Received: 27 December 2023 | Accepted: 2 January 2024

DOI: 10.1111/jgs.18829

COMMENTARY

Journal of the American Geriatrics Society

Evaluation of medical therapies in the nursing home population: Gaps, challenges, and next steps

Kathleen T. Unroe MD, MHA, MS[1,2,3] | **Debra Saliba MD, MPH, AGSF**[4,5,6,7] | **Susan E. Hickman PhD**[2,3,8] | **Sheryl Zimmerman PhD**[9,10,11] | **Cari Levy MD, PhD**[12,13] | **Jerry Gurwitz MD**[14]

[1]Division of General Internal Medicine and Geriatrics, Indiana University School of Medicine, Indianapolis, Indiana, USA

[2]Indiana University Center for Aging Research, Regenstrief Institute Inc., Indianapolis, Indiana, USA

[3]Research in Palliative and End-of-Life Communication and Training (RESPECT) Center, Indiana University School of Medicine, Indianapolis, Indiana, USA

[4]US Department of Veterans Affairs Greater Los Angeles Healthcare System (VAGLAS) Health Services Research and Development Service (HSR&D) Center of Innovation, Los Angeles, California, USA

[5]David Geffen School of Medicine, University of California, Los Angeles, California, USA

[6]Anna and Harry Borun Center for Gerontological Research, University of California Division of Geriatrics, Los Angeles, California, USA

[7]RAND Corporation, Santa Monica, California, USA

[8]Indiana University School of Nursing, Indianapolis, Indiana, USA

[9]School of Social Work, University of North Carolina, Chapel Hill, North Carolina, USA

[10]Cecil G. Sheps Center for Health Services Research, University of North Carolina, Chapel Hill, North Carolina, USA

[11]Center for Excellence in Assisted Living (CEAL), School of Social Work, University of North Carolina, Chapel Hill, North Carolina, USA

[12]Division of Geriatric Medicine, University of Colorado School of Medicine Anschutz Campus, Aurora, Colorado, USA

[13]Denver Veterans Affairs Medical Center, Aurora, Colorado, USA

[14]Division of Geriatric Medicine, UMass Chan Medical School, Worcester, Massachusetts, USA

Correspondence
Kathleen T. Unroe, Division of General Internal Medicine and Geriatrics, Indiana University School of Medicine, 1101 West 10 Street, Indianapolis, Indiana, USA.
Email: kunroe@iu.edu

In the United States, 15,600 nursing homes (NHs) provide care to nearly 1.4 million people each year, with over 20% of Medicare beneficiaries discharged to a NH after hospitalization for post-acute care.[1] Actively managed, prevalent conditions among NH residents include hypertension (77%), depression (49%), and diabetes (35%), and a majority have Alzheimer's disease or cognitive impairment.[1] Multimorbidity, functional impairment, and polypharmacy are ubiquitous among the NH population.

Despite NHs' critical role in the nation's post-acute and long-term care infrastructure, there are persistent challenges to optimizing resident outcomes. Recently, increasingly sophisticated analytic techniques have been used to focus on the multiple quality and operational concerns related to inadequately trained and insufficient staff, high staff turnover and instability,[2–4] lack of accountability and transparency,[5] and racial disparities in access to care, quality of care, and quality of life.[6] Less evaluation and research activity have focused on building and testing interventions and therapies within this setting. Very few

This paper is part of a special collection edited by Janice Schwartz, titled *A changing landscape for evaluation of new therapies for older adults and diverse populations: National and international perspectives.* Once complete, you can explore the rest of the collection here: https://agsjournals.onlinelibrary.wiley.com/hub/journal/15325415/special-collections.

high quality clinical trials have been conducted in the NH setting,[7,8] and, unfortunately, evidence often does not exist to guide and inform optimal clinical decision-making and care for this unique and vulnerable population.

THE NEED FOR CLINICAL TRIALS IN NHs

The COVID-19 pandemic highlighted the pressing need for trials in NHs.[9] While estimates vary, conservatively 166,773 NH residents died from COVID-19 between early 2020 and December 2022.[10] However, only a small fraction of residents participated in related clinical trials.[11] This omission was consequential in that despite evidence that monoclonal antibody treatment reduced hospitalizations and mortality from COVID-19 infection, there were delays delivering these treatments equitably and consistently to NH residents because they were not considered in the development of these therapies.[12] Inclusion of NH residents in COVID-19 therapeutics trials might have identified specific issues relating to dosing, administration, and monitoring, spurred creation of training materials specifically for NH staff, and promoted the development of consistent policies to identify appropriate candidates and deliver treatments promptly, safely, and optimally.

