


COMMENTARY

Coronavirus disease 2019 and clinical research in U.S. nursing homes

Charlene C. Quinn RN, PhD¹  | **Alyce S. Adams PhD²** |
Jay S. Magaziner PhD, MSHyg¹ | **Jerry H. Gurwitz M.D.^{3,4}**

¹University of Maryland School of Medicine, Baltimore, MD

²Stanford School of Medicine, Stanford, CA

³Meyers Primary Care Institute, A Joint Endeavor of University of Massachusetts Medical School, Fallon Health and Reliant Medical Group, Worcester, MA

⁴Division of Geriatric Medicine, University of Massachusetts Medical School, Worcester, MA

Correspondence

Charlene C. Quinn, RN, PhD, FAAN, Associate Professor, University of Maryland School of Medicine, Project Director, AGING Initiative Nursing Home Clinical Trials Network, 655 W Redwood St., HH 215, Baltimore, MD 21201.

Email: cquinn@som.umaryland.edu

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The ongoing coronavirus disease 2019 (COVID-19) pandemic has revealed the extreme vulnerability of residents of our nation's more than 15,000 nursing homes. Fewer than 1% of America's population reside in nursing homes, but as reported by the COVID-19 Tracking Project, "this tiny fraction of the country accounts for 35% of U.S. COVID-19 deaths."¹ Moreover, COVID-19 has disproportionately affected nursing homes with a higher proportion of Black and Hispanic residents.²

Despite these sobering statistics, the U.S. clinical research enterprise has largely ignored the nursing home population in conducting clinical research on COVID-19. Of the 1.3 million residents of U.S. nursing homes, only a few hundred have participated in randomized controlled trials relating to COVID-19.³ And while nursing home residents were prioritized for vaccination in the initial COVID-19 allocation phase in the United States,⁴ this population was effectively excluded from the pivotal clinical trials of vaccines assessing efficacy and safety.⁵

The dire need for scientific evidence to address the escalating crisis in nursing homes became apparent nearly immediately following the onset of the pandemic. Infection prevention and control strategies, therapeutics, vaccine safety and efficacy, and vaccine rollout efforts all would have benefited from rigorous research-based approaches. However, such efforts were impossible not only due to

the chaos and lockdowns of nursing homes that occurred with the rapid spread of the virus, but because of circumstances in nursing homes that have existed for decades.

In this Commentary, we describe issues that have challenged the conduct of clinical research in nursing homes before and during the pandemic, and which will continue to challenge such efforts into the future.

AN UNDER-RESOURCED, ORGANIZATIONALLY CHALLENGED INDUSTRY

Regardless of size, location, or profit status, nursing homes have not been immune to economic challenges resulting from COVID-19. Nursing homes depend on an 85% occupancy rate to break even, with occupancy rates declining far below this during the pandemic. Medicaid covers more than 60% of all nursing home residents, but only 70–80% of the costs of care. As a result, nursing homes that are heavily dependent on Medicaid reimbursement are poorly resourced, have lower staffing levels, have more quality problems, and are at the greatest risk for sale, merger, acquisition, or closure.⁶ Furthermore, 70% of nursing homes are owned by for-profit entities, which can create perverse financial incentives with adverse consequences for resident care.⁷

Beyond these financial challenges, the pandemic has highlighted concerns relating to nurse home staffing and quality of care.⁸ High rates of nursing staff turnover, with median annual nursing staff turnover exceeding 90%,⁹ are a long-standing issue relating to low compensation, poor working conditions, high resident-to-staff ratios, and a high proportion of unlicensed personnel. Turnover of top management in nursing homes is also high with estimates exceeding 40% per year.¹⁰

The cumulative effect of these financial and organizational challenges places clinical research on a low priority for many nursing homes.

REGULATIONS IMPACTING RESEARCH IN NURSING HOMES

Gustavson and colleagues described the many challenges of conducting research in nursing homes due to federal and state regulatory oversight.¹¹ Clinical research generally requires access to protected health information, as researchers may wish to use administrative data and electronic health records to identify, recruit, and characterize study participants, examine care, and measure outcomes.¹² These data are subject to the Health Information Portability and Accountability Act (HIPAA) Privacy Rule and nursing homes do not typically have privacy boards or IRBs to determine if release of data for specific research purposes complies with privacy regulations. Furthermore, any institution “engaged in research” supported by the U.S. Department of Health and Human Services (HHS) is required to have an approved Federal-wide Assurance for the Protection of Human Subjects committing to compliance with Common Rule requirements on file with the Office for Human Research Protections in HHS.¹²

While fully “engaging” nursing homes in research may be “ideal” for planning and conducting clinical research from the perspective of researchers and funders, the direct involvement of nursing home staff in research may trigger concerns about coercion when training and research-related tasks fall beyond the scope of their work and compete with time devoted to resident care.

