Advanced Research and Development Authority (BARDA) within the Administration for Strategic Preparedness and Response (ASPR) recently launched the Decentralized Clinical Operations for Healthcare and Research (D-COHRe) program,[20] which seeks to enhance and create sustainable decentralized clinical capabilities. This program will be able to support pandemic preparedness and create capability to conduct clinical trials where patients seek care, as well as assess benefits of utilizing DCTs, including participant diversity.

For all types of trials, FDA is taking action to reduce barriers that may lead to the exclusion of certain populations in clinical research. For example, FDA published a proposed rule related to oversight of human subjects research in September 2022[21] that would remove pregnant people from the categories of persons considered vulnerable to coercion and undue influence. Similarly, it would remove "handicapped, or mentally disabled persons" from the list and instead include "persons with impaired decision-making capacity." These changes, if implemented, will reduce unnecessary barriers to the inclusion of pregnant people and persons with disabilities that do not impair their ability to give informed consent with or without support. FDA also recently published final guidance[22] with recommendations regarding informed consent, including specific considerations to take into account when enrolling children, children who are wards of the state, non-English speaking participants, participants with low literacy and numeracy, participants with physical or sensory disabilities, and adult participants with impaired consent capacity. This guidance will support more inclusive study design.

In addition to its regulatory activities, FDA also has programs that seek to improve access to clinical research for underserved populations. For example, FDA's Project Equity[23] works to improve access to clinical trials of

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[17] Decentralized clinical trials are defined as clinical trials in which some or all of the trial-related activities occur at locations other than traditional clinical trial sites.

[18] FDA (2023). Decentralized Clinical Trials for Drugs, Biological Products, and Devices: Draft Guidance. Docket Number FDA-2022-D-2870. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/decentralized-clinical-trials-drugs-biological-products-and-devices, last accessed December 1, 2023.

[19] FDA (2023). Framework for the Use of Digital Health Technologies in Drug and Biological Product Development. Available at: https://www.fda.gov/media/166396/download, last accessed December 1, 2023.

[20] ASPR (2024). D-COHRe Funding: Decentralized Clinical Operations for Healthcare and Research. Available at: https://drive.hhs.gov/dcohre.html, last accessed April 24, 2024.

[21] FDA (2022). Protection of Human Subjects and Institutional Review Boards Proposed Rule, 87 FR 58733. Available at: https://www.federalregister.gov/documents/2022/09/28/2022-21088/protection-of-human-subjects-and-institutional-review-boards, last accessed December 1, 2023.

[22] FDA (2023). Informed Consent: Final Guidance. Docket Number FDA-2006-D-0031. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent, last accessed December 1, 2023.

[23] FDA (2023). Project Equity. Available at: https://www.fda.gov/about-fda/oncology-center-excellence/project-equity, last accessed December 1, 2023.

oncology medical products for populations that have historically been underrepresented in clinical research such as racial and ethnic minorities, individuals who live in rural areas, sexual and gender minorities, and individuals with economic, linguistic, or cultural barriers to healthcare services.

Finally, the HHS 2023 Equity Action Plan[24] commits HHS to continuing to make progress in diversifying clinical research. Plan actions include ensuring better representation of people impacted by health conditions in studies and clinical trials and engaging diverse populations throughout the entirety of the research process and study design to build trust and improve transparency and accountability.

Planning for diverse clinical research

Diverse clinical research studies do not happen by accident; rather, research studies must be designed with the intention to recruit and retain diverse research participants. Furthermore, research should aspire not just to include diverse populations, but to include diverse populations in a way that is representative of the population affected by the disease or condition. HHS is exploring these issues and implementing new requirements for grantees, contracts, and drug/device applications.

For example, programs administered by ACL, the Advanced Research Projects Agency for Health (ARPA-H), ASPR, and others include diversity in grant/contract requirements. The National Institute on Disability, Independent Living and Rehabilitation Research (NIDILRR) at ACL requires all research grantees to demonstrate that people with disabilities from racial and ethnic minority backgrounds will be included in study samples in sufficient numbers to generate knowledge/products relevant to the diversity of the study population.[25] ASPR has incorporated FDA regulatory guidance on diversity in clinical trials into BARDA's medical countermeasure programs.[26] Equity and diversity are core pillars of ARPA-H's research programs – for example, projects in the new Novel Innovations for Tissue Regeneration in Osteoarthritis (NITRO) program[27] will be required to engage a full-time equity officer to ensure compliance with FDA guidance on diversity plans. Similarly, ARPA-H's Advanced Analysis for Precision cancer Therapy (ADAPT) program's equity requirements ensures that the population participating in the program's clinical trials reflects the diversity of Americans who are impacted by cancer.[28]