GAPS THAT CAN BE FILLED WITH CLINICAL TRIALS IN NHs

There are numerous areas ripe for clinical trials in NHs relevant to medical therapies, including the study of vaccines, drugs and biologics, and devices. In addition, prevention trials can address communicable diseases and common harmful conditions including pressure injuries, infections, and falls; intervention trials can address neuropsychiatric symptoms of dementia,[13] depression, loneliness, and anxiety; and health services intervention trials can address rehabilitation services, deprescribing initiatives,[14] approaches to routine care,[15] end-of-life care quality, risks of hospitalization,[16] and other innovative models of care delivery in NHs. Concerns and challenges regarding care and outcomes in NHs necessitate rigorous clinical trials designed for the NH setting to build and advance the science of caring for residents of NHs and improve the quality of care provided in these settings.

CHALLENGES CONDUCTING CLINICAL TRIALS IN NHs

Unfortunately, NHs are considered by many to be challenging settings in which to conduct research (see Table 1).[17–20] Conducting trials in NHs requires identification and navigation of operational barriers, which may impact the initiation of research efforts and the adherence to research protocols.[21] NHs experience high turnover[22] in both staff and leadership positions,[23] which makes it challenging to cultivate initial engagement and maintain engagement over time.[24] Limited occupancy and workforce shortages lead to risk of closures and changes in ownership, which can adversely affect the performance of multi-site trials.[25] Additional challenges to recruitment[26,27] include varying policies regarding research, fear of liability, and concerns about increased workload for NH leadership and staff, which may not be adequately funded.[24] Medical providers may restrict

TABLE 1 Challenges to conducting research on medical therapies in nursing homes.

Operational barriers	High turnover of staff and administrators
Business and financial challenges	Risk of ownership changes and closure
Regulations	Complex federal and state regulatory requirements (sometimes conflicting)
Recruitment challenges	Inconsistent policies regarding human research; liability concerns; lack of Institutional Review Board infrastructure
Inadequate staffing	Concerns about time demands of research on staff
Medical provider "gatekeeping"	May limit access to study subjects due to apprehension about increased responsibilities including need to communicate with residents and families, and lack of compensation for efforts
Health literacy	Informed consent challenges and impact
Cognitively impaired residents	Need for engagement with surrogate decision-makers
Frailty, functional impairment, and multimorbidity	Challenges in performing testing and obtaining samples
Research design and methodologic challenges	High attrition due to illness, hospitalization, and death
Outcome measures	Surrogate measures versus "what matters most"
Industry partners	Lack of understanding of nursing home setting and the lack of research experience and infrastructure to conduct research in this setting

research access to their residents due to concerns about restrictive clinical protocols, billing, or compensation.[28]

In addition to challenges engaging NHs, recruitment of vulnerable NH residents requires attention to special considerations and regulatory protections.[29] Materials need to be developed with a focus on health literacy and attention to the needs of minoritized populations through both representation and cultural tailoring to ensure equity. A key recruitment barrier is the reality that NH residents are constrained by their illnesses, treatments, and stresses of care transitions. As in other settings, some patients and families may object to a trial design that includes the possibility of being randomized to a control or placebo arm rather than active treatment.[25] Further, it can be difficult to determine when a resident has sufficient cognitive capacity to consent, thereby requiring a longer consent process as well as monitoring over time in the event of loss of capacity.[25,30] When residents do lack capacity, there are often additional challenges in identifying and reaching the legally authorized representative to obtain consent.[31] Finally, staff recruitment is often difficult due to concerns about time demands, the impact of research on their workload, and lack of compensation for their efforts.[25]

NEXT STEPS IN CONDUCTING CLINICAL TRIALS IN NHs

To overcome these challenges, intervention and trial design must take the setting and needs of residents and staff into account and consider attrition due to turnover, dropout, hospitalization, illness, and mortality when designing a clinical trial.[25,28] Attention must also be paid to identifying suitable outcome measures[25,30] that align with "what matters most" to NH residents and reflect resident diversity.[32] The lack of NH setting-relevant research experience perpetuates conditions that inhibit research and create barriers to both small and multi-site trials. Those researchers who have successfully conducted trials in the NH setting and have strong research connections across industry partners (e.g., for profit, not-for-profit, government owned) NH leaders operators and interprofessional care providers are limited to a few centers.[17,33]

