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Permalink

<https://escholarship.org/uc/item/5v22h148>

Journal

Journal of General Internal Medicine, 38(8)

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Publication Date

2023-06-01

DOI

10.1007/s11606-023-08182-8

Peer reviewed

Research Inclusion Across the Lifespan: A Good Start, but There Is More Work to Be Done



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ABSTRACT

While older adults account for a disproportionate amount of healthcare spending, they are often underrepresented in clinical research needed to guide clinical care. The purpose of this perspective is to make readers aware of new data on age at enrollment for participants included in National Institutes of Health (NIH)-funded clinical research. We highlight key findings of relevance to general internal medicine and suggest ways readers could support the inclusion of older adults in clinical research. Data from the NIH Research Inclusion Statistics Report show that there were 881,385 participants enrolled in all NIH-funded clinical research in 2021, of whom 170,110 (19%) were 65 years and older. However, on average, studies included a far lower percentage of older adults. Additionally, there were many conditions for which overall enrollment rates for older adults were lower than would be expected. For example, while 10% of participants in studies related to diabetes were ≥ 65 years old, older individuals represent 43% of all prevalent diabetes in the USA. Researchers should work with clinicians to advocate for older adults and ensure their participation in clinical research. Best practices and resources for overcoming common barriers to the inclusion of older adults in research could also be disseminated.

J Gen Intern Med 38(8):1966–9
DOI: 10.1007/s11606-023-08182-8

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Despite accounting for only 16% of the US population, adults 65 years and older account for approximately 33% of all spending on physician and clinical services, 38% of inpatient hospital admissions, and 84% of all hospital discharges to skilled nursing facilities.^{1–4} High healthcare use among older adults is driven, in part, by the higher prevalence of chronic diseases at an older age, with older adults often accumulating multiple chronic conditions.^{5,6}

Given what we know about the epidemiology of chronic disease and the need for clinical research to guide the care of patients, one might expect that older adults would make up a sizable proportion of most study populations. However, new data released by the National Institutes of Health (NIH) show that older adults are commonly underrepresented in clinical research.⁷ The purpose of this *JGIM* Perspective is to make readers aware of new data on age at enrollment from the NIH Research Inclusion Statistics Report, emphasize key findings of relevance to general internal medicine, and highlight available resources to facilitate the inclusion of older adults.

The inequitable distribution of older adults in clinical research is not a new problem. Prior reports have shown that research studies often enroll older adults at a lower proportion than the proportion of older adults in the disease population.^{8–10} This underrepresentation occurs when research studies set upper age cutoffs; use exclusion criteria that are more likely to affect older adults, such as comorbid conditions; or fail to accommodate age-related barriers to participation, such as anticipating the need for longer study visits for older adults with mobility or sensory limitations.^{11–13} What is new, however, is the NIH-wide scale of data collection and reporting on age at enrollment and the availability of resources to help achieve the goals of the NIH Inclusion Across the Lifespan Policy.

The NIH issued the Inclusion Across the Lifespan policy in 2017, requiring that all applications submitted after January 2019 include “individuals of all ages, including children and older adults...unless there are scientific or ethical reasons not to include them.”^{14,15} All submissions must include a plan for enrolling individuals across the lifespan. Scientific review groups are tasked with rating the age-related inclusion and exclusions as either acceptable or unacceptable which, in turn, impacts funding decisions. The policy also stipulates that grant recipients must upload a de-identified participant-level dataset including age at enrollment with the annual progress report.

For the first time, results from the NIH-wide collection of participant-level age-at-enrollment data were published online as part of the 2021 NIH Research Inclusion Statistics Report. Columns in the table include the Research, Condition, and Disease Categorization (RCDC), a computerized

Received August 5, 2022
Accepted March 20, 2023
Published online March 31, 2023

reporting process used by NIH to classify funded research, as well as the funding NIH Institute or Center. Data on age are presented in columns that include the total number of participants and the number and percentage of participants <18 years old (child), 18 to 64 years old (adult), 65 years and older (older adult), or unknown/not reported. In addition to the overall percentage, a column is provided for the median percentage defined as the percent of individuals in a typical project within an RCDC category, separately for each age group.

To summarize some key findings of age at enrollment from this report, we identified the number and percentage of adults 65 years and older and the median percentage for all clinical research, all clinical trials, and a select number of clinical conditions of high importance to general internal medicine (RCDC categories for cardiovascular disease (CVD), cancer, hypertension, diabetes, and depression). We filtered the Population for “All studies” to capture studies that included all age groups as well as studies that restricted their population to a specific age group (i.e., studies of only older adults). We also filtered Institute/Center for “Total, NIH” to provide enrollment data across all funding groups within NIH. Applying these filters showed that there were 881,385 participants enrolled in NIH-funded clinical research in 2021, of whom 170,110 (19%) were 65 years and older. Of the 254,836 participants included in the RCDC category “Clinical Trials and Supportive Activities,” 18% were 65 years and older (Figure).

