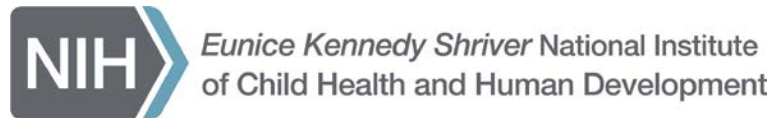


NICHD Director's Report

Diana W. Bianchi, M.D.

June 11, 2020



Talk Outline

- Budget
- COVID-19
- NICHD Strategic Plan Implementation
- Maternal Mortality
- INCLUDE (INvestigating Co-occurring conditions across the Lifespan to Understand Down syndromE)
- NICHD Staff Updates

FY 2020 and FY 2021 Appropriations

- Federal government currently funded through September 30, 2020
- FY 2021 Proposed President's Budget
 - 12% cut to NIH
 - Testified at House Subcommittee on March 4
- COVID-19 Stimulus Funds
 - H.R. 748 Coronavirus Aid, Relief, and Economic Security Act (CARES Act)
 - \$945.4 million to NIH to “prevent, prepare for, or respond to coronavirus, domestically or internationally”
 - Specific funding for NIAID, NHLBI, NIBIB, NCATS, NLM, and the OD





COVID-19

Large Trans-NIH Efforts: ACTIV

VIEWPOINT

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) An Unprecedented Partnership for Unprecedented Times

Francis S. Collins, MD, PhD
Office of the Director,
National Institutes of
Health, Bethesda,
Maryland.

Paul Stoffels, MD
Johnson & Johnson,
New Brunswick,
New Jersey.

It has been more than a century since the world has encountered a pandemic like coronavirus disease 2019 (COVID-19), and the rate of spread of COVID-19 around the globe and the associated morbidity and mortality have been staggering.¹ To address what may be the greatest public health crisis of this generation, it is imperative that all sectors of society work together in unprecedented ways, with unprecedented speed. In this Viewpoint, we describe such a partnership.

First reported in Wuhan, China, in December 2019, COVID-19 is caused by a highly transmissible novel coro-

academic experts. Participants sought urgently to identify research gaps and to discuss opportunities to collaborate in an accelerated fashion to address the complex challenges of COVID-19.

These critical discussions culminated in a decision to form a public-private partnership to focus on speeding the development and deployment of therapeutics and vaccines for COVID-19. The group assembled 4 working groups to focus on preclinical therapeutics, clinical trial capacity, and In addition to the founding memb

To address what may be the greatest public health crisis of this generation, it is imperative that all sectors of society work together in unprecedented ways, with unprecedented speed.

Figure. The Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Partnership

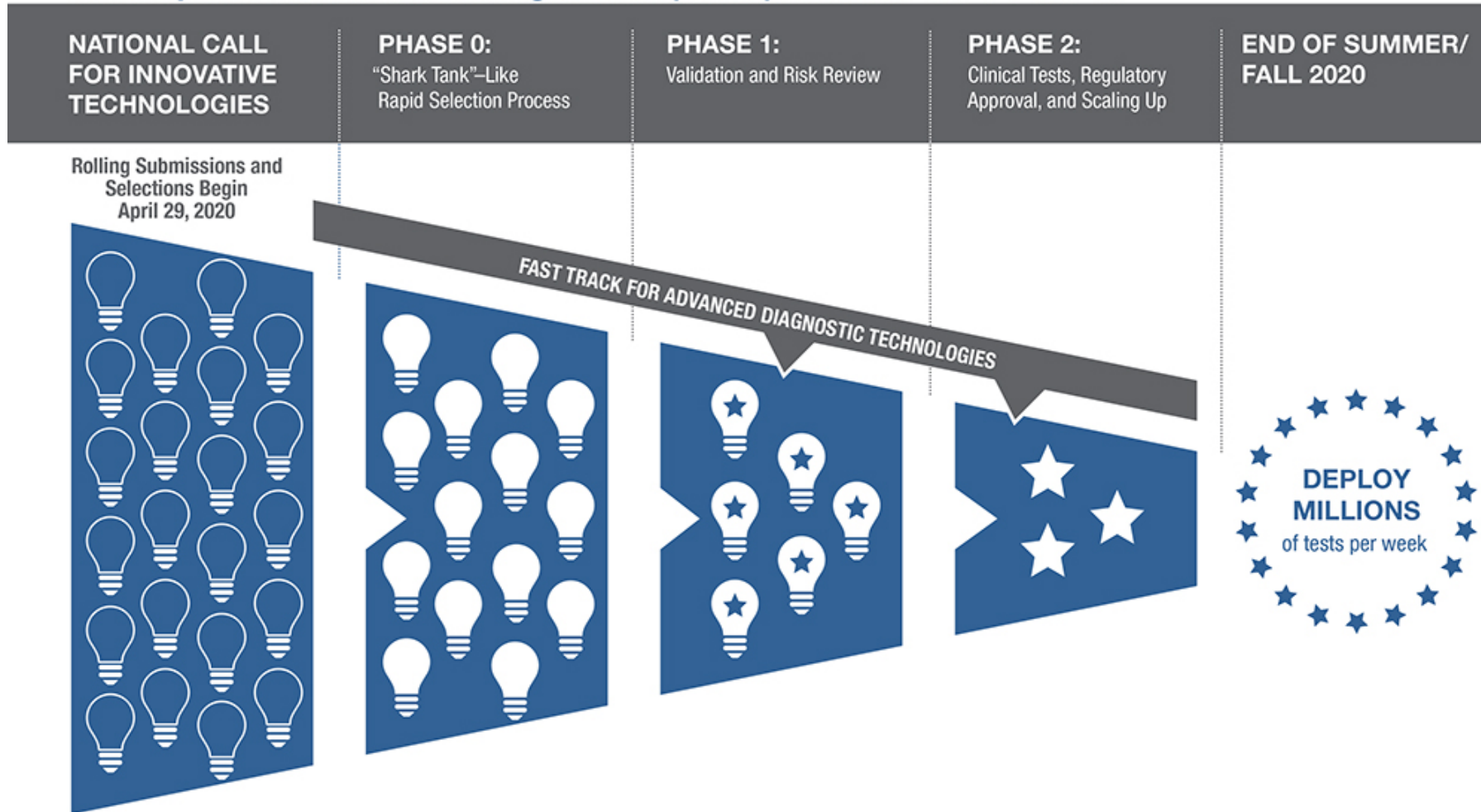


COVID-19 indicates coronavirus disease 2019; FDA, Food and Drug Administration; and NIH, National Institutes of Health.



Large Trans-NIH Efforts: RADx

NIH Rapid Acceleration of Diagnostics (RADx) Initiative for COVID-19



**RADx-TECH
RADx-UP
RADx-RAD
RADx-ATP**



COVID-19: NICHD's Goals and Objectives

We are working to accelerate research and better understand the impact of COVID-19 infection on our populations: pregnant and lactating women, children, and people with intellectual, developmental, and physical disabilities.

- **First**, we engaged across NICHD to advance scientific understanding of SARS-CoV-2 and COVID-19, by:
 - **Identifying existing opportunities in our networks and intramural laboratories**
 - **Participating in trans-NIH funding opportunities and notices of special interest (NOSIs)**
 - **Working with the Department of HHS and our federal colleagues to address emerging concerns**



NICHD Intramural Research Efforts

More than a dozen NICHD intramural research labs rapidly responded to the need for COVID-19 research, temporarily shifting their focus and resources

Viral-like particle production

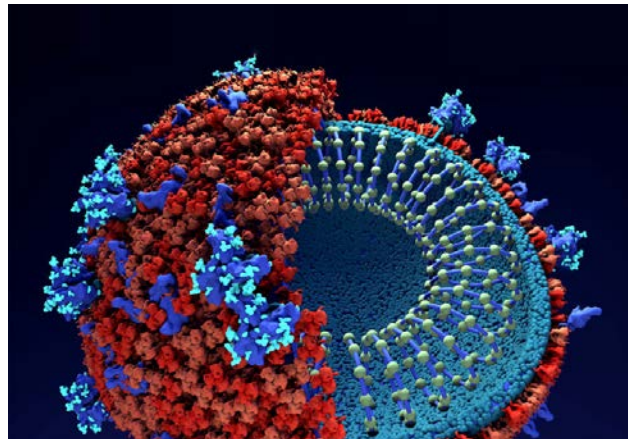
Production of viral-like particles that express SARS-CoV-2 spike protein and other envelope proteins suitable for vaccine production

Viral cell targets in the lung

Studies using human lung tissue to identify viral cell targets and preclinical studies of antiviral therapeutics; others using bronchial tissues to study virus inhibitors using EM

Point of Care multimodal biosensor

Development and testing of a biosensor used during pathogenesis and recovery using modalities such as NIRS (near-infrared spectroscopy), pulse oximetry and skin temperature



Preclinical therapeutic target identification and testing

Studying targets of the essential proteins in the enveloped virus, inhibitors of specific kinases, and inhibitors of specific host cell proteins for therapeutics

Molecular Biology of SARS-CoV-2

Studies of the physicochemical properties of the spike protein, its interaction with the host receptors, membrane activity, properties of the envelope protein, and requirements for blocking the virus at the molecular level

***In planning:** Studies of innate immune responses, nanomaterial protectants, therapeutic targets, roles of specific cofactors and binding sites*



NICHD Extramural Research Efforts

Pregnancy Registry

Conducted a COVID-19 pregnancy registry landscape analysis and began collaboration to connect the dots between registries

Opportunistic Pharmacokinetic Studies

The Pediatric Trials Network is performing opportunistic PK/PD characterization of several drugs used for treatment



Protocols and Toolkits

NIEHS, NLM, and collaborators catalogued protocols and tools in the PhenX Toolkit and Disaster Research Response (DR2)

Networks and Cohorts

Catalogued relevant networks and cohorts to promote collaboration as part of the multiple trans-NIH efforts

IC Planned and Future Research Activities

Determining out-year commitments needed to support IC-specific and Trans NIH efforts



Multisystem Inflammatory Syndrome in Children (MIS-C)

Coronavirus Live updates U.S. map World map Reopening tracker Lives lost Your life at home Your money

Children are falling ill with perplexing inflammatory syndrome thought to be linked to covid-19

Number of cases remains small, but officials are on high alert because of severity



Health

Young adults are also affected by Kawasaki-like disease linked to coronavirus, doctors say



Washington Post

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People™

Search

Coronavirus



Advanced Search

Coronavirus Disease 2019 (COVID-19)

CDC > Coronavirus Disease 2019 (COVID-19) > Daily Life & Coping > Caring for Children



Coronavirus Disease 2019 (COVID-19)

Symptoms

Testing

For Parents: Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19

Other Languages

Print Page

EurekaAlert!

AAAS

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COVID-19

NEWS RELEASES

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ABOUT

NEWS RELEASE 28-APR-2020

Boston Children's Hospital to lead nationwide study on COVID-19 in children

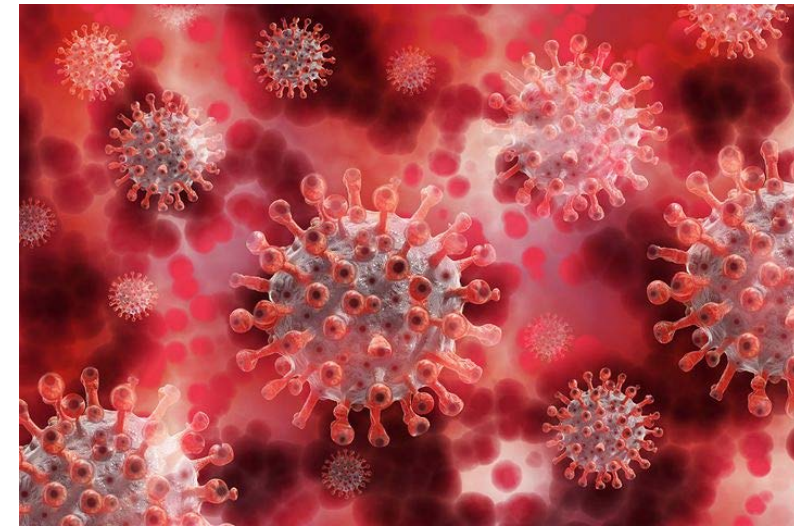