HHS agencies also provide resources to help investigators design studies with diverse participation. For example, FDA recently published draft guidance on post-marketing approaches to obtain data on populations underrepresented in trials[29] - particularly important for populations that are often excluded in the study

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[24] HHS (2023). Agency Equity Action Plan. Available at: https://www.hhs.gov/sites/default/files/hhs-equity-action-plan.pdf, last accessed February 28, 2024.

[25] ACL (2021). Research that Reflects the Rich Racial and Ethnic Diversity of People with Disabilities. Available at: https://acl.gov/news-and-events/acl-blog/research-reflects-rich-racial-and-ethnic-diversity-people-disabilities, last accessed December 1, 2023.

[26] ASPR (2023). BARDA Stories: Advancing Inclusion in Clinical Trials. Available at: https://medicalcountermeasures.gov/stories/clinicaltrials/, last accessed December 1, 2023.

[27] ARPA-H (2023). NITRO: Novel Innovations for Tissue Regeneration in Osteoarthritis. Available at: https://arpa-h.gov/engage/programs/nitro/, last accessed December 1, 2023.

[28] ARPA-H (2024). ADAPT: Advanced Analysis for Precision cancer Therapy. Available at: https://arpa-h.gov/research-and-funding/programs/adapt, last accessed April 24, 2024.

[29] FDA (2023). Postmarketing Approaches to Obtain Data on Populations Underrepresented in Clinical Trials for Drugs and Biological Products: Draft Guidance. Docket Number FDA-2022-D-2629. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarketing-approaches-obtain-data-populations-underrepresented-clinical-trials-drugs-and, last accessed December 1, 2023.

protocol for pivotal trials. NIH has also published a myriad of resources for grantees for designing studies that are inclusive of women and racial and ethnic minorities.[30]

The regulations at 45 CFR part 46.111(a)(3) require that selection of subjects is equitable, taking into account the purposes and setting of the research. IRBs are responsible for making these determinations of what it means to be equitable. These issues in the context of representative research – and whether a lack of representation means that the research is uninformative – were discussed at the October 2023 Secretary's Advisory Committee on Human Research Protections (SACHRP) meeting and continue to be explored.

The Food and Drug Omnibus Reform Act of 2022 (FDORA) included several new provisions related to diversity in clinical trials – in particular, section 3601 of FDORA established new requirements for drug and device sponsors to submit diversity action plans to FDA. Specifically, sponsors of any Phase 3 or other pivotal drug study will be required to submit diversity action plans by the time of submitting their study protocol; likewise, sponsors of device trials will be required to submit diversity plans with their Investigational Device Exemption (IDE) application, 510(k), requests for classification, or premarket approval application. FDA will publish draft guidance in response to this requirement, which will replace the April 2022 draft guidance on diversity plans.[31]

Improving data reporting

Transparency and accountability are essential elements of improving the representativeness of clinical research. The 2016 Final Rule "Clinical Trials Registration and Results Information Submission" (42 CFR Part 11) mandates the reporting of sex, age, race, and ethnicity data if those data were collected during the trial. Because trials may collect race and ethnicity data in different ways, ClinicalTrials.gov allows sponsors to submit race/ethnicity data using pre-specified, standardized categories, or as user-defined categories. An analysis of the impact of this policy found that over 90% of studies reported race and ethnicity data after the reporting requirement was implemented, as compared to 42% pre-requirement.[32] A majority of studies reporting race and ethnicity used the Office of Management and Budget (OMB) standard race and ethnicity groups, facilitating secondary data analysis. FDA has taken steps to improve compliance with ClinicalTrials.gov requirements, including sending pre-notices of noncompliance[33], and issuing a 2020 final guidance on civil money penalties related to noncompliance.[34] Currently, there are no reporting requirements for other patient characteristics, such as gender identity or urban versus rural populations.

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[30] NIH (2022). Inclusion of Women and Minorities as Participants in Research Involving Human Subjects. Available at: https://grants.nih.gov/policy/inclusion/women-and-minorities.htm, last accessed December 1, 2023.

