



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

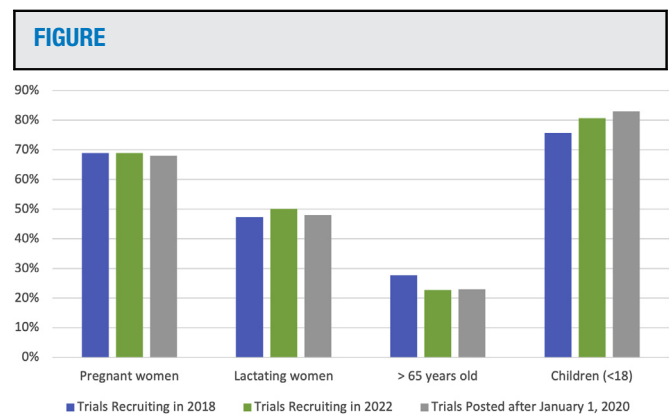
Gaps in evidence-based medicine: underrepresented populations still excluded from research trials following 2018 recommendations from the Health and Human Services Task Force on Research Specific to Pregnant Women and Lactating Women

OBJECTIVE: Despite being at higher risk for COVID-19–related complications, pregnant and lactating women were excluded from the initial trials leading to Emergency Use Authorizations for COVID-19 vaccinations.¹ These exclusions came 2 years after the United States Department of Health and Human Services (HHS) Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) provided recommendations to Congress and HHS on how to increase inclusion of traditionally excluded groups in research.²

Lack of randomized controlled trials including pregnant and lactating patients limits clinicians' ability to make evidence-based recommendations. The explicit exclusion of these groups from trials means that clinicians must rely on less sound data, often from observational studies or expert opinions, when making recommendations. Although these exclusions are framed as protective, they result in a lack of evidence-based care and harm patients as effects, dosing changes, and metabolic changes are not studied. Patients in other commonly excluded groups are exposed to the same harms, with limited evidence available to steer decision-making for patients with disabilities, the elderly, and children. This study aimed to determine if National Institutes of Health (NIH)–funded trials were more likely to include underrepresented groups after the 2018 PRGLAC recommendations.

STUDY DESIGN: All actively recruiting NIH-funded phase 3 and 4 trials were downloaded from [ClinicalTrials.gov](https://clinicaltrials.gov) on January 7, 2022. These trials were reviewed for inclusion criteria and population of interest. Data collected from this date were then compared with data published before these recommendations.³

RESULTS: Of 419 actively recruiting trials, explicit exclusion was noted in 69% for pregnant individuals, 50% for lactating women, 81% for children, 23% for older adults, and 15% for individuals with disabilities. In comparison with previous data,³ explicit exclusion did not change for any group (Figure). Of the 289 trials that did not explicitly exclude pregnant women, many focused on populations that by nature exclude pregnant and lactating individuals,



Explicit exclusion in clinical trials

Figure shows explicit exclusion in clinical trials before Health and Human Services Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) recommendations, after recommendations, and in trials posted after January 1, 2020.

Thiele. Underrepresented populations still excluded from research trials following 2018 recommendations from the Health and Human Services Task Force on Research Specific to Pregnant Women and Lactating Women. Am J Obstet Gynecol 2022.

including postmenopausal-age adults, cisgender males, and young children.

To account for time needed to incorporate PRGLAC recommendations, we isolated trials published after January 1, 2020, and found that among these 160 trials, there was no change in the exclusion of underrepresented groups relative to data published before the recommendations.

CONCLUSION: The continued exclusion of pregnant and lactating women from trials extends gaps in knowledge and data for clinicians to use in managing and counseling women. Despite a concerted effort to increase research in these populations, exclusion persists, even in the setting of a pandemic with unique opportunities for inclusion. After PRGLAC recommendations were presented, pregnant women were removed as a vulnerable population from the Common Rule.⁴ However, there have been no changes to NIH justification

criteria for the inclusion or exclusion of these groups, nor specific policies requiring a justification for their exclusion from NIH-funded research trials. Although principal investigators must justify exclusion of nonpregnant women and minorities, there is no requirement for such justification when excluding pregnant or lactating individuals or those with disability.⁵ Thus, unsurprisingly, there have been no changes in the inclusion of underrepresented populations among the recruiting trials. ■

Lisa Thiele, BS
Department of Obstetrics and Gynecology
The University of Texas Southwestern Medical Center
5323 Harry Hines Blvd.
Dallas, TX 75390
lisa.thiele@utsouthwestern.edu

Jennifer Thompson, MD
Parkland Health & Hospital System
Dallas, TX
Department of Obstetrics and Gynecology
The University of Texas Southwestern Medical Center
Dallas, TX

Jessica Pruszynski, PhD
Department of Obstetrics and Gynecology
The University of Texas Southwestern Medical Center
Dallas, TX

Catherine Y. Spong, MD
Department of Obstetrics and Gynecology
University of Texas Southwestern Medical Center
Dallas, TX
Parkland Health & Hospital System
Dallas, TX

C.Y.S. was the chair of the Task Force on Research Specific to Pregnant Women and Lactating Women from its inception until July 1, 2018. The remaining authors report no conflict of interest.

REFERENCES

1. Rubin R. Pregnant people's paradox-excluded from vaccine trials despite having a higher risk of COVID-19 complications. *JAMA* 2021;325:1027–8.
2. PRGLAC. Task. force on research specific to pregnant women and lactating women. 2018. Available at: https://www.nichd.nih.gov/sites/default/files/2018-09/PRGLAC_Report.pdf. Accessed April 17, 2022.
3. Spong CY, Bianchi DW. Improving public health requires inclusion of underrepresented populations in research. *JAMA* 2018;319:337–8.
4. Task Force on Research Specific to Pregnant Women and Lactating Women. Research implementation plan. 2020. Available at: https://www.nichd.nih.gov/sites/default/files/inline-files/PRGLAC_Implement_Plan_083120.pdf. Accessed July 5, 2022.
5. National Institute of Health. Guidelines for inclusion of pregnant women in research. 2022. Available at: <https://orwh.od.nih.gov/toolkit/nih-policies-inclusion/guidelines>. Accessed July 5, 2022.

© 2022 Elsevier Inc. All rights reserved. <https://doi.org/10.1016/j.ajog.2022.07.009>