NICHD Director's Report

Diana W. Bianchi, M.D.
NICHD Director
June 11, 2019

Talk Outline

- FY 2020 Appropriations
- Updates on Selected NICHD Initiatives
  - Maternal Mortality
  - Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)
  - INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome (INCLUDE)
  - Data and Specimen Hub (DASH)
- Institute and Center Leadership at NIH

House Appropriations Hearing for NIH FY 2020 Budget

- Testified at the FY 2020 House appropriations hearing with Drs. Collins, Fauci (NIAID), Gibbons (NHLBI), Lowy (NCI), and Volkow (NIDA)
- Fielded questions about:
  - Maternal mortality
  - Task Force on Research Specific to Pregnant Women and Lactating Women
  - Newborn screening
  - Postpartum depression
  - Pediatric research

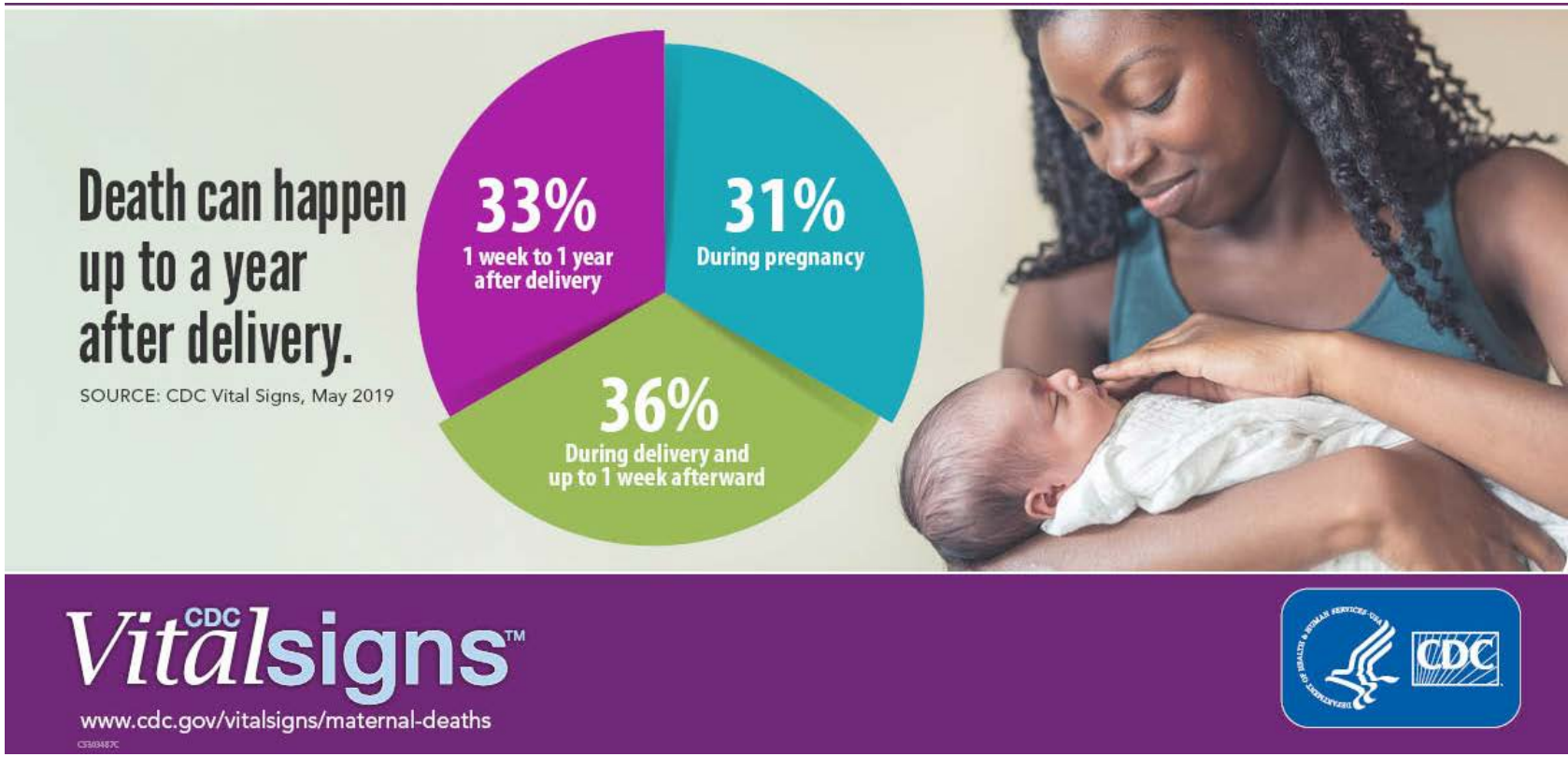
Next Steps in FY 2020 Appropriations

- Strong bipartisan support expressed for NIH funding
- House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies marked up a bill that included:
  - $41.1 billion for NIH (+2 billion)
  - $1.580 billion for NICHD (+80 million over FY 2019)
  - $12.6 million for Gabriella Miller Kids First program
- House Appropriations Full Committee markup held May 8
- 5 of 12 appropriations bills (including Labor-HHS) packaged together to be considered on House floor this week
- Senate markup expected in June

Maternal Mortality – New CDC Analysis

- Every 12 hours a woman dies in the US as a complication of childbirth
- ~60% of maternal deaths deemed preventable
- Data confirm persistent racial disparities
- Obstetric emergencies cause most deaths at delivery
- Heart disease and stroke caused more than 1 in 3 deaths
- Cardiomyopathy leading cause of death 1 week to 1 year postpartum

Data from 2011-2015 national pregnancy-related death data and 2013-2017 data from maternal mortality review committees in 13 states



Maternal Mortality: A Public Health Priority

- NICHD is sponsoring a series of meetings aimed at updating the research agenda on maternal mortality
- Community Engagement Forum on Improving Maternal Health – April 8