These data provide the necessary starting point for understanding inclusion across the lifespan for all NIH-funded clinical research studies and for monitoring age at enrollment going forward. Additionally, there are findings that deserve immediate attention. First, for many RCDC groups, the median percentage is much lower than the overall percentage, with many being less than 1%. For example, older

adults accounted for 54% ($n=18,670$) of participants in CVD clinical research studies, but half of all CVD studies enrolled 4% or fewer older adults. This suggests that the overall percentage was driven by a few studies that enrolled a large percentage of older adults. As studies within an RCDC group address different clinical research problems and test different research hypotheses, low enrollment in most studies means that many clinical questions remain unanswered for older adults.

Second, there are many conditions and research focus areas for which overall enrollment rates for older adults were lower than would be expected. As these conditions often have different clinical presentations, management strategies, and treatment goals at an older age, failing to include representative study populations undermines our ability to optimize and innovate care for the growing number of older adults. For example, while 10% of participants in studies related to diabetes were ≥ 65 years old (Fig. 1), older individuals represent 43% of all prevalent diabetes in the USA.¹⁶ Similarly, 56% of incident cancer in the US is among those aged ≥ 65 years, but only 26% of participants in cancer-related studies were ≥ 65 years.¹⁷ On average, those ≥ 65 years old make up 23% of rural populations among all US states and account for more than 50% of the rural population in Vermont, Maine, Mississippi, West Virginia, and Arkansas.¹⁸ Yet, older adults only made up 11% of studies on rural health and 18% of studies on telehealth. Given the long time horizon from participation in clinical research to impact on clinical care and population health, low enrollment of older adults in 2021, will have lasting effects over the next several decades.

Findings from the 2021 NIH Research Inclusion Statistics Report highlight the urgent need to address the low study-level inclusion for conditions and research areas of high priority for older adults. In addition to NIH policies, there are several ways general internal medicine researchers and

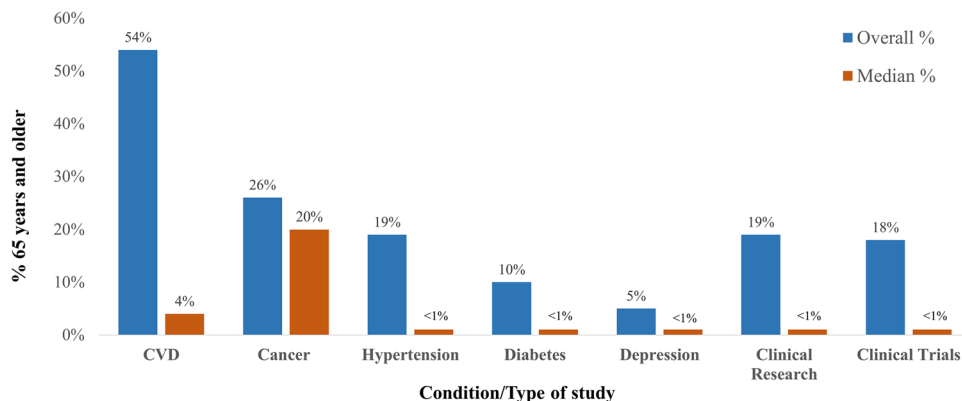


Figure 1 Percentage of adults 65 years and older by Research, Condition, and Disease Categorization (RCDC) enrolled in National Institutes of Health (NIH) funded clinical research studies in 2021. Data were obtained from Table #1867-21-1 (Broad Age Groups) and filtered on “All studies” for Population and “Total, NIH” for Institute/Center. Overall percentages were presented in the table, calculated as the number of adults 65 years and older divided by the total number of participants in that RCDC group. The median percentage is described by the NIH as the percentage of individuals included in a typical project associated with the RCDC group.

Table 1 Common Barriers to Inclusion of Older Adults in Research and Examples of New Resources to Address These Barriers

Barrier	Resource	Description
Older adults have limited knowledge and experience with clinical trials	Recruiting Older Adults into Research (ROAR) project from the National Institute on Aging (NIA) ²⁶	Toolkit developed for older adults includes flyers, an easy-to-read booklet, and tip sheets describing what to expect when participating in research. The toolkit is available in English, Spanish, and Chinese.
Investigators are not aware of barriers to the inclusion of older adults	Inclusion of Older Adults in Clinical and Translational Research Toolkit from the Clinical and Translational Science Awards (CTSA) national Inclusion of Special Populations Working Group ²⁷	Toolkit developed for research audiences includes nine modules that raise awareness about benefits and challenges of recruiting older adults for research. Each module includes a downloadable slide set and detailed notes.
Research teams do not address common challenges to participation	The 5Ts Framework developed with support from the CTSA and NIA Older Americans Independence Centers ²⁸	Framework provides practical recommendations organized by “T”: target population, team, time, tips to accommodate, and tools. Recommendations and resources are available through the 5Ts website.