THE NEED FOR SPECIAL PROTECTIONS FOR RESEARCH SUBJECTS

There have long been concerns about the special circumstances surrounding human subjects research in nursing homes and the vulnerability of residents to coercion or undue influence. The Common Rule stipulates that all human subjects must provide consent to research unless consent can be waived. Hearing loss, vision loss, and

cognitive impairment are common among the nursing home population impacting ability to consent for research. When a resident lacks capacity to consent, the investigator may obtain informed consent from the subject’s legally authorized representative. The issue of who can be a legally authorized representative is determined by the local or state laws.¹³ This can add additional complexity to the conduct of a clinical trial involving facilities located in different states, even when nursing homes are owned by the same corporation. While some programmatic or environmental interventions implemented at the facility or unit of care level may meet criteria for a waiver of informed consent, randomized trials of new therapeutics or vaccines do not.

THE LACK OF A CLINICAL RESEARCH INFRASTRUCTURE IN NURSING HOMES

The successful conduct of clinical trials in nursing homes generally requires strong relationships between investigators and nursing home leadership and clinical staff, but few of the nation’s 15,000 nursing homes have ongoing formal relationships with academic health centers or university-affiliated investigators. The small number of university-based investigators who perform clinical trials in nursing homes tend to operate these endeavors like “cottage industries” relying on personal relationships formed over years with a small-to-modest number of local facilities or with a single nursing home chain. These investigator-driven efforts often become “one-offs,” meaning that once the clinical trial is completed, the relationship between the investigator and the participating nursing homes ends. With the advent of a new trial, the investigator must start anew identifying and engaging with potential study nursing homes, in many cases needing to develop relationships with new owners, administrators, directors of nursing, and medical directors due to high levels of leadership turnover.

THE POSSIBILITY OF A COORDINATED RESEARCH APPROACH TO COVID-19 IN NURSING HOMES

Lane and Fauci have written, “scientifically robust and ethically sound clinical research remains the quickest and most efficient pathway to effective treatment and prevention strategies for patients with COVID-19.”¹⁴ Yet, many have lamented that beyond our success with vaccines, the United States was not up to the task

of conducting randomized controlled trials relevant to COVID-19, and not for “lack of intent, effort, or resources.”¹⁵ This underperformance has been attributed to the structure of the U.S. clinical research enterprise that while vast, has never functioned as a coordinated system in setting priorities, designing trials, and fostering collaboration.¹⁵

For the reasons described in this Commentary, a coordinated research approach to COVID-19 in nursing homes never stood a chance. One attempt to work-around these challenges was BLAZE-2, a phase 3 randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of anti-spike neutralizing monoclonal antibodies in preventing SARS-CoV-2 infection and COVID-19 in skilled nursing and assisted living facility residents and staff (funded by NIAID and Eli Lilly and Company).¹⁶ The study employed a decentralized, non-academic health center-centric research approach that required no nursing home-based research infrastructure and no established relationships with individual nursing homes or chains. Mobile units comprised of refitted recreational vehicles pulling trailers arrived at facilities experiencing outbreaks. Mobile units handled drug preparation, infusion, and lab work. While falling far below recruitment goals, this ambitious effort was able to enroll 1097 study participants, of which 300 were residents of nursing homes.³

CONCLUSION

Ouslander and Grabowski described COVID-19 in nursing homes as a “perfect storm” resulting from a confluence of circumstances including a highly vulnerable population residing in a congregate setting, overwhelming staffing challenges, and inadequate resources. They argued that “we now have the opportunity to improve nursing homes to protect residents and their caregivers ahead of the next storm... and that it is time to reimagine how we pay for and regulate care to achieve this goal.”¹⁷ The same type of reimagining needs to occur to create a more effective environment for clinical research in U.S. nursing homes. This will require a collective national effort to create a nursing home clinical research infrastructure involving a broad group of stakeholders (including residents and families), that is centrally supported and administered, easily adaptable to be able to pivot as necessary, and which is devised to endure far beyond the tragedy of this pandemic.

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CONFLICT OF INTEREST

Authors have no conflict of interest or financial disclosures related to this manuscript.

AUTHOR CONTRIBUTIONS

All authors contributed equally to the manuscript.

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ORCID

Charlene C. Quinn  <https://orcid.org/0000-0002-6066-2984>

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