  - Community-based and healthcare provider groups discussed community engagement strategies to improve maternal health
  - More than 400 participants, in-person and virtually
  - Facebook Live received 11,000 views within the first week following the Forum

Dr. LaQuandra Nesbitt
Director, DC Department of Health

Maternal Mortality: A Public Health Priority

- Manuscript - “Importance of Research in Reducing Maternal Morbidity and Mortality” – accepted for publication by American Journal of Obstetrics and Gynecology
- *Maternal Mortality in the United States: Future Research Directions* workshop – May 2-3
  - Goal: Develop a research agenda to address maternal mortality in the U.S.
  - Discussions included:
    - Data quality and trends
    - Disparities
    - Social determinants
    - Clinical causes
- NIH is establishing a working group with CMS to explore opportunities to use their data to address research questions
- NICHD is supporting a NASEM study on choice of birth settings, including risk factors, social determinants that influence risk, and maternal health outcomes,
  - Recommendations expected in 2020
- Upcoming workshop – co-morbid conditions (e.g., obesity, hypertension, diabetes) to be held in early 2020

Pregnancy and Lactation

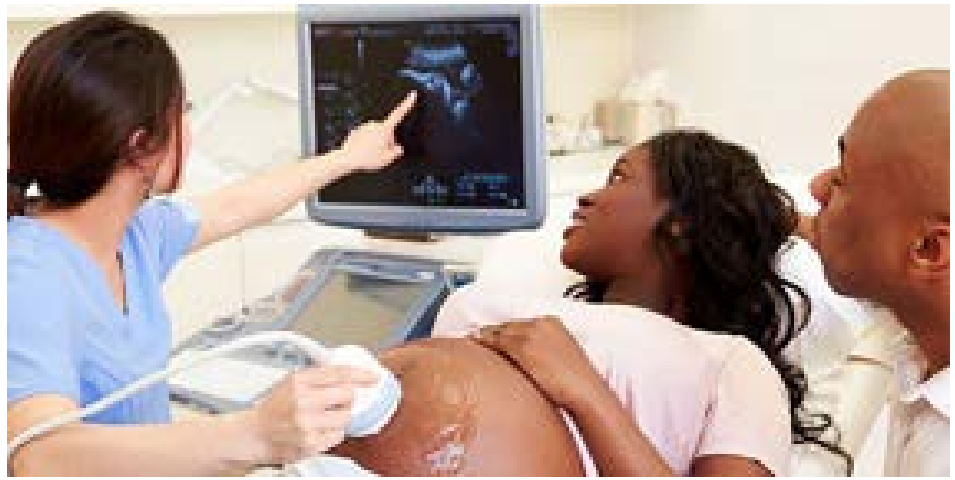
- 6.3M women in the US become pregnant each year
  - >90% take medications; 70% of these are prescribed
  - 98% of medications have data insufficient to determine teratogenicity risk
  - 98% of dosing studies do not include pregnant women
- Pregnancy is complex
  - Fetus/placenta change over gestation, timing of exposure is important
  - Physiologic changes in mother due to pregnancy
  - Impact of external factors: maternal obesity, environment
  - Co-existing chronic or acute medical conditions in mother
- Concerns re: liability
- Lactation
  - 500,000 women have difficulty making milk
  - Must consider benefits of breastfeeding vs. medications
  - Limited assays for assessment of medications in breast milk