Existing infrastructure and collaborative initiatives, however, can be leveraged to address barriers to NH research and build the science of NH care. The Long-Term Care Data Cooperative (LTCDC), funded by the National Institute on Aging (NIA), is directly addressing barriers to accessing and utilizing medical record data, increasing access to linked secondary data sources, and maintaining a community of NH owners, operators, and administrators who can be more fully engaged in research, including trials of medical therapies. Specifically, the LTCDC is merging and harmonizing different electronic medical record vendor databases to increase utility of combined data. It complements major NIA-funded initiatives such as the Imbedded Pragmatic Alzheimer's disease and AD-Related Dementias Clinical Trials (IMPACT) Collaboratory's focus on pragmatic trials addressing AD/ADRD care across healthcare settings and the AGING Initiative's focus on interdisciplinary research for older adults with multiple chronic conditions.[34] Together, these NIA initiatives provide foundational work addressing the identification and capture of important clinical outcomes, laying the groundwork for a NH clinical trials network.[17,35]

In addition, the NIA is making a commitment to building the science of NH care through its 2023 call for applications for a NH explanatory clinical trials network.[36] The hope is that this new network, once funded and established, will build a collaborative community of NH leaders, staff, residents and care partners, and researchers who will together identify research priorities and develop action plans to address these priorities. Future network activities would also include the evaluation of medical therapies in NHs. Such a network holds the potential to foster the development of consensus-based best practices for NH-based clinical trials, create toolkits and research guidance, and foster collaborations.

A FRAMEWORK FOR MAKING A NH CLINICAL TRIALS NETWORK A REALITY

We propose a framework based on the literature and our experiences conducting NH research that outlines the interrelated key elements that are essential for NH clinical trials to be successful (Figure 1). As depicted in the figure, designing the intervention includes consideration of NH-specific issues in the planning of the research protocol and the therapies, instruments, or care processes to be tested. Specifically, researchers should anticipate the study's potential burden on NH staff and residents, which often goes unappreciated, and should proactively identify potential regulatory issues.[29] Ensuring diversity, equity, and inclusion in a trial's design, conduct, analyses, and dissemination, is critical. There are significant rates of racial disparities in access to care, quality of care, and quality of life among minoritized residents in comparison to white residents, and it is important to ensure the generalizability of study findings and understand differences in the effects of a treatment between important subgroups of residents. If evidence generated in clinical trials is to reduce disparities, health equity must be baked into all aspects of a trial. Recruiting both NHs and individual

