Multicenter Clinical Trials: Leveraging Network Infrastructure to Advance Research and Outcomes for Women, Children, and Pregnant and Lactating Individuals

NACHHD June Council 2022

Bob Tamburro, MD, MS on Behalf of the Division of Extramural Research
Initiative Background

- NICHD has long supported multicenter clinical studies
- NICHD formed its first clinical research networks in 1985
  - Neonatal Intensive Care Units
  - Maternal-Fetal Medicine Units
- Perform large scale clinical trials
- Network support resulted in clinical practice changes

Amniocentesis: HEW Backs Test for Prenatal Diagnosis of Disease

The study, which was conducted by researchers at nine major medical centers,* was coordinated and supported by the National Institute of Child Health and Human Development (NICHD). The study was designed to answer two basic questions about the use of amniocentesis during the middle 3 months of pregnancy.

*The participating institutions were: Children’s Memorial Hospital, Chicago; Eunice Kennedy Shriver Center, Boston; Johns Hopkins University School of Medicine, Baltimore; Mount Sinai School of Medicine, New York; University of California at Los Angeles—Harbor General Hospital, Torrance; University of California School of Medicine, San Diego; University of Michigan School of Medicine, Ann Arbor; University of Pennsylvania School of Medicine, Philadelphia; Yale University School of Medicine, New Haven.

7 November 1975
Network Clinical Trials

Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment


Low-dose aspirin for the prevention of preterm delivery in nulliparous women with a singleton pregnancy (ASPIRIN): a randomised, double-blind, placebo-controlled trial

A Trial of Hyperimmune Globulin to Prevent Congenital Cytomegalovirus Infection


Effect of Therapeutic Hypothermia Initiated After 6 Hours of Age on Death or Disability Among Newborns With Hypoxic-Ischemic Encephalopathy: A Randomized Clinical Trial

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Effect of Physiologic Point-of-Care Cardiopulmonary Resuscitation Training on Survival With Favorable Neurologic Outcome in Cardiac Arrest in Pediatric ICUs: A Randomized Clinical Trial

The ICU-RESUS and Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network Investigators

Estrozole versus Clomiphene for Infertility in the Polycystic Ovary Syndrome

S. Lagro, M.D., Robert G. Brzyski, M.D., Ph.D., Michael P. Diamond, M.D., stos Courfandis, M.D., Ph.D., William D. Schlaff, M.D., Peter Casson, M.D., Mary M. Christman, M.D., Hao Huang, M.D., M.P.H., Qingshang Yan, Ph.D., uben Alvero, M.D., Daniel J. Haisenleider, Ph.D., Kurt T. Barnhart, M.D., right Bates, M.D., Rebecca Usadi, M.D., Scott Lucidi, M.D., Valerie Baker, M.D., russell, M.D., Stephen A. Krawetz, Ph.D., Peter Snyder, M.D., Dara Ohl, M.D., tte Santoro, M.D., Esther Eisenberg, M.D., M.P.H., and Hoping Zhang, Ph.D. for the NICHD Reproductive Medicine Network
Initiative Background

- NIH proposed to enhance clinical trial stewardship
- Individual Institutes/Centers asked to develop their own clinical trial FOAs
- **Four principles** for continued commitment of NICHD Network infrastructure for rigorous multisite clinical trials
  - Notice (NOT-HD-19-034): *Infrastructure for NICHD Multisite Clinical Trials*
  - Webinar: *Strategic Plan 2020 Implementation: NICHD’s vision for multisite clinical trials infrastructure*
    - [https://www.youtube.com/watch?v=kzgFRuH9rnE](https://www.youtube.com/watch?v=kzgFRuH9rnE)
Enhance the rigor and reproducibility of clinical trial protocols

Promote greater availability of multisite clinical trial infrastructure to support trials from a wider range of investigators

Facilitate data sharing and access to biospecimens to efficiently expand research capacity for all investigators

Facilitate greater involvement of diverse populations in multisite clinical trials
NICHD Strategic Plan 2020

• **Goal #1:** Promoting an Inclusive Scientific Workforce
• **Goal #2:** Facilitating Data Sharing and Access to Biospecimens
• **Goal #6:** Improving Clinical Trial Oversight and Management
Initiative Background

• Process is needed to operationalize guiding principles
• NICHD conducted extensive assessment to inform this process
  • Request For Information (NOT-HD-19-041)
  • Landscape Analysis of best clinical practices across the NIH