Brief Review of PRGLAC Recommendations

- Report submitted to HHS Secretary and Congress in September 2018
- Key recommendations included:
  - Change existing culture that has limited scientific knowledge of therapeutic product safety, effectiveness, and dosing for pregnant and lactating women
  - Protect pregnant women *through* research instead of *from* research
  - 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

Plan for PRGLAC – Phase 2

- Charter extended until March 2021
- Will hold 2 meetings of the full Task Force per year (required in legislation)
  - Charge call held on May 22, 2019
  - August 22-23, 2019
- Establish four working groups to address subsets of the recommendations and develop plans for implementation
  - Research/Training
  - Regulatory
  - Communication
  - Discovery
- Existing members divided into the four working groups
- Will add additional *ad hoc* members as needed to fill in missing expertise



PRGLAC - Strong Federal Partners

- Federal partners are included in all PRGLAC working groups
- Recent FDA draft guidances
  - Scientific and Ethical Considerations for Inclusion of Pregnant Women in Clinical Trials (April 2018)
  - Clinical Lactation Studies: Considerations for Study Design (May 2019)
  - Post-approval Pregnancy Safety Studies Guidance for Industry (May 2019)
- FDA Center of Excellence for Perinatal and Maternal Health (PHCE) recently established
  - Funded 14 proposals from across FDA, from end-user testing to improve communications around pregnancy and lactation labeling to testing placental drug transfer using tissue chips

The NIH INCLUDE Project

- Trans-NIH initiative included in FY 2018 budget legislation
- Purpose: to investigate conditions that affect individuals with Down syndrome and the general population
- Three components to address key quality-of-life issues:
  1. Conduct targeted, high-risk, high-reward basic science studies on chromosome 21
  2. Assemble a large study population of individuals with Down syndrome
  3. Include individuals with Down syndrome in existing clinical trials
- Unique double benefit: understanding both **Down syndrome** and **shared common conditions** (risks or resiliencies)

The NIH INCLUDE Project

- $22.2M awarded in FY18 across NIH
- NICHD issued 4 FOAs in FY19; awards made by September
- Workshops in development
  - “Planning a Virtual Down Syndrome Cohort across Lifespan”
  - “The State of the Science for Meaningful Clinical Trials in Down syndrome”
- **New NICHD project**
  - Leveraging NICHD’s Pediatric Trials Network to establish infrastructure for Down syndrome clinical trials
  - Develop training programs on effective ways for practitioners to work with IDD populations

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

DASH Data and Specimen Hub

https://dash.nichd.nih.gov

Study Topics in DASH (*biospecimens available)

- Autism Spectrum Disorders
- Birth Defects
- Cerebral Palsy
- Children's Bone Health & Calcium
- Diabetes
- Driving Risk
- Early Learning
- High-Risk Pregnancy & Pregnancy Loss
- HIV/AIDS*
- Infant Care & Health
- Infant Mortality
- Infertility & Fertility
- Labor & Delivery
- Neuroscience
- Necrotizing Enterocolitis
- Obesity & Overweight
- Obstetrics
- Pediatric Injury
- Pelvic Floor Disorder
- Pharmacology
- Preconception & Prenatal Care
- Preeclampsia & Eclampsia
- Pregnancy*
- Preterm Labor & Birth*
- Primary Ovarian Insufficiency
- Rehabilitation Medicine
- Sleep
- Spinal Cord Injury
- Stillbirth
- Stroke
- Sudden Infant Death Syndrome
- Traumatic Brain Injury
- Turner Syndrome
- Women's Health