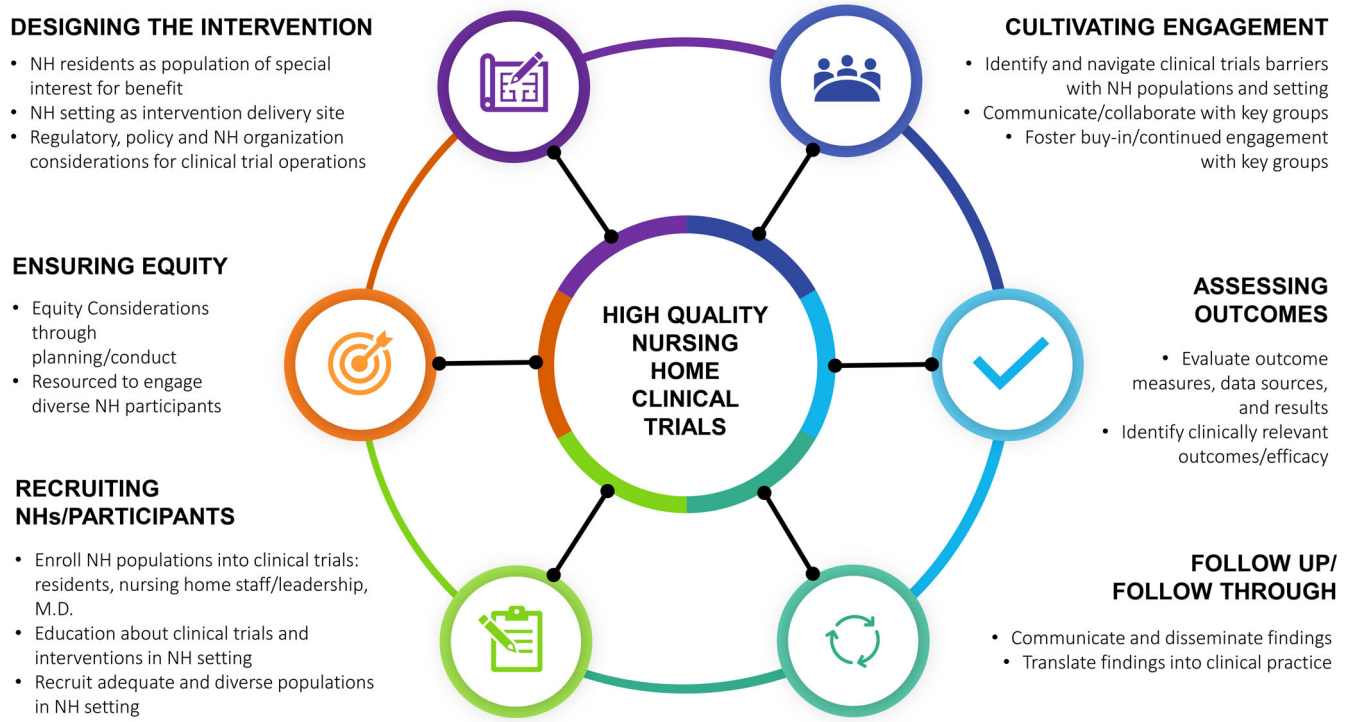

FIGURE 1 Key elements for successful nursing home (NH) clinical trials.

participants can be complex; NH leaders must agree to participate or allow access to potential staff and resident participants. Thus, the value of a given intervention must be communicated to residents, clinical providers, staff, and leadership. Cultivating and maintaining engagement throughout the project recognize that initial recruitment is only the start; researchers must have plans to monitor and respond to internal or external threats to ongoing involvement of NH partners and research participants. Assessing outcomes, necessary in any trial, includes identifying appropriate metrics and reliable data sources that can be harmonized across sites and trials. Finally, following up and following through emphasize the importance of communicating results (i.e., dissemination) and developing sustainable paths to rapid and efficient implementation of successful interventions, critical for moving interventions toward embedment in clinical processes and workflows in the "real world" without the usual multi-year delays following the completion of a trial and publication of study results.

In addition to leveraging existing infrastructure and collaborations, our framework embraces a comprehensive perspective of NH research that has not been utilized previously in this setting. It has the potential to guide the establishment and efforts of a NH clinical trials network designed to spur high quality evidence generation to improve residents' lives and the quality of their care.

NHs will continue to play a critical role in our healthcare system, providing care for populations with functional impairment, cognitive impairment, and significant medical complexity. A dedicated, coordinated approach to support research focused on the evaluation of medical therapies and care innovations is needed to answer pressing clinical questions and target efforts and resources where they are most needed.

"Nursing homes will continue to play a critical role in our healthcare system, providing care for populations with functional impairment, cognitive impairment, and significant medical complexity. A dedicated, coordinated approach to support research focused on the evaluation of

medical therapies and care innovations is needed to answer pressing clinical questions and target efforts and resources where they are most needed."

AUTHOR CONTRIBUTIONS

All authors participated in the writing of the manuscript.

CONFLICT OF INTEREST STATEMENT

Dr. Unroe is the founder and CEO of Probari, Inc., a healthcare start-up supporting nursing home care. The other authors have no conflicts.

SPONSOR'S ROLE

None.