[31] FDA (2022). Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials: Draft Guidance. Docket Number FDA-2021-D-0789. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-plans-improve-enrollment-participants-underrepresented-racial-and-ethnic-populations, last accessed December 1, 2023.

[32] Fain KM, Nelson JT, Tse T, Williams RJ. Race and ethnicity reporting for clinical trials in ClinicalTrials.gov and publications. Contemp Clin Trials. 2021 Feb;101:106237. doi: 10.1016/j.cct.2020.106237. Epub 2020 Dec 5. PMID: 33290865; PMCID: PMC8612121.

[33] FDA (2021). FDA Takes Action for Failure to Submit Required Clinical Trial Results Information to ClinicalTrials.Gov. Available at: https://www.fda.gov/news-events/press-announcements/fda-takes-action-failure-submit-required-clinical-trial-results-information-clinicaltrialsgov, last accessed December 1, 2023.

[34] FDA (2020). Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank: Final Guidance. Docker Number FDA-2018-D-0787. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/civil-money-penalties-relating-clinicaltrialsgov-data-bank, last accessed December 1, 2023.

In addition, HHS has several ongoing activities to improve the collection and reporting of demographic characteristics of clinical research participants. For example, through the Sentinel Initiative, FDA is supporting work to evaluate ways to enhance data reporting in Sentinel[35], FDA's national medical product monitoring system, and a narrative review describing methods to overcome limitations in data reporting was recently published.[36] FDA's Project Equity[37] also aims to conduct and present analyses of data generated through clinical trials and other data sources to evaluate outcomes across subgroups, as these analyses are critical to ensuring that all impacted populations have access to safe and effective therapies that will work for them.

Exploring appropriate incentives for sponsors and participants

In order to achieve sustained increases in diversity in clinical research participation, the product approval process and provider payment policies need to align to properly incentivize sponsors. The Centers for Medicare and Medicaid Services (CMS) have two proposed policies to align payment incentives with representative research and encourage research participation. In June 2023, CMS published a draft guidance document[38] that includes a proposed criterion that the Coverage with Evidence Development (CED) study population reflects the demographic and clinical diversity among the Medicare beneficiaries who are the intended population of the intervention. At a minimum, this includes attention to the intended population's racial and ethnic backgrounds, gender, age, disabilities, important comorbidities, and dependent on data availability, relevant social determinants of health. Additionally, the guidance includes proposed criterion about the study protocol, including that the protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly groups that are underrepresented in clinical studies, how the inclusion and exclusion requirements affect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. The protocol would also be required to include plans for analyzing demographic subpopulations and clinically relevant subgroups as identified in existing evidence.

CMS also finalized changes in its 2024 Medicare Physician Fee Schedule Final Rule[39] related to improving payment, including new payment codes, for social determinants of health risk assessment, community health integration services and principal illness navigation services. The new code for principal illness navigation services explicitly includes "providing the patient with information/resources to consider participation in clinical trials or clinical research as applicable."

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[35] Sentinel Initiative (2022). Improving Capture of Race and Ethnicity Data in Sentinel. Available at: https://www.sentinelinitiative.org/methods-data-tools/methods/improving-capture-race-and-ethnicity-data-sentinel, last accessed December 1, 2023.

[36] Ter-Minassian M, DiNucci AJ, Barrie IS, Schoeplein R, Chakravarty A, Hernández-Muñoz JJ. Improving data capture of race and ethnicity for the Food and Drug Administration Sentinel database: a narrative review. Ann Epidemiol. 2023 Oct;86:80-89.e2. doi: 10.1016/j.annepidem.2023.07.006. Epub 2023 Jul 20. PMID: 37479122.

[37] FDA (2023). Project Equity. Available at: https://www.fda.gov/about-fda/oncology-center-excellence/project-equity, last accessed December 1, 2023.

[38] CMS (2023). Coverage with Evidence Development: Proposed Guidance. Available at: https://www.cms.gov/medicare-coverage-database/view/medicare-coverage-document.aspx?mcdid=35, last accessed December 1, 2023.

[39] CMS (2023). Medicare and Medicaid Programs; CY 2024 Payment Policies Under the Physician Fee Schedule and Other Changes to Part B Payment and Coverage Policies; Medicare Shared Savings Program Requirements; Medicare Advantage; Medicare and Medicaid Provider and Supplier Enrollment Policies; and Basic Health Program Final Rule, 88 FR 78818. Available at: https://www.federalregister.gov/documents/2023/11/16/2023-24184/medicare-and-medicaid-programs-cy-2024-payment-policies-under-the-physician-fee-schedule-and-other, last accessed January 8, 2024.