• Centralized approach
  • NICHD supports Network infrastructure
  • Any qualified investigator can use the infrastructure
  • All applications/protocols undergo NIH peer review

• A dedicated funding opportunity announcement is proposed to solicit clinical trial applications to leverage the NICHD Network Infrastructure
Goals of the Initiative

*Enhancing rigor and reproducibility*

- Develop new protocol proposal and selection processes to increase transparency and rigor of Network study selection
- Future trials to be conducted within the Network infrastructure:
  - Will be submitted as individual NIH applications
  - Will undergo NIH peer review
  - Funding decisions will be made by NICHD
Goals of the Initiative

*Promoting greater availability of multisite clinical trial infrastructure to support trials from a wider range of investigators*

• Investigators from outside the Network will now be able to propose studies to be conducted in the Network

• Investigators from Network Clinical Centers will also be eligible to propose studies via the proposed funding opportunity announcement

• Studies will need to align with the purpose, goals and objectives of the Network and NICHD priorities
Goals of the Initiative

Facilitating data sharing and access to biospecimens

• Networks will be required to share data and biospecimens according to the NIH Policy for Data Management and Sharing

• Study consent forms to allow broad sharing and future use of study data

• Common Data Element use will be a priority of Network studies
Goals of the Initiative

Facilitating greater involvement of diverse populations in multisite clinical trials

• Ensuring diverse populations in multisite clinical trials
  • Participants
  • Investigators
• Trials will be expected to maximize inclusion of diverse study participants
• Develop diversity in the workforce (NOT-OD-20-031)
Operationalizing the Process

- Essential features of that approach
  - High priority science aligned with our Networks
  - Rigorous pre-application process
  - Peer Review process
  - Funding procedure
Operationalizing the Process

• Scientific areas
  • Start with a small focus and expand progressively
  • Identify Network synergies

• Rigorous pre-application process
  • Feasibility assessment
  • Alignment of science
    o Current state of the field
    o Societal needs
    o Network mission
    o Institute priorities
MFMU and NRN Request For Applications

Reissue of RFA-HD-16-019


RFA-HD-23-016

RFA-HD-23-017, U24 Resource-Related Research Project (Cooperative Agreements)

NICHD Neonatal Research Network (NRN): Data Coordinating Center (U24 Clinical Trial Optional)

U24 Resource-Related Research Projects – Cooperative Agreements

Reissue of RFA-HD-18-010


RFA-HD-23-001

RFA-HD-23-002, U24 Resource-Related Research Projects – Cooperative Agreements

Reissue of RFA-HD-13-013


RFA-HD-23-017

RFA-HD-23-016, UG1 Clinical Research Cooperative Agreements - Single Project

NICHD Maternal-Fetal Medicine Units (MFMU) Network: Clinical Centers (UG1 Clinical Trial Optional)

UG1 Clinical Research Cooperative Agreements - Single Project

Reissue of RFA-HD-16-020


RFA-HD-23-002

RFA-HD-23-001, U24 Resource-Related Research Project (Cooperative Agreements)

NICHD Maternal-Fetal Medicine Units (MFMU) Network: Data Coordinating Center (U24 Clinical Trial Optional)

U24 Resource-Related Research Projects – Cooperative Agreements

Reissue of RFA-HD-13-013


RFA-HD-23-001
Operationalizing the Process

• Scientific areas
  • Start with a small focus and expand progressively
  • Identify Network synergies
• Rigorous pre-application process
  • Feasibility assessment
  • Alignment of science
    o Current state of the field
    o Societal needs
    o Network mission
    o Institute priorities
Operationalizing the Process

• Peer Review process
  • Network Clinical trials will undergo NIH peer review
  • Special emphasis panel

• Funding procedure
  • Cost neutral
  • Various models (e.g. StrokeNet)
  • Model that optimizes Network infrastructure
Moving forward

• Much work left to be done
• Expected Impact
  • Expand the breadth and diversity of our science and investigators
  • Enhance rigor and transparency of Network clinical trials
  • Perform clinical trials in the most efficient and cost-effective manner
  • Assure alignment with the NICHD Strategic Plan
  • Identify novel and innovative interventions
  • Foster nimbleness and flexibility for emerging health crises
  • Augment the impact of the science that we support
Team Effort

Core Group
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Scientific Programmatic Branch Chiefs

Administrative Support
- Ashley Walton
“It is not important for us to be right, but that we get it right.”

- Rohan Hazra 2022
Thank you, National Advisory Child Health and Human Development Council for allowing me to present and for all the great work that you do to support the mission of the NICHD!