

Progress Towards Including Pregnant and Lactating People in Clinical Trials

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Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)



- **2016: Congress established PRGLAC** via the 21st Century Cures Act to identify and address gaps in knowledge regarding safe and effective therapies and vaccines for pregnant and lactating women.
- **Representation from all sectors:** multiple NIH institutes, CDC, FDA, AHRQ, HRSA, HHS, VA, professional societies, industry, academia, non-profit organizations. NICHD as lead.
- 2018: PRGLAC Report to Congress included **15 recommendations** to promote the inclusion of pregnant and lactating women in clinical trials.
- HHS Secretary extended PRGLAC charter, requesting guidance on implementation.



- 2020: PRGLAC issued an **Implementation Plan**.
- On March 13, 2021, PRGLAC's charter expired, ***but implementation continues!***



Brief Overview of PRGLAC Recommendations

- Key recommendations included:
 - Protect pregnant people *through* research instead of *from* research.
 - Change the existing culture that has limited scientific knowledge of therapeutic product safety, effectiveness, and dosing for pregnant and lactating women.
 - Remove pregnant women as a vulnerable population through Common Rule.
 - Expand workforce of clinicians and researchers with expertise in obstetric and lactation pharmacology and therapeutics.
 - Remove regulatory barriers.
- All 15 recommendations and full Task Force report are available online:
<https://www.nichd.nih.gov/About/Advisory/PRGLAC>

IMPLEMENTATION UPDATE



RECOMMENDATIONS

1. Include and integrate pregnant women and lactating women in the clinical research agenda.
2. Increase the quantity, quality, and timeliness of research on safety and efficacy of therapeutic products used by pregnant women and lactating women.
9. Develop programs to drive discovery and development of therapeutics and new therapeutic products for conditions specific to pregnant women and lactating women.
11. Leverage established and support new infrastructures/collaborations to perform research in pregnant women and lactating women.

ACTIONS

- The [Maternal-Pediatric Precision in Therapeutics \(MPRINT\) Hub](#) serves as a national resource for expertise in maternal and pediatric therapeutics to conduct and foster therapeutics-focused research in obstetrics, lactation, and pediatrics, while enhancing inclusion of people with disabilities.
- [Maternal-Fetal Medicines Unit \(MFMU\) Network](#) studies the efficacy of antivirals and other therapeutics for pregnant women with COVID-19.



The MPRINT Hub: Advancing Frontiers in Health through Maternal and Pediatric Precision In Therapeutics



- Address underrepresentation of women and children in clinical trials
- MPRINT Hub is a service center and science catalyst:
 - Enhancing the availability of knowledge, regulatory science, and drug development tools
 - Catalyze and accelerate maternal and pediatric therapeutics towards precision medicine
 - Synergize with other resources and networks
 - Facilitating safer, more inclusive, and more cost-effective trials

**MPRINT Hub:
Knowledge Core
and Centers of
Excellence**



MPRINT Centers of Excellence in Therapeutics

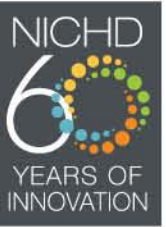


- **Current awards**

- Effects of maternal antibiotics on breastmilk and infant outcomes ([UCSD](#))
 - Develop and validate novel assays and models to describe and predict maternal and infant antibiotic PK during breastfeeding
 - Impact of maternal antibiotics on establishing normal infant microbiome and gut metabolome
 - Potential downstream effects of antibiotic exposure on infant immune function and cytochrome P450 drug metabolizing enzymes
- Maternal and pediatric precision therapeutics and NOWs ([Vanderbilt](#))
 - Community engaged approach to illuminate knowledge, attitudes & priorities for pharmacogenomics
 - Validate pharmacogenomic associations using the strategy of EHR phenotyping
 - Identify and quantify variants with unknown function in diverse individuals



IMPLEMENTATION UPDATE



RECOMMENDATION

3. Expand the workforce of clinicians and research investigators with expertise in obstetric and lactation pharmacology and therapeutics.

ACTIONS

- NICHD provides training and career development awards that include research on pregnant and lactating persons at <https://www.nichd.nih.gov/grants-contracts/training-careers>.
- MPRINT Hub webinar series focused on educating the biomedical community on research approaches that can be applied to pregnant and lactating persons, as well as pediatric populations.