ORCID

Susan E. Hickman https://orcid.org/0000-0003-1514-8430

Cari Levy https://orcid.org/0000-0002-7485-280X

TWITTER

Kathleen T. Unroe *kathleenunroe*

REFERENCES

1. Sengupta M, Penn Lendon J, Caffrey C, Melekin A, Singh P. Post-acute and long-term care providers and services users in the United States, 2017–2018. *Vital Health Stat 3*. 2022;2022(47):1-93.
2. Loomer L, Grabowski DC, Yu H, Gandhi A. Association between nursing home staff turnover and infection control citations. *Health Serv Res*. 2022;57(2):322-332. doi:10.1111/1475-6773.13877
3. Sinha S, Mukamel DB, Saliba D, Ladd H, Konetzka RT. New dimensions of staffing patterns in nursing homes and nursing home quality: comparing staffing instability to staffing turnover. *J Am Med Dir Assoc*. 2023;24(8):1099-1105.e7. doi:10.1016/j.jamda.2023.04.009
4. Mukamel DB, Saliba D, Ladd H, Konetzka RT. Association of Staffing Instability with Quality of nursing home care. *JAMA Netw Open*. 2023;6(1):e2250389. doi:10.1001/jamanetworkopen.2022.50389
5. Stevenson D, Peterson H, Skinner R, et al. Trends in ownership structures of U.S. nursing homes and the relationship with facility traits and quality of care (research brief). Washington DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. November 13, 2023.
6. Shippee TP, Davila H, Ng W, et al. Evidence to inform policy and practice: mechanisms to address racial/ethnic disparities in nursing home quality of life. Innov. *Aging*. 2022;6(4):igac037. doi:10.1093/geroni/igac037
7. Ouslander JG, Reyes B, Yang Z, et al. Nursing home performance in a trial to reduce hospitalizations: implications for future trials. *J Am Geriatr Soc*. 2021;69(8):2316-2326. doi:10.1111/jgs.17231
8. Miller LG, McKinnell JA, Singh RD, et al. Decolonization in nursing homes to prevent infection and hospitalization. *N Engl J Med*. 2023;389(19):1766-1777. doi:10.1056/NEJMoa2215254
9. Quinn CC, Adams AS, Magaziner JS, Gurwitz JH. Coronavirus disease 2019 and clinical research in U.S. nursing homes. *J Am Geriatr Soc*. 2021;69(7):1748-1751. doi:10.1111/jgs.17191
10. Centers for Medicare and Medicaid Services. COVID-19 Nursing Home Data. 2024. Retrieved February 2024. https://data.cms.gov/covid-19/covid-19-nursing-home-data.
11. Cohen MS, Nirula A, Mulligan MJ, et al. Effect of Bamlanivimab vs placebo on incidence of COVID-19 among residents and staff of skilled nursing and assisted living facilities: a randomized clinical trial. *JAMA*. 2021;326(1):46-55. doi:10.1001/jama.2021.8828
12. Palat ST, Eber LB, Lum H, Levy C. Monoclonal antibody use in post-acute and long-term care: a call to action. *J Am Med Dir Assoc*. 2021;22(12):2516-2517. doi:10.1016/j.jamda.2021.10.010
13. Ishii S, Streim JE, Saliba D. Potentially reversible resident factors associated with rejection of care behaviors. *J Am Geriatr Soc*. 2010;58(9):1693-1700. doi:10.1111/j.1532-5415.2010.03020.x
14. Sloane PD, Zimmerman S, Ward K, et al. A 2-year pragmatic trial of antibiotic stewardship in 27 community nursing homes. *J Am Geriatr Soc*. 2020;68(1):46-54. doi:10.1111/jgs.16059
15. Weintraub JA, Zimmerman S, Ward K, et al. Improving nursing home Residents' Oral hygiene: results of a cluster randomized intervention trial. *J Am Med Dir Assoc*. 2018;19(12):1086-1091. doi:10.1016/j.jamda.2018.09.036
16. Ouslander JG, Lamb G, Perloe M, et al. Potentially avoidable hospitalizations of nursing home residents: frequency, causes, and costs: [see editorial comments by Drs. Jean F. Wyman and William R. Hazzard, pp 760-761]. *J Am Geriatr Soc*. 2010;58(4):627-635. doi:10.1111/j.1532-5415.2010.02768.x
17. Gurwitz JH, Quinn CC, Abi-Elias IH, et al. Advancing clinical trials in nursing homes: a proposed roadmap to success. *J Am Geriatr Soc*. 2022;70(3):701-708. doi:10.1111/jgs.17696
18. Simmons S, Resnick B, Schnelle J, Ouslander JG. Clinical trials in nursing homes: challenges and practical solutions, *Clinical Trials in Older Adults*. 2015;231-253.
19. Ouslander JG, Schnelle JF. Research in nursing homes: practical aspects. *J Am Geriatr Soc*. 1993;41(2):182-187. doi:10.1111/j.1532-5415.1993.tb02055.x
20. Zimmerman S, Resnick B, Ouslander J, et al. Pragmatic trials and improving long-term care: recommendations from a National Institutes of Health conference. *Geriatr Nurs*. 2022;44:288-292.
21. Levy C, Zimmerman S, Mor V, et al. Pragmatic trials in long-term care: challenges, opportunities, recommendations. *Geriatr Nurs*. 2022;44:282-287.
22. Tilden VP, Thompson SA, Gajewski BJ, Buescher CM, Bott MJ. Sampling challenges in nursing home research. *J Am Med Dir Assoc*. 2013;14(1):25-28. doi:10.1016/j.jamda.2012.08.015