Similarly, research needs to be conducted in a way that does not disincentivize potential participants from joining clinical research. Financial barriers associated with clinical trial participation is a major barrier – as discussed above – and providing compensation to offset costs is an important consideration when evaluating approaches to increase diversity in clinical research participation. FDA's August 2023 guidance on Informed Consent clarifies existing policies on reimbursement and payment to research participants.[40] HHS is actively exploring these issues. For example, the Office for Human Research Protections (OHRP) held an exploratory workshop on payment for research participation in 2022[41] and SACHRP provided recommendations on the ethical considerations of paying research participants in 2019.[42]

Building infrastructure and workforce to support diversity in clinical research

Clinical research has historically been conducted primarily in research-oriented settings such as universities or academic medical centers. This can significantly reduce opportunities for populations who do not live close to these facilities to participate in research. Building community research infrastructure could dramatically increase the accessibility of clinical research to diverse populations across the U.S. In addition to the physical location of research facilities, expanding the reach of clinical research into communities by increasing diversity in the research workforce is also critical to building trust with populations that may not see themselves well-represented in academic or hospital settings.

HHS has many initiatives and programs that seek to expand the reach of clinical research into communities. For example, one of the core principles of ARPA-H's newly announced Advancing Clinical Trial Readiness (ACTR) program is to enable 90% of all eligible Americans to take part in a clinical trial within a half hour of their home.[43] By taking advantage of novel technologies such as artificial intelligence, digital health technologies, and machine learning, and expanding the types of locations that can run clinical trials, this program has the potential to significantly reduce barriers to access clinical research for diverse participants across the country. NIH also has several programs to build capacity in underserved areas. One example is NIH's Institutional Development Award (IDeA) Networks for Clinical and Translational Research, which targets areas with historically low levels of NIH funding and supports a more diverse clinical research workforce. The NIH's Trial Innovation Network (TIN) develops tools and provides clinical trial support that improves trial efficiency including recruitment of diverse populations into trials by increasing decentralized trial methods and providing methods to address diverse participant needs in addition to addressing system and trial barriers to recruitment.[44,45] The TIN developed the on-line program Faster Together, Enhancing the Recruitment of Marginalized Communities Clinical Trials for research teams to identify and develop solutions together to

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[40] FDA (2023). Informed Consent: Final Guidance. Docket Number FDA-2006-D-0031. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent, last accessed December 1, 2023.

[41] OHRP (2022). 2022 OHRP Exploratory Workshop: Beyond Altruism – Exploring Payment for Research Participation. Available at: https://www.hhs.gov/ohrp/education-and-outreach/exploratory-workshop/2022-workshop/index.html, last accessed April 24, 2024.

[42] OHRP (2019). Attachment A – Addressing Ethical Concerns Offers of Payment to Research Participants. Available at: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html, last accessed April 24, 2024.

[43] ARPA-H (2023). Biden-Harris Administration's ARPA-H initiative invests to improve clinical trials and drive better health outcomes. Available at: https://arpa-h.gov/news/actr/, last accessed December 1, 2023.

[44] Harris, P. A., Dunsmore, S. E., Atkinson, J. C., Benjamin, D. K., Bernard, G. R., Dean, J. M., ... & Lloyd, W. (2023). Leveraging the Expertise of the CTSA Program to Increase the Impact and Efficiency of Clinical Trials. JAMA network open, 6(10), e2336470-e2336470.

[45] Hanley, D. F., Bernard, G. R., Wilkins, C. H., Selker, H. P., Dwyer, J. P., Dean, J. M., ... & Harris, P. A. (2023). Decentralized clinical trials in the trial innovation network: Value, strategies, and lessons learned. Journal of Clinical and Translational Science, 7(1), e170.

address the barriers and facilitators their study team or sites may have to minority recruitment.[46] NIH also supports community health centers through its Community Partnerships to Advance Science (ComPASS) program,[47] which seeks to increase diversity and inclusion in research by cultivating community trust and partnerships, building research capacity among the community and relevant partners, and enhancing community organization competitiveness for future funding. NIH's Research Centers in Minority Institutions (RCMI) program[48] develops and strengthens the research infrastructure necessary to conduct state-of-the-art biomedical research and foster the next generation of researchers from underrepresented populations. BARDA's D-COHRe program[49] aims to leverage the shift in decentralized care and enhance clinical study capabilities by partnering with organizations focused on providing decentralized clinical care, directly to where the patients seek it.

