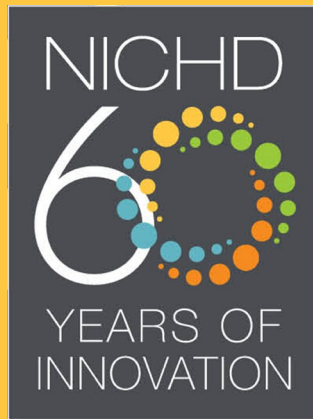




Multicenter Clinical Trials: Leveraging Network Infrastructure to Advance Research and Outcomes for Women, Children, and Pregnant and Lactating Individuals

NACHHD June Council 2022

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



Eunice Kennedy Shriver National Institute
of Child Health and Human Development



Initiative Background

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

- 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

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

ORIGINAL ARTICLE

A Trial of Hyperimmune Globulin to Prevent Congenital Cytomegalovirus Infection

B.L. Hughes, R.G. Clifton, D.J. Rouse, G.R. Saade, M.J. Dinsmoor, U.M. Reddy, R. Pass, D. Allard, G. Mallett, L.M. Fette, C. Gyamfi-Bannerman, M.W. Varner, W.H. Goodnight, A.T.N. Tita, M.M. Costantine, G.K. Swamy, R.S. Gibbs, E.K. Chien, S.P. Chauhan, Y.Y. El-Sayed, B.M. Casey, S. Parry, H.N. Simhan, P.G. Napolitano,

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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 Investigator Groups

ORIGINAL ARTICLE

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

Edward M. Connor, Rhoda S. Sperling, Richard Gelber, Pavel Kiselev, Gwendolyn Scott, Mary Jo O'Sullivan, Russell VanDyke, Mohammed Bey, William Shearer, Robert L. Jacobson, Eleanor Jimenez, Edward O'Neill, et al., for the Pediatric AIDS Clinical Trials Group Protocol 076 Study Group*

JAMA | Original Investigation

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

JAMA | Original In

Effect of U Ligament Behavior on Surgical at 5 Years in the OPTIMAL

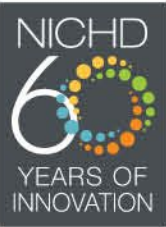
Abbot R. Laptook, MD; Seetha Shankaran, MD; Jon E. Tyson, MD, MPH; Breda Munoz, PhD; Edward F. Bell, MD; Ronald N. Goldberg, MD; Nehal A. Parikh, DO, MS; Namasivayam Ambalavanan, MD; Claudia Pedroza, PhD; Athina Pappas, MD; Abhik Das, PhD; Aasma S. Chaudhary, BS, RRT; Richard A. Ehrenkranz, MD; Angelita M. Hensman, MS, RNC-NIC; Krisa P. Van Meurs, MD; Lina F. Chalak, MD, MSCS; Amir M. Khan, MD; Shannon E. G. Hamrick, MD; Gregory M. Sokol, MD; Michele C. Walsh, MD, MS; Brenda B. Poindexter, MD, MS; Roger G. Faix, MD; Kristi L. Watterberg, MD; Ivan D. Frantz III, MD; Ronnie Guillet, MD, PhD; Uday Devaskar, MD; William E. Truog, MD; Valerie Y. Chock, MD, MS-Epi; Myra H. Wyckoff, MD; Elisabeth C. McGowan, MD; David P. Carlton, MD; Heidi M. Harmon, MD, MS; Jane E. Brumbaugh, MD; C. Michael Cotten, MD, MHS; Pablo J. Sánchez, MD; Anna Maria Hibbs, MD; Rosemary D. Higgins, MD; for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

ORIGINAL ARTICLE

etrozole versus Clomiphene for Infertility in the Polycystic Ovary Syndrome

ard S. Legro, M.D., Robert G. Brzyski, M.D., Ph.D., Michael P. Diamond, M.D., stos Coutifaris, M.D., Ph.D., William D. Schlaff, M.D., Peter Casson, M.D., ory M. Christman, M.D., Hao Huang, M.D., M.P.H., Qingshang Yan, Ph.D., uben Alvero, M.D., Daniel J. Haisenleder, 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., Dana Ohl, M.D., tte Santoro, M.D., Esther Eisenberg, M.D., M.P.H., and Heping Zhang, Ph.D., for the NICHD Reproductive Medicine Network*

Initiative Background



Building Better Clinical Trials through Stewardship and Transparency

By Mike Lauer and Carrie Wolinetz

Posted September 16, 2016



- 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*
 - <https://grants.nih.gov/grants/guide/notice-files/NOT-HD-19-034.html>
 - Webinar: *Strategic Plan 2020 Implementation: NICHD's vision for multi-site clinical trials infrastructure*
 - <https://www.youtube.com/watch?v=kzgFRuH9rnE>