23. Gandhi A, Yu H, Grabowski DC. High nursing staff turnover in nursing homes offers important quality information: study examines high turnover of nursing staff at US nursing homes. *Health Aff*. 2021;40(3):384-391.
24. Levy C, Au D, Ozkaynak M. Innovation and quality improvement: safe or sabotage in nursing homes? *J Am Med Dir Assoc*. 2021;22(8):1670-1671. doi:10.1016/j.jamda.2021.06.026
25. Lam HR, Chow S, Taylor K, et al. Challenges of conducting research in long-term care facilities: a systematic review. *BMC Geriatr*. 2018;18(1):242. doi:10.1186/s12877-018-0934-9
26. Daddato A, Wald HL, Horney C, et al. A randomized trial of heart failure disease management in skilled nursing facilities (SNF connect): lessons learned. *Clin Trials*. 2017;14(3):308-313. doi:10.1177/1740774517690529
27. Unroe KT, Ersek M, Tu W, et al. Using palliative leaders in facilities to transform Care for People with Alzheimer's disease (UPLIFT-AD): protocol of a palliative care clinical trial in nursing homes. *BMC Palliat Care*. 2023;22(1):105. doi:10.1186/s12904-023-01226-0
28. Gismondi PM, Hamer DH, Leka LS, Dallal G, Fiatarone Singh MA, Meydani SN. Strategies, time, and costs associated with the recruitment and enrollment of nursing home residents for a micronutrient supplementation clinical trial. *J Gerontol A Biol Sci Med Sci*. 2005;60(11):1469-1474. doi:10.1093/gerona/60.11.1469
29. Gustavson AM, Drake C, Lakin A, et al. Conducting clinical research in post-acute and long-term nursing home care settings: regulatory challenges. *J Am Med Dir Assoc*. 2019;20(7):798-803. doi:10.1016/j.jamda.2019.04.022
30. Greenspan S, Nace D, Perera S, et al. Lessons learned from an osteoporosis clinical trial in frail long-term care residents. *Clin Trials*. 2012;9(2):247-256. doi:10.1177/1740774511430516
31. Wood F, Prout H, Bayer A, et al. Consent, including advanced consent, of older adults to research in care homes: a qualitative study of stakeholders' views in South Wales. *Trials*. 2013;14(1):247. doi:10.1186/1745-6215-14-247
32. Tinetti ME, McAvay GJ, Chang SS, et al. Contribution of multiple chronic conditions to universal health outcomes. *J Am Geriatr Soc*. 2011;59(9):1686-1691. doi:10.1111/j.1532-5415.2011.03573.x
33. Verbeek H, Zwakhalen SMG, Schols JMGA, Kempen GIJM, Hamers JPH. The living lab in ageing and long-term care: a sustainable model for translational research improving quality of life, quality of care and quality of work. *J Nutr Health Aging*. 2020;24(1):43-47. doi:10.1007/s12603-019-1288-5
34. Mitchell SL, Mor V, Harrison J, McCarthy EP. Embedded pragmatic trials in dementia care: realizing the vision of the NIA IMPACT Collaboratory. *J Am Geriatr Soc*. 2020;68:S1-S7.
35. Hanson LC, Bennett AV, Jonsson M, et al. Selecting outcomes to ensure pragmatic trials are relevant to people living with dementia. *J Am Geriatr Soc*. 2020;68:S55-S61. doi:10.1111/jgs.16619
36. RFA-AG-24-016: Nursing Home EXplanatory Clinical Trials Network (NEXT) (U24 Clinical Trial Required). Accessed December 11, 2023. https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-24-016.html.

How to cite this article: Unroe KT, Saliba D, Hickman SE, Zimmerman S, Levy C, Gurwitz J. Evaluation of medical therapies in the nursing home population: Gaps, challenges, and next steps. *J Am Geriatr Soc*. 2024;1-6. doi:10.1111/jgs.18829