Similarly, the Native American Research Centers for Health program at NIH funds federally recognized American Indian/Alaska Native (AI/AN) tribes and organizations for health research, research career enhancement, and research infrastructure enhancement activities. Other programs in the Department seek to enhance membership of underserved and underrepresented populations in funded research teams (see for example: ACL[50], Agency for Healthcare Research and Quality (AHRQ)[51], FDA[52]) or support the career development of individuals in underrepresented or underserved populations (see for example: Centers for Disease Control and Prevention (CDC)[53,54], Health Resources and Services Administration (HRSA)[55], NIH[56,57,58]). These examples represent just a few of the many grants and programs across HHS agencies that seek to support a diverse and inclusive clinical research workforce.

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[46] Coursera (2024). Faster Together, Enhancing the Recruitment of Marginalized Communities in Clinical Trials. Available at: https://www.coursera.org/learn/faster-together-recruitment, last accessed April 24, 2024.

[47] NIH (2024). Community Partnerships to Advance Science Program. Available at: https://commonfund.nih.gov/compass, last accessed April 24, 2024.

[48] NIH (2022). Research Centers in Minority Institutions Program. Available at: https://www.nimhd.nih.gov/programs/extramural/research-centers/rcmi/, last accessed December 1, 2023.

[49] ASPR (2024). D-COHRe Funding: Decentralized Clinical Operations for Healthcare and Research. Available at: https://drive.hhs.gov/dcohre.html, last accessed April 24, 2024.

[50] ACL (2022). National Institute on Disability, Independent Living, and Rehabilitation Research Final Rule, 87 FR 50000. Available at: https://www.federalregister.gov/documents/2022/08/15/2022-17422/national-institute-on-disability-independent-living-and-rehabilitation-research, last accessed December 1, 2023.

[51] AHRQ (2023). Competitive Revision Supplements to Existing AHRQ Grants and Cooperative Agreements to Enhance Workforce Diversity in Health Services Research. Funding Opportunity Announcement Number PA-22-175. Available at: https://grants.nih.gov/grants/guide/pa-files/PA-22-175.html, last accessed December 1, 2023.

[52] FDA (2023). FDA OMHHE Health Equity Innovation Award: Racial & Ethnic Minority Acceleration Consortium for Health Equity (REACH). Funding Opportunity Announcement Number RFA-FD-23-010. Available at: https://grants.nih.gov/grants/guide/rfa-files/RFA-FD-23-010.html, last accessed December 1, 2023.

[53] CDC (2023). Supporting a Diverse Workforce. Available at: https://www.cdc.gov/infrastructure/dwd/strategic-priorities/diverse-workforce.html, last accessed December 1, 2023.

[54] CDC (2021). Programs for Diversity and Health Equity. Available at: https://www.cdc.gov/stem/workforce/inclusive-STEM-workforce.html, last accessed December 1, 2023.

[55] HRSA (2023). Maternal Health Research Collaborative for Minority-Serving Institutions (MH-RC-MSI) Research Centers (RCs). Available at: https://www.hrsa.gov/grants/find-funding/HRSA-23-112, last accessed December 1, 2023.

[56] NIH (2023). K99/R00 MOSAIC Postdoctoral Career Transition Award to Promote Diversity. Available at: https://www.ninds.nih.gov/funding/training-career-development/postdoctoral-fellows/mosaic-postdoctoral-career-transition-award-promote-diversity, last accessed December 1, 2023.

[57] NIH (2023). K99/R00 BRAIN Initiative Advanced Postdoctoral Career Transition Award to Promote Diversity. Available at: https://www.ninds.nih.gov/funding/training-career-development/postdoctoral-fellows/brain-initiative-advanced-postdoctoral-career-transition-award-promote-diversity, last accessed December 1, 2023.

[58] NIH (2023). Research Opportunities for New and "At-Risk" Investigators to Promote Workforce Diversity. Funding Opportunity Announcement Number PAR-22-181. Available at: https://grants.nih.gov/grants/guide/pa-files/PAR-22-181.html, last accessed December 1, 2023.