- **Centralized resource for researchers to store de-identified data and to access data and associated biospecimens from NICHD supported studies**
- **Can help investigators meet NIH's data sharing requirements for their own studies**
- **Data sharing launched in August 2015; biospecimen request launched in March 2019**
- **Governed by the NICHD DASH Committee**
- **Aims to accelerate scientific findings to ultimately improve human health**

134 Studies | **35** Study Topics | **141** Data Requests | **15** Data Use Publications | **8** Studies Offering Biospecimens

Questions? Contact supportdash@mail.nih.gov

For NICHD studies not archived in DASH, visit: https://dash.nichd.nih.gov/Resource/LinksToOtherArchives

Last Updated 05/31/2019

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

DASH Data and Specimen Hub

https://dash.nichd.nih.gov

Study Topics with Biospecimens in DASH	
HIV/AIDS Pregnancy	Preterm Labor & Birth More to come!

Biospecimens Currently Available	
Amniotic Fluid Blood Breastmilk DNA/RNA/Proteins Saliva	Serum Plasma Tissue Samples Urine Vaginal Fluid

New DASH Function:

Managing Requests for NICHD Biospecimens

- **Genomic and Proteomic Network for Preterm Birth Research (GPN)**
  Expression profiling, GWAS case control, and longitudinal cohort studies
- **NICHD International Site Development Initiative (NISDI)**
  4 studies of pregnant women with HIV, their infants with and exposed to HIV, and children with and exposed to HIV in Latin American Countries
- **Mothers and Infants Cohort Study (MICS)**
  Study of perinatal transmission of HIV and developmental outcomes of children with HIV

8 Studies Offering Biospecimens

Questions? Contact supportdash@mail.nih.gov

For NICHD studies not archived in DASH, visit: https://dash.nichd.nih.gov/Resource/LinksToOtherArchives

Last Updated 04/30/2019

Sample Publications from DASH Data Reuse

Maternal and Neonatal Outcomes of Induction of Labor Compared with Planned Cesarean Delivery in Women with Preeclampsia at 34 Weeks' Gestation or Longer

Tetsuya Kawakita, MD[1] Katherine Bowers, PhD[2]

[1] Department of Obstetrics and Gynecology, MedStar Washington Hospital Center, Washington, District of Columbia
[2] Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

Am J Perinatol 2018;35:95–102.

Abstract

Objective This study aims to
in women with preeclampsia.
Study Design A retrospectiv
nancies, preeclampsia (mild, s
ean at ≥ 34 weeks' gestation
(intensive care unit [ICU] adm
omy), composite severe neona
ischemic encephalopathy, an
admission, transient tachypne
(RDS). Adjusted odds ratios (aO
controlling for confounders.
Results Of 5,506 women with
women underwent induction.
associated with an increased ri
risks of ICU admission (aOR: 3.
composite neonatal outcome
0.60; 95% CI: 0.43–0.84), TTN (

Keywords

BMJ Open

Impact of gestational weight gain and prepregnancy body mass index on the prevalence of large-for-gestational age infants in two cohorts of women with type 1 insulin-dependent diabetes: a cross-sectional population study

Ketrell L McWhorter,[1,2,3] Katherine Bowers,[2] Lawrence M Dolan,[4] Ranjan Deka,[1] Chandra L Jackson,[3] Jane C Khoury[2,4]

To cite: McWhorter KL, Bowers K, Dolan LM, *et al*. Impact of gestational weight gain and prepregnancy body mass index on the prevalence of large-for-gestational age infants in two cohorts of women with type 1 insulin-dependent diabetes: a cross-sectional population study. *BMJ Open* 2018;**8**:e019617. doi:10.1136/bmjopen-2017-019617

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2017-019617).

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Accepted 12 February 2018

ABSTRACT

Objectives Despite improvements in treatment modalities, large-for-gestational age (LGA) prevalence has remained between 30% and 40% among infants of mothers with type 1 insulin-dependent diabetes mellitus (TIDM). Our objective was to estimate LGA prevalence and examine the association between gestational weight gain (GWG) and prepregnancy body mass index (BMI) with LGA among mothers with TIDM.
Design Cross-sectional study.
Setting Regional data in Cincinnati, Ohio, from the Diabetes in Pregnancy Program Project (PPG), a prospective cohort for the period 1978–1993; national data from Consortium on Safe Labor (CSL), a multicentre cross-sectional study for the period 2002–2008.
Participants The study included 333 pregnancies in the PPG and 358 pregnancies in the CSL. Pregnancies delivered prior to 23 weeks' gestation were excluded. Women with TIDM in the PPG were identified according to physician confirmation of ketoacidosis, and/or c-peptide levels, and by International Classification of Diseases, ninth version codes within the CSL. LGA was identified as birth weight >90th percentile according to gestational age, race and sex.
Main outcome measures LGA at birth.
Results Mean±SD maternal age at delivery was 26.4±5.1 years for PPG women and 27.5±6.0 years for CSL women, p=0.008. LGA prevalence did not significantly differ between cohorts (PPG: 40.2% vs CSL: 36.6%, p=0.32). More women began pregnancy as overweight in the later cohort (PPG (16.8%) vs CSL (27.1%), p<0.001). GWG

Nonmedically Indicated Induction of Labor Compared with Expectant Management in Nulliparous Women Aged 35 Years or Older

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[2] Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio
[3] Division of Endocrinology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

Am J Perinatol 2019;36:45–52.

Abstract

Objective This article con
≥ 35 years who experience
expectant management.
Study Design This was a re
a singleton and cephalic
compared between wome
gestation and those with e
(aORs) with 95% confiden
predefined covariates.
Results Of 3,819 nullipara
Overall at 39 weeks' gestati
or improved with NMII. At
expectant management was
38, and 39 weeks' gestatio
management was associate
decreased odds of neonatal
Conclusion In nulliparous
decreased odds of cesarea
odds of NICU admission
management.

Keywords
- cesarean delivery
- expectant management
- induction of labor
- macrosomia
- neonatal intensive care unit

Journal of Perinatology (2017) 37, 335–339

www.nature.com/jp

ORIGINAL ARTICLE

Racial and social predictors of longitudinal cervical measures: the Cervical Ultrasound Study

EW Harville[1], KS Miller[2] and LR Knoepp[3]

OBJECTIVE: To evaluate whether the racial and socioeconomic disparities are present in adverse cervical parameters, and, if so, when such disparities develop.
STUDY DESIGN: A prospective cohort study was conducted. 175 women with a prior preterm birth had up to four endovaginal ultrasounds between gestational weeks 16 and 24 (Cervical Ultrasound Trial of the MFMU). Each sociodemographic factor (race/ethnicity, marital status, insurance funding and education) was examined as a predictor of short cervix or U/funnel shape, using multiple logistic and linear regression. Changes in the cervical length and shape across pregnancy and after pressure were also examined.
RESULTS: The strongest associations were seen between race and government-funded insurance and short cervix and U shape per funneling (race and length <25 mm per funnel: adjusted odds ratio (OR) 5.52, 2.24 to 13.63; government-funded insurance and length <30 mm per funnel: adjusted OR 3.10, 1.34 to 7.15). Changes in cervical length were not associated with sociodemographics.
CONCLUSION: African-American race and, to a lesser extent, insurance funder, are associated with cervical length and shapes that have been associated with preterm birth, and those properties are present largely early in pregnancy.

Journal of Perinatology (2017) **37,** 335–339; doi:10.1038/jp.2016.240; published online 12 January 2017

INTRODUCTION

Even in the absence of clinical cervical insufficiency, shorter cervix is associated with preterm birth (PTB).[1] In the United States, the most striking epidemiologic feature of PTB is the disparity between African-American women and other racial/ethnic groups;[2] gradient relationships, with those at highest social risk also having the highest medical risk, are also seen between other socioeconomic indicators, such as poverty and education, and PTB.[3] A study of 5092 Dutch women found that white ethnicity was associated with longer cervical length, while women of African origin had the shortest mean cervical length.[4] There are also racial disparities in cervical insufficiency: an analysis of the US Natality file found that African Americans are more prone to cervical insufficiency than European Americans,[5] although other socioeconomic risk factors for preterm birth, such as marital status and education, were not related. While genetics have a role in cervical structure and function,[6] immigrant studies do not suggest genetic differences as a major cause for between-population disparities.[7,8]

The key role of the cervix in parturition has led to examination of cervical measures (length, shape, length after pressure, changes in length or shape, funneling) especially when repeated, as possible predictors of PTB. The Cervical Ultrasound Study (CRVUS) associated with increased risk of early preterm birth in CRVUS, results were imprecise.

We are not aware of studies that have more extensively examined the relationship between social factors and cervical length and changes in length or shape early in pregnancy. Although cervical length is the major cervical property known to be clinically predictive of preterm birth,[10] cervical shape and changes in length and shape are also associated with, if not diagnostic for, PTB. A major goal of this research field is to determine the pathophysiologic mechanisms that create health disparities and the times during which interventions are most likely to be useful. In this analysis, we consider social influences on cervical length, shape, and changes.

MATERIALS AND METHODS

This study is a secondary analysis of the 'Mid-trimester endovaginal sonography in women at high risk for spontaneous preterm delivery' study (Cervical Ultrasound Study/CRVUS) of the Maternal-Fetal Medicine Units (MFMU) Network. The goal of the study was to determine the predictive value of longitudinal cervical sonographic data collected prior to 24 weeks in predicting spontaneous preterm birth at <35 weeks' gestation, including for cervical characteristics other than length. The study has been described in detail previously.[1] 187 participants were recruited between 1997 and 1999 from nine sites (University of Alabama, Wayne

Institute and Center Leadership at NIH

New Director for National Institute on Deafness and Other Communication Disorders (NIDCD)

- Debara L. Tucci, M.D., M.S., M.B.A., is expected to join NIDCD in September 2019
- Dr. Tucci comes to NIH from the Division of Head and Neck Surgery & Communication Sciences at Duke University
- 10 of 27 IC Directors are now women

NIH ICs and Directors

National Cancer Institute – Doug Lowy (Acting)

National Eye Institute – Paul Sieving

National Heart, Lung, and Blood Institute – Gary Gibbons

National Human Genome Research Institute – Eric Green

National Institute on Aging – Richard Hodes

National Institute on Alcohol Abuse and Alcoholism – George Koob

National Institute of Allergy and Infectious Diseases – Tony Fauci

National Institute of Arthritis and Musculoskeletal and Skin Diseases – Bob Carter (Acting)**

National Institute of Biomedical Imaging and Bioengineering – Bruce Tromberg

***Eunice Kennedy Sh*river National Institute of Child Health and Human Development – Diana Bianchi**

National Institute on Deafness and Other Communication Disorders – Debara Tucci

National Institute of Dental and Craniofacial Research – Martha Somerman

National Institute of Diabetes and Digestive and Kidney Diseases – Griffin Rodgers

National Institute on Drug Abuse – Nora Volkow

National Institute of Environmental Health Sciences – Linda Birnbaum

National Institute of General Medical Sciences – Jon Lorsch

National Institute of Mental Health – Josh Gordon

National Institute on Minority Health and Health Disparities – Eliseo Perez-Stable

National Institute of Neurological Disorders and Stroke – Walter Koroshetz

National Institute of Nursing Research – Ann Cashion (Acting)**

National Library of Medicine – Patricia Brennan

National Institutes of Health Clinical Center – James Gilman

Center for Information Technology – Andrea Norris

Center for Scientific Review – Noni Byrnes

Fogarty International Center – Roger Glass

National Center for Advancing Translational Sciences – Christopher Austin

National Center for Complementary and Integrative Health – Helene Langevin

We are Hiring!

- Executive Officer – final stages of hiring process
- Deputy Director – interviews concluded
- Extramural Branch Chief Positions: Pregnancy and Perinatology, Child Development and Behavior
- Medical and Program Officers in Division of Extramural Research

Thank You and Questions