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

Total Funding $223M

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

Specialized Center--Cooperative Agreements (U54)

U10 initially set up for single study

U01 initially set up for single study

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

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

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

• NHLBI: RCT of antihtn 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
Maternal Health Research Coordination across NIH

Implementing 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