



Advancing NIH Research on the Health of Women: A 2021 Conference

Harnessing the power of research: Optimizing infrastructure to optimize maternal outcomes

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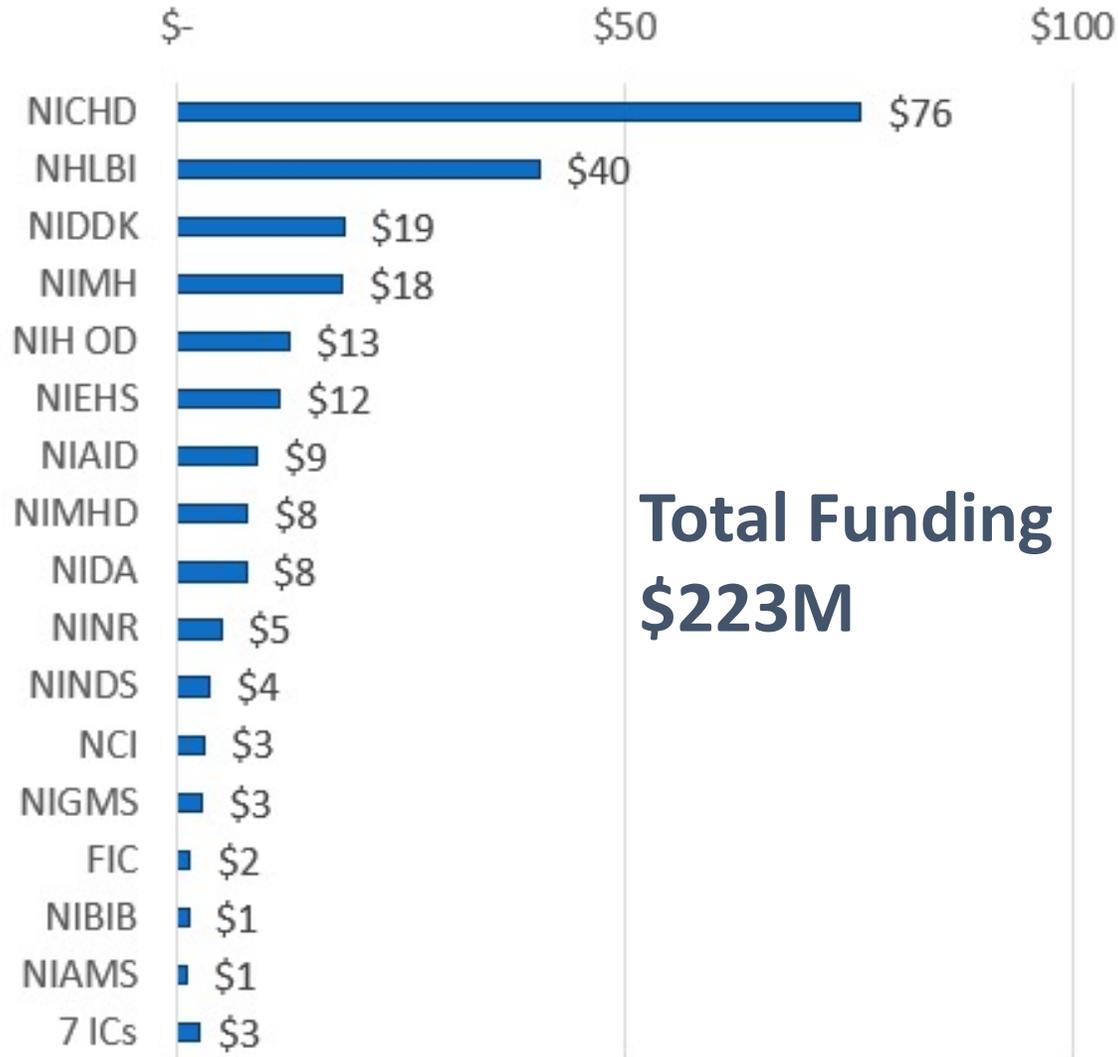
Greater NIH Funding for Maternal Health is Needed

- NIH budget \$419 million allocated to pregnancy research, represented only 1.2% of the total NIH budget (2018)
- “These data represent an alarming underestimation of disease burden related to pregnancy.”
- “We should not forget that although only approximately 1% of the US population is pregnant, pregnant women carry 100% of the future of humankind.”