Building and sustaining relationships with communities

In addition to all the specific policies and issues discussed above, enhancing diverse research participation requires building and sustaining relationships with underserved communities – to build trust, increase awareness, and improve engagement. HHS is continuously identifying ways to engage with non-governmental and other interested groups and disseminate information about clinical research to diverse populations. Programs such as the NIH-funded Community Engagement Alliance (CEAL) Against COVID-19 Disparities[59], designed with the explicit goal of engaging communities in research, have been incredibly successful in engaging diverse populations (discussed in more detail below). HHS agencies have used a variety of approaches to engage and build relationships with communities, including public meetings[60], public workshops[61], and even podcasts.[62] Programs such as the FDA's Office of Minority Health and Health Equity Diversity in Clinical Trials Initiative seek to increase diverse participation in clinical trials through education, outreach, and by providing patient resources in a wide range of languages.[63] Others such as the National Center for Advancing Translational Sciences (NCATS) Trial Innovation Network (TIN) are engaging with diverse partners such as Historically Black Colleges and Universities, minority-serving institutions, and rural organizations with the goal of building trust with communities that do not often engage with clinical research. These relationship-building activities are a core pillar of HHS' broader activities to enhance diversity in research participation.

TRANSLATING POLICY TO ACTION

The COVID-19 pandemic posed a unique challenge to the clinical research enterprise. The need for social distancing to mitigate the spread of SARS-CoV-2, the virus that causes COVID-19, upended traditional clinical research approaches, while the urgent need for new safe and effective diagnostics, therapeutics, and vaccines required research to be done at an unprecedented pace. Furthermore, the COVID-19 pandemic drew attention to long-standing health disparities among racial and ethnic minority groups, when early data showed that Black and Hispanic populations were disproportionately likely to be infected, to be hospitalized, and to die from COVID-19.[64] As HHS worked to respond to the COVID-19 pandemic and support the development of safe and effective diagnostics, vaccines, and other products, diverse participation in research studies remained a

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[59] NIH (2023). NIH Community Engagement Alliance (CEAL). Available at: https://covid19community.nih.gov/, last accessed December 1, 2023.

[60] ACL (2023). Interagency Committee on Disability Research. Available at: https://icdr.acl.gov/reports, last accessed December 1, 2023.

[61] FDA (2023). Discussing Approaches to Enhance Clinical Study Diversity Public Workshop: November 29-30, 2023. Available at: https://www.fda.gov/drugs/news-events-human-drugs/discussing-approaches-enhance-clinical-study-diversity-public-workshop-11292023, last accessed December 1, 2023.

[62] FDA (2023). Guidance Recap Podcast | Podcast for Patients – Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs. Available at: https://www.fda.gov/drugs/guidances-drugs/guidance-recap-podcast-podcast-patients-enhancing-diversity-clinical-trial-populations-eligibility, last accessed December 1, 2023.

[63] FDA (2022). Clinical Trial Diversity. Available at: https://www.fda.gov/consumers/minority-health-and-health-equity/clinical-trial-diversity, last accessed December 1, 2023.

[64] KFF (2022). COVID-19 Cases and Deaths, Vaccinations, and Treatments by Race/Ethnicity as of Fall 2022. Available at: https://www.kff.org/racial-equity-and-health-policy/issue-brief/covid-19-cases-and-deaths-vaccinations-and-treatments-by-race-ethnicity-as-of-fall-2022/ https://www.kff.org/racial-equity-and-health-policy/issue-brief/covid-19-cases-and-deaths-vaccinations-and-treatments-by-race-ethnicity-as-of-fall-2022/, last accessed February 28, 2024.

top priority. Here, we highlight a few examples from the COVID-19 response that exemplify learnings and best practices toward recruitment of diverse populations for clinical research.

The Phase 3 trials for Moderna's vaccine candidate – the COVID-19 Efficacy (COVE) study – provides an example of balancing speed with diverse representation. The COVE trial was sponsored by Moderna with funding and technical support from BARDA and the National Institute of Allergy and Infectious Diseases (NIAID) at NIH. Acknowledging the urgent need to include those individuals at greatest risk of severe COVID-19, the recruitment strategy for this trial was designed intentionally to enroll diverse participants. Moderna highlighted some of its strategies in a retrospective paper.[65] These included developing local enrollment strategies that accounted for the unique communities of each study location; real-time review of enrollment data and resultant revisions to recruitment strategies; using registries such as NIAID's COVID-19 Prevention Network (CoVPN) to identify potential clinical trial participants; adding additional sites in strategic locations; and revising recruitment materials as needed. Moderna attributes its success in achieving a final study population that was representative of the intended treatment population to these flexible strategies.