IMPLEMENTATION UPDATE



RECOMMENDATION

7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women.

ACTIONS

- Congressionally-mandated study with NASEM to convene a panel with specific legal, ethical, regulatory, and policy expertise to develop a framework for addressing medicolegal and liability issues when planning or conducting research specific to pregnant people and lactating people.
- The current workshop!



IMPLEMENTATION UPDATE



RECOMMENDATION

10. Implement a proactive approach to protocol development and study design to include pregnant women and lactating women in clinical research.

ACTIONS

- NICHD's [MFMU Network](#) is studying the efficacy of antivirals and other therapeutics for pregnant women with COVID-19.
- The MFMU completed the Tranexamic Acid (TXA) for the Prevention of Obstetrical Hemorrhage after Cesarean Delivery trial, testing whether, in pregnancies with cesarean deliveries, giving TXA following cord clamping can reduce maternal deaths and the need for blood transfusions.
- Researchers in NICHD's Global Network for Women's and Children's Health Research, in collaboration with the Bill & Melinda Gates Foundation, will assess whether a single oral dose of the antibiotic azithromycin during labor reduces the risk of maternal and infant bacterial infection and death in seven low- and middle-income countries.
- NICHD has open grant solicitations on "[Translational Research in Maternal and Pediatric Pharmacology and Therapeutics](#)" encouraging proposals that address the PRGLAC recommendations.



IMPLEMENTATION UPDATE



RECOMMENDATION

12. Utilize and improve existing resources for data to inform the evidence and provide a foundation for research on pregnant women and lactating women.

ACTIONS

- [The Office of the Secretary's Patient-Centered Outcomes Research Trust Fund \(OS-PCORTF\)](#) funded projects to improve electronic health record data for research on maternal health and pregnancy.
 - NICHD [Severe Maternal Morbidity and Mortality EHR Data Infrastructure](#)
 - CDC [MATernal and Infant Network to Understand Outcomes Associated with Treatment for Opioid Use Disorder during Pregnancy \(MAT-LINK\)](#)
 - CDC [Enhancing Surveillance of Maternal Health Clinical Practices and Outcomes with FQHCs' EHRs Visit Data](#)
- The [NICHD Data and Specimen Hub \(DASH\)](#) is a centralized resource that allows researchers to share and access de-identified data from studies funded by NICHD and serves as a portal for requesting biospecimens from selected DASH studies.



Future Pandemic Preparedness: *Include Pregnant and Lactating People in Research*



- Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)
 - Representation across all sectors
 - Issued **recommendations** in 2018 and an **implementation plan** in 2020
 - <https://www.nichd.nih.gov/About/Advisory/PRGLAC>
- Change the culture to protect pregnant people *through* research instead of *from* research
- **Need to plan for the inclusion of pregnant and lactating people for evaluation of treatments and vaccines in future pandemics**

Viewpoint

February 10, 2021

Involving Pregnant Individuals in Clinical Research on COVID-19 Vaccines

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IMPLEMENTATION UPDATE



Recommendations: Future Work Needed

4. Remove regulatory barriers to research in pregnant women.
 - In 2019 pregnant women were removed as an explicit example of a vulnerable population in 45CFR46 by the HHS Office for Human Research Protection.
 - Awaiting FDA harmonization with the Common Rule.



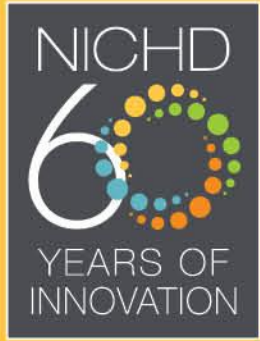
IMPLEMENTATION UPDATE



Recommendations: Future Work Needed

5. Create a public awareness campaign to engage the public and health care providers in research on pregnant women and lactating women.
6. Develop and implement evidence-based communication strategies with health care providers on information relevant to research on pregnant women and lactating women.
8. Develop separate programs to study therapeutic products used off-patent in pregnant women and lactating women using the NIH BPCA as a model.
13. Optimize registries for pregnancy and lactation.





Thank You!