Notice Number: NOT-HD-19-034

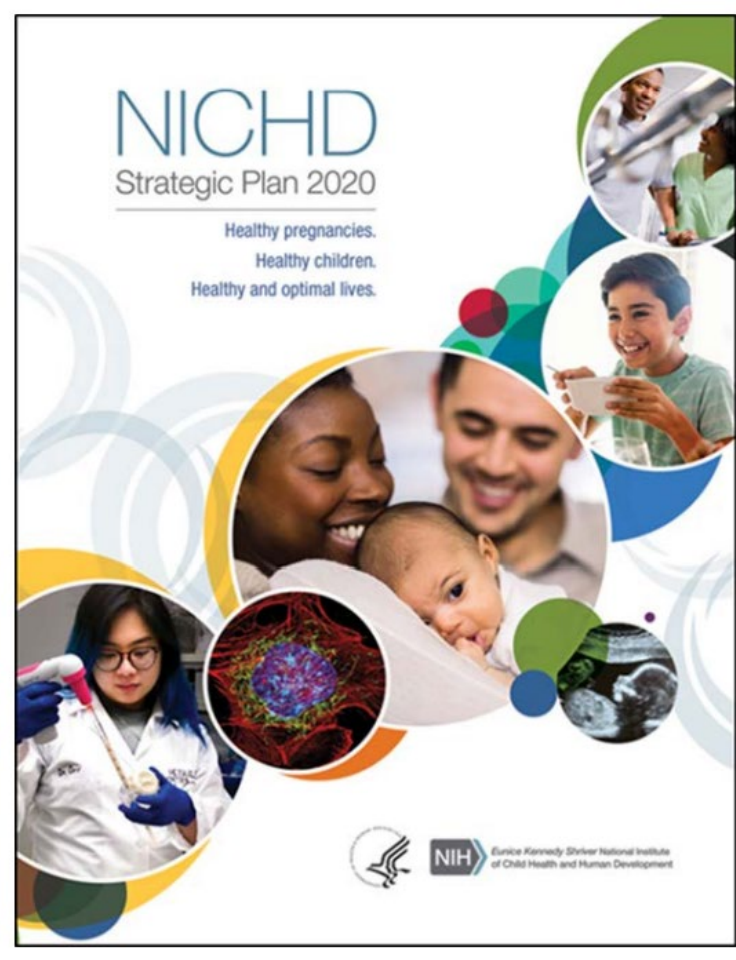
Key Dates

Release Date: October 10, 2019

Related Announcements

- ***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)
 - <https://grants.nih.gov/grants/guide/notice-files/NOT-HD-19-041.html>
 - 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
 - Current state of the field
 - Societal needs
 - Network mission
 - Institute priorities



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

[UG1 Clinical Research Cooperative Agreements - Single Project](#)

Reissue of [RFA-HD-16-019](#)

- **May 19, 2022** - Notice of Pre-Application Webinars for the Maternal-Fetal Medicine Units Network and Neonatal Research Network Funding Opportunity Announcements. See Notice [NOT-HD-22-023](#)

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](#)

- **May 19, 2022** - Notice of Pre-Application Webinars for the Maternal-Fetal Medicine Units Network and Neonatal Research Network Funding Opportunity Announcements. See Notice [NOT-HD-22-023](#)

RFA-HD-23-001

[RFA-HD-23-002](#), [UG1 Clinical Research Cooperative Agreements - Single Project](#)

NICHD Neonatal Research Network (NRN): Clinical Centers (UG1 Clinical Trial Optional)

[UG1 Clinical Research Cooperative Agreements - Single Project](#)

Reissue of [RFA-HD-16-020](#)

- **May 19, 2022** - Notice of Pre-Application Webinars for the Maternal-Fetal Medicine Units Network and Neonatal Research Network Funding Opportunity Announcements. See Notice [NOT-HD-22-023](#)

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](#)

- **May 19, 2022** - Notice of Pre-Application Webinars for the Maternal-Fetal Medicine Units Network and Neonatal Research Network Funding Opportunity Announcements. See Notice [NOT-HD-22-023](#)

RFA-HD-23-017

[RFA-HD-23-016](#), [UG1 Clinical Research Cooperative Agreements - Single Project](#)



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
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 - Network mission
 - 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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- David Weinberg
- Yasaman Shirazi
- Dennis Twombly
- Bill Duval
- Kathryn Adams
- Rebekah Rasooly
- Rohan Hazra

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- Cathy Wedeen

Clinical Trials Working Group

- Maria Stagnitto
- Sue Marden

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!**