Rice et al, AJOG, 2020

- COVID-19 vaccine: most recent example of how pregnant people are left out of critical research
- Pregnancy research is critical for people who could become pregnant -- not just those who are already pregnant

NIH Research: Maternal Morbidity & Mortality Funding by IC, FY 2020



Analysis conducted by National Institutes of Health, Office of Research on Women's Health (NIH/ORWH)

*Note: Type 1 Diabetes Special Statutory Funding Program combined with NIDDK.
NIH Roadmap funding combined with NIH OD.
<https://report.nih.gov/funding/categorical-spending/#>*

Greater Investment in Clinical Research Infrastructure is Needed

- Clinical research to address causes of maternal morbidity and mortality requires:
 - Large sample sizes
 - Ethnic/racial/SES diversity
 - Geographic diversity
 - Health delivery system diversity
 - Academic and community hospitals/clinics, FQHC, private practices
 - \$\$\$: Beyond scope of “typical R01” 500K/year direct costs
 - Duration - takes more than 5 years



NICHD Maternal-Fetal Medicine Units Network (MFMU)

- Established in 1986
- 12 Centers (36 hospitals) participate collaboratively in common protocols
- Conducts mainly randomized trials to reduce maternal and infant deaths and complications
- Large number of deliveries covered (165,000)
- Racial/ethnic, geographic diversity



GOALS: To reduce maternal, fetal, and infant morbidity and to provide the rationale for evidence-based, cost-effective obstetric practice.



MFMU Trial: Tranexamic acid (TXA) for the Prevention of Obstetric Hemorrhage After Cesarean Delivery

WOMAN Trial: international, randomized, double-blind, placebo-controlled trial

- Conclusion: TXA safely reduces death due to bleeding in women with postpartum hemorrhage
- Established safety & efficacy of TXA for treatment of obstetric hemorrhage

Lancet 2017;389:2105-16

MFMU TXA Trial: 11,000 women randomized to TXA vs. placebo

- Designed to assess efficacy of TXA for prevention of obstetric hemorrhage
- Timely recruitment (2018- 2021)
- IND: complex FDA regulatory requirements

Clinical research



OBSTETRIC-FETAL PHARMACOLOGY
RESEARCH CENTERS

Specialized Center--Cooperative Agreements (U54)

NICHD: Cooperative multidisciplinary research to enhance the understanding of obstetric pharmacokinetics and pharmacodynamics of medications through pregnancy



Nulliparous Pregnancy Outcomes Study
Monitoring Mothers-to-be



funded by the National Institutes of Health

NICHD/NHLBI: Adverse pregnancy outcomes (n=10,000) →
Cardiovascular outcomes 2-7 years

U10 initially set up for single study



U01 initially set up for single study

NIDDK: Early glycemia →
prediction of GDM and adverse maternal and neonatal outcomes →
(n=2150)
-Can be leveraged for longer term outcomes

Clinical research



Cesarean Section Optimal Antibiotic Prophylaxis (C/SOAP) Trial

- NHLBI: RCT of antihypertensive treatment vs. no treatment for mild chronic hypertension, n=2400
- Primary outcome: preeclampsia with severe features; fetal or neonatal death, placental abruption, or indicated PTB <35 weeks
- NICHD: RCT of azithromycin vs placebo in addition to standard antibiotic prophylaxis before cesarean to decrease infection, n= 2,013
- Primary Outcome reduced from 12% to 6%

Invest more in clinical research site infrastructure for maternal health research

- Increase MFMU (or similar) network funding to expand site diversity and recruitment capacity
 - Requirements for site geographic, sociodemographic and care type diversity; Reach large numbers of eligible participants in timely way; Lower start-up/set-up costs for launching critical trials
- Leverage network/consortium infrastructures better
 - Promote use of that infrastructure for critical studies across ICs and investigators
 - RFAs and other FOAs for maternal health research encouraged to use the network infrastructure

Maternal Health Research Coordination across NIH

NIH Pediatric Research Consortium (N-PeRC)

- N-PeRC is a trans-NIH initiative that began in June 2018 to capitalize on pediatric research expertise and resources across NIH's 27 institutes and centers through increased collaboration.
- NICHD is the lead NIH institute for the consortium.
- NIH support for pediatric research: >\$4 billion.
- N-PeRC aims to harmonize these activities across institutes, explore gaps in the overall pediatric research portfolio, and share best practices to advance science.
- The consortium meets several times a year to discuss scientific opportunities and potential new areas of collaboration, including efforts to enhance research training for the next generation of pediatricians.