In the fall of 2020, NIH launched CEAL,[66] a research network designed to work with communities and community-based organizations to identify promising engagement and outreach practices that communicate trustworthy, science-based information to communities experiencing health disparities. CEAL has made a significant impact in the two and half years since its launch.[67] Twenty-one CEAL teams across 21 states, the District of Columbia, and Puerto Rico have reached nearly 91 million people in 101 counties. These CEAL teams are collaborating with almost 1,000 organizations, including health care providers and hospital systems, academic and research organizations, schools, associations, and independent businesses. Most importantly, over half of those partners are community-service, faith-based, grassroots, nonprofit, social service, and civic community-based organizations. Working with these partners, CEAL research teams have held more than 3,000 local events reaching over 600,000 participants. CEAL teams have recruited over 2,600 clinical research participants for research on topics such as COVID-19 vaccine confidence. As the focus on the pandemic shifts, CEAL research teams continue to address issues related to the social determinants of health – many that affected communities well before the pandemic hit.

In 2021, NIH launched the Researching COVID to Enhance Recovery (RECOVER) Initiative, which is a nationwide effort dedicated to understanding why some people develop long-term symptoms following COVID-19, and how to detect, treat, and prevent Long COVID.[68] RECOVER is committed to enrolling a study population that is inclusive and representative of the communities most affected by Long COVID. Study sites partner with local communities to raise awareness about Long COVID and offer opportunities to participate in the RECOVER clinical trials. Researchers developed the trials with extensive feedback from patient representatives and experts in the symptom areas and proposed interventions. The RECOVER Patient and Community Engagement Strategy[69] details a myriad of roles that patients and community members may have in decision-making, from study design through dissemination of results. This active involvement of patients and community members in

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[65] Hill J, Montross D, Ivarsson M. Diversity and inclusion in clinical trials: Evolution throughout the development of an mRNA COVID-19 vaccine. Front Public Health. 2023 Apr 26;11:1113003. doi: 10.3389/fpubh.2023.1113003. PMID: 37181705; PMCID: PMC10169614.

[66] NIH (2023). NIH Community Engagement Alliance (CEAL). Available at: https://nihceal.org/, last accessed December 1, 2023.

[67] NIH (2023). History of CEAL. Available at: https://ceal.nih.gov/history-ceal, last accessed December 1, 2023.

[68] RECOVER (2023). RECOVER: Researching COVID to Enhance Recovery. Available at: https://recovercovid.org/, last accessed December 1, 2023.

[69] RECOVER (2022). RECOVER Patient and Community Engagement Strategy. Available at: https://recovercovid.org/sites/default/files/docs/RECOVEREngagementStrategy.pdf, last accessed December 1, 2023.

the initiative reinforces trust in the research and facilitates sustained engagement in the initiative by diverse community members.

Beyond COVID-19 activities, the *All of Us* Research Program (allofus.nih.gov) at NIH[70] represents an outstanding example of how NIH is expanding the diversity of participants in clinical research. The program aims to enroll one million individuals and longitudinally track their health over decades. Data collected includes biospecimens for whole genome sequencing, electronic health records, and extensive survey data. The program has enrolled more than 786,000 participants to date: 46 percent are diverse by race and ethnicity and 87 percent of participants are historically underrepresented in biomedical research, which includes persons of lower socioeconomic status particularly based on income and education, underserved rural residents, sexual gender minority populations, people with disabilities, and people who encounter challenges accessing healthcare. The program has more than 120 community engagement partners, agreements with multiple large healthcare provider organizations, and multiple mobile van units to support the enrollment of diverse populations all over the United States. Additionally, the program engages diverse researchers to use the data, with more than 133 registered institutions that serve populations that have been historically underrepresented in the sciences, including racial and ethnic minority populations, with over 78 percent of its 10,000+ researchers who are from underrepresented groups in the biomedical workforce including more than 50 percent women and more than 32 percent by race and ethnicity. Participants are also offered multiple return of value pathways, including genomic results that include heredity disease risk for multiple health conditions, as well as a personalized report on how their individual genetics interacts with several prescription medications.

DISCUSSION OF GAPS AND FUTURE ACTION

While progress has been made in increasing diversity of clinical research participation, opportunities for additional action remain. HHS is actively engaged in the foundational work of understanding the problems and gaps that limit diversity in clinical research. This report also highlights a range of proposed, newly implemented, or soon-to-be implemented policy changes – from CMS coverage and payment policies to new diversity planning requirements for FDA drug and device applications. As these policies are put into place, it will be essential to monitor the impact on how investigators design, execute, and report on clinical research, as well as the actual impact on diverse participation. Understanding the impact of these policies may inform the need for additional or different policy actions in the future.

Equitable compensation

Equitable compensation policies have the potential to enhance participation in research by underserved populations, particularly because many may face greater financial hardship associated with research participation. These hardships may be due to inadequate insurance coverage, the need to travel to research sites, the need to take leave from work or obtain alternative childcare, or other factors. Equitable compensation should consider these factors and the ways in which barriers may be experienced differently across underserved populations, but also must be ethical and not coercive. As outlined in sections above, HHS is working to better understand the financial barriers to participate in clinical research and explore ways in

[70] NIH (2024). All of Us Research Program. Available at: https://allofus.nih.gov/, last accessed April 24, 2024.

which equitable compensation may enable greater diversity in research participants. This topic represents an area where additional research and exploration is needed to identify appropriate policy actions.

Defining and incentivizing representativeness

Discussions on this issue have evolved in recent years from simply focusing on inclusion of diverse participants, but rather to ensure that diversity is reflective of the population affected by a condition or potential users of a therapy being tested. This includes sex or gender, age, race, and ethnicity, but also other factors such as disability status that may be relevant for a given condition or treatment population. This concept of representativeness is complicated by the fact that underrepresentation in foundational research about disease prevalence can contribute to a poor understanding of the ways in which specific populations are impacted by a disease or condition. Researchers may not always know what the "representative" population looks like; however, research should still endeavor to be as representative as possible. Additional work is needed to explore what it means for research to be representative, and how this concept may be better incorporated in the research process at the stages of obtaining funding, seeking IRB approval, and evaluating recruitment in real time. A related, but separate, issue is designing clinical research studies that have sufficient inferential power to conduct subgroup analyses. This issue is beyond the scope of the current report, but it is an important consideration in developing clinical research studies that can generate evidence for all impacted populations.

Furthermore, work is needed to examine the need for additional incentives for sponsors to achieve representative enrollment in clinical development programs. Given the related policies being implemented around designing study protocols, including diversity action plans and CED study protocols, it is not clear whether additional incentives in this space would encourage more representative trial designs.

Data reporting

Transparency and accountability around reporting of demographic data associated with clinical research participants is critical for monitoring progress and identifying gaps moving forward. Research has shown significant gains in demographic reporting (specifically race/ethnicity) since the Clinical Trials Registration and Results Information Submission Rule took effect in 2017; further, most submissions used the pre-standardized race/ethnicity categories available on ClinicalTrials.gov, facilitating secondary data analysis.[71] Currently, no published studies have evaluated demographic reporting after early 2020, and it is not clear how FDA's regulatory enforcement activities may impact compliance with data submission requirements. Therefore, additional research is warranted to better understand how data reporting has continued to evolve in recent years and the potential costs or benefits of imposing more standardized data reporting requirements or expanding to include additional required data elements beyond age, sex or gender, and race/ethnicity.

Coordination

Partnerships between HHS agencies on these topics are already robust because of the interrelatedness of many of the policy issues. However, when examining gaps and future actions, HHS may also consider the need for and value of a formalized coordinating structure across the Department and identify areas (such as equitable compensation) where a Department-wide strategy is required.

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[71] Fain KM, Nelson JT, Tse T, Williams RJ. Race and ethnicity reporting for clinical trials in ClinicalTrials.gov and publications. Contemp Clin Trials. 2021 Feb;101:106237. doi: 10.1016/j.cct.2020.106237.

CONCLUSION

This document highlights just a few of the many ways HHS is working to enhance diversity in clinical research and expanding the focus of these efforts beyond age, sex or gender, race, and ethnicity to include all elements of diversity that may impact the experience of a condition or prospects for treatment. As part of HHS' core goals around health equity, HHS will continue to conduct research on barriers and best practices in recruiting and retaining diverse research participants; explore and evaluate the need for new policies at all stages of the clinical research process to enhance diverse research participation.

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