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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 (PRGLAC)

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Background:

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 two years after the 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 a clinician's 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 opinion when making recommendations. While 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.

Objective:

The objective of this study was to determine if 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 on January 7th, 2022. These trials were reviewed for inclusion criteria and population of
interest. Data collected from this date was then compared to published data prior to 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 prior data, [3] explicit exclusion did not change for any group (Figure 1). Of the 289 trials that did not explicitly exclude pregnant women, many focused-on populations that by nature exclude pregnant and lactating individuals including postmenopausal aged adults, cis-gendered males, and young children.

To account for time needed to incorporate PRGLAC recommendations, we isolated trials posted later than January 1st, 2020, and found that among these 160 trials, there was no change in the exclusion of underrepresented groups from data published prior to the recommendations.

Conclusions:

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 criteria for justification for these groups for inclusion or exclusion – nor specific policies requiring a justification for their exclusion from NIH funded research trials. While PIs must justify exclusion of nonpregnant women and
minorities, there is no requirement for an explanation of the exclusion of pregnant or lactating individuals or those with disability.[5] As such, there have been no changes in the inclusion among recruiting trials.

References


2. PRGLAC Report to HHS and Congress (2018)


Figure 1. Explicit exclusion in clinical trials prior to PRGLAC recommendations, after recommendations, and in trials posted after January 1st, 2020.