NEED NIH Obstetric Research Consortium

- Prioritize research on pregnancy
- Catalog of research across NIH
- Identification of Gaps
- Coordination of research
- RFAs to target gaps-Life course approach
- Enhance research training



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Maternal Health Research Coordination across NIH

I mplementing a Maternal health and Pregnancy Outcomes Vision for Everyone (IMPROVE) Initiative

- Address leading causes of pregnancy-related severe maternal morbidity/maternal mortality by building an evidence base for improved care and outcomes
- Administrative supplements for NIH grants to Add or Expand Research Focused on Maternal Mortality 37 awards totaling \$7.2M
- Needs sustained funding to issue RFAs to target specific gaps
- **Ultimate Goal: One NIH committee empowered not just to track maternal health research but to lead the agenda**
- Empowered to direct how the maternal health funding gets used/allocated
Annual report on priorities, activities and OUTPUT.

Collaboration across HHS

GOAL: Committee with representation across HHS agencies. Single agency coordinating and tracking maternal health research across HHS and how best to leverage resources

- **NIH**
- **FDA**
- **CDC**
- **HRSA**
- **AHRQ**
- **SAMHSA**
- **IHS**
- **CMS**
- + **PCORI**

Separate program for therapeutic products in pregnant people

- Best Pharmaceuticals for Children Act (BPCA) enacted by law in 2002
- Goals:
 - 1) Encourage the pharmaceutical industry to perform pediatric studies to improve labeling for patented drug products used in children, by granting an additional 6 months patent exclusivity
 - 2) NIH to prioritize therapeutic areas and sponsor clinical trials and other research for off-patent drug products that need further study in children
- Funding: Congress appropriates \$25 million of NIH budget each FY
 - NICHD contributes 25 % of BPCA funding from its annual budget.
 - Remaining funds are from more than 20 other NIH institutes
- **NEED Pregnant and lactating people equivalent!**
 - Recommendation by the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) to the HHS secretary in 2020 Report

Driving priority maternal health research objectives

- Grant application review: Standing CSR study section specific to Women's Health to include **Ob-Gyn**, internal medicine, adolescent medicine, epidemiology, health equity, implementation science expertise
- Increased funding targeted to URM investigators and geographically diverse institutions
- Increased funding of Physician scientists to focus on maternal health
 - Individual K grants and bridge funding
- Single IRB process efficiency

Driving priority maternal health research objectives

- Funding of Translational research:
 - Basic and clinical sciences (bench to bedside) (T0-T2)
 - Real world care and outcomes (T3 translation)
 - Community and population health (T4 translation)
- “Patient Voice Core” component to RFAs/IIGs to ensure investigators have expertise and support to incorporate patient-reported outcomes, appropriate quality of life measures
- Community-Based Participatory Research (CBPR) component to RFAs/IIG
 - NIHMD CBPR program: Improved transdisciplinary and intervention research methods and approaches addressing health disparities
 - Recruitment and engagement of faculty who can build trust and alliances with community so patient-based research studies are perceived as an investment in the community rather than community-based experimentation

Conclusions

- Increase funding of maternal health research
- “BPCA equivalent” for therapeutic products in pregnant and lactating people
- Expand MFMU (or similar) Network to include more sites to increase number of deliveries, enhance diversity of populations studied
 - Use infrastructure to perform studies proposed from Investigator initiated grants and RFAs for timely and efficient conduct
- Establish CSR specific study section for Women’s Health
- Increase pool and diversity of investigators focused on maternal health by increasing individual Ks and bridge funding
- Trans-NIH Obstetric Research Consortium to direct/lead agenda
- Expand translational research (across HHS) to include Health services and Implementation research to address racial and ethnic disparities in maternal health