clinicians could support the inclusion of older adults in clinical research. As researchers and institutional leaders, those in general medicine have the opportunity to impose higher standards of inclusion of older adults in their own work and in their roles on grant study sections, institutional review boards, and journal editorial boards. General medicine clinicians may have a less direct influence on the representation of older adults in research. However, as older adults often look to their healthcare providers for advice on participating in research,^{19,20} general medical practitioners are well positioned to advocate on behalf of their older patients. There are also opportunities to help identify high-priority clinical questions and ensure that findings are more likely to be adopted in routine practice by contributing to “partnered research” efforts.^{21–23}

Immediate steps could also be taken to disseminate best practices for overcoming common barriers to the inclusion of older adults in research.^{24,25} Barriers to participation can be considered from multiple perspectives including that of older adults who face decisions about participating, research investigators who design and obtain funding for studies, and research staff who are tasked with enrolling participants. For example, barriers can arise when older adults have limited experience and knowledge about research, when research investigators do not recognize the benefits and challenges of participation, or when research teams have not adopted best practice strategies for recruiting older adults. Luckily, there are a growing number of nationally available resources for addressing barriers to the inclusion of older adults in research (Table 1).^{26–28} Our team has developed the 5Ts Framework to support the inclusion of diverse populations of older adults in research by communicating practical strategies to research teams who lack expertise in aging.¹¹ Each “T” is a useful reminder of the many strategies that have already been developed and used to recruit thousands of older adults in

research studies. The 5Ts help investigators identify the appropriate *target population*, build *teams* that include aging expertise, anticipate additional *time* to engage older adults, follow practical *tips* for accommodating age-related limitations to study participation and use *tools* that measure outcomes that are important to older adults. However, the 5Ts and other approaches to including older adults in research have not yet gained traction outside of geriatrics research.

Achieving health equity will require, in part, that clinical research funding is allocated to studies that enroll populations in proportion to the burden of disease. Towards this goal, the Inclusion Across the Lifespan has made major progress in planning, implementation, and reporting and the NIH should be commended for this effort. Research teams, participants, their families, and caregivers should also be acknowledged for the tremendous work that resulted in the enrollment of tens of thousands of older adults—during a global pandemic—into NIH-funded clinical research in a single year. However, these enrollment data also show that for many research areas inclusion falls far short of building the equitable evidence base we need to ensure older adults are not left out of innovations in clinical care.

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Funding Support was provided through the National Institute on Aging (RO1AG062502, P30AG028716). This work was also supported by the Durham Center of Innovation to Accelerate Discovery and Practice Transformation (ADAPT), (CIN 13-410) at the Durham VA Health Care System. The views expressed here/in this manuscript are those of the authors and do not necessarily represent the views of the National Institutes of Health; or the Department of Health and Human Services.

Data Availability Data summarized here is available from the NIH Inclusion Statistics Report: <https://report.nih.gov/RISR>.

Declarations

Conflict of Interest The authors declare that they do not have a conflict of interest.

REFERENCES

- Administration for Community Living. 2020 Profile of Older Americans. U.S. Department of Health and Human Services. Washington, D.C. <https://acl.gov/aging-and-disability-in-america/data-and-research/profile-older-americans>. Accessed August 1, 2022.
- U.S. Centers for Medicare and Medicaid Services. National Health Expenditure Data. U.S. Department of Health and Human Services. Baltimore, MD 2014. www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Age-and-Gender. Accessed August 1, 2022.
- Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUPnet). Rockville, MD. 2019. <https://datatools.ahrq.gov/hcupnet>. Accessed August 1, 2022.
- Burke RE, Juarez-Colunga E, Levy C, Prochazka AV, Coleman EA, Ginde AA. Patient and Hospitalization Characteristics Associated With Increased Postacute Care Facility Discharges From US Hospitals. *Med Care*. 2015;53(6):492-500.
- Bowling CB, Sloane R, Pieper C, et al. Association of Sustained Blood Pressure Control with Lower Risk for High-Cost Multimorbidities Among Medicare Beneficiaries in ALLHAT. *J Gen Intern Med*. 2021;36(8):2221-2229.
- Goodman RA, Ling SM, Briss PA, Parrish RG, Salive ME, Finke BS. Multimorbidity Patterns in the United States: Implications for Research and Clinical Practice. *J Gerontol A Biol Sci Med Sci*. 2016;71(2):215-220.
- National Institutes of Health. NIH RCDC Inclusion Statistics Report. U.S. Department of Health and Human Services. 2021. <https://report.nih.gov/RISR/#/>. Accessed 2 May 2022.
- Bourgeois FT, Orenstein L, Ballakur S, Mandl KD, Ioannidis JPA. Exclusion of Elderly People from Randomized Clinical Trials of Drugs for Ischemic Heart Disease. *J Am Geriatr Soc*. 2017;65(11):2354-2361.
- Lockett J, Sauma S, Radziszewska B, Bernard MA. Adequacy of Inclusion of Older Adults in NIH-Funded Phase III Clinical Trials. *J Am Geriatr Soc*. 2019;67(2):218-222.
- Zulman DM, Sussman JB, Chen X, Cigolle CT, Blaum CS, Hayward RA. Examining the evidence: a systematic review of the inclusion and analysis of older adults in randomized controlled trials. *J Gen Intern Med*. 2011;26(7):783-790.
- Bowling CB, Whitson HE, Johnson TM. 2nd. The 5Ts: Preliminary Development of a Framework to Support Inclusion of Older Adults in Research. *J Am Geriatr Soc*. 2019;67(2):342-346.
- Mody L, Miller DK, McGloin JM, et al. Recruitment and retention of older adults in aging research. *J Am Geriatr Soc*. 2008;56(12):2340-2348.
- Vaughan CP, Dale W, Allore HG, et al. AGS Report on Engagement Related to the NIH Inclusion Across the Lifespan Policy. *J Am Geriatr Soc*. 2019;67(2):211-217.
- Bernard MA, Clayton JA, Lauer MS. Inclusion Across the Lifespan: NIH Policy for Clinical Research. *JAMA*. 2018;320(15):1535-1536.
- National Institutes of Health. Revision: NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects. Bethesda, MD: National Institutes of Health; 2017. Notice NOT-OD-18-116. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-116.html>. Accessed May 2, 2022.
- Centers for Disease Control and Prevention. Prevalence of Both Diagnosed and Undiagnosed Diabetes. December 29, 2021. <https://www.cdc.gov/diabetes/data/statistics-report/diagnosed-undiagnosed-diabetes.html>. Accessed May 4, 2022.
- National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Cancer of Any Site. <https://seer.cancer.gov/statfacts/html/all.html>. Accessed May 4, 2022.
- United States Census Bureau. The Older Population in Rural America: 2012-2016. Report number ACS-41. September 23, 2019. <https://www.census.gov/library/publications/2019/acs/acs-41.html>. Accessed June 3, 2022.
- Chen DT, Miller FG, Rosenstein DL. Clinical research and the physician-patient relationship. *Ann Intern Med*. 2003;138(8):669-672.
- Comis RL, Miller JD, Colaizzi DD, Kimmel LG. Physician-related factors involved in patient decisions to enroll onto cancer clinical trials. *J Oncol Pract*. 2009;5(2):50-56.
- Bosworth HB. The changing face of general internal medicine and lessons learned from geriatric medicine. *J Gen Intern Med*. 2014;29(6):824-826.
- Goldstein KM, Gierisch JM, Tucker M, Williams JW, Jr., Dolor RJ, Henderson W. Options for Meaningful Engagement in Clinical Research for Busy Frontline Clinicians. *J Gen Intern Med*. 2021;36(7):2100-2104.
- Zickmund SL, Frosch DL, Carman KL. Patient and Veteran Engagement in Health Research: the Emergence of a Field of Study. *J Gen Intern Med*. 2022;37(Suppl 1):3-5.
- National Institute of Health. Inclusion Across the Lifespan II Workshop Report. U.S. Department of Health and Human Services. <https://grants.nih.gov/sites/default/files/IAL-II-Workshop-Report.pdf>. Accessed May 2, 2022.
- Petrovsky DV, Ethoan LN, Loizos M, et al. Key recommendations from the 2021 "inclusion of older adults in clinical research" workshop. *J Clin Transl Sci*. 2022;6(1):e55.
- National Institute on Aging. Recruiting Older Adults into Research (ROAR) Toolkit. U.S. Department of Health and Human Services. Available at: <https://www.nia.nih.gov/health/recruiting-older-adults-research-roar-toolkit>
- NCATS CTSA Inclusion of Older Adults as a Model for Special Populations Working Group. Presentation Materials Library: Inclusion of Older Adults in Clinical and Translational Research. Available at: <https://clic-ctsa.org/education/kits/presentation-materials-library-inclusion-older-adults-clinical-and-translational>
- Bowling CB, Thomas J. 5Ts Framework. Available at: <https://5tsframework.duke.edu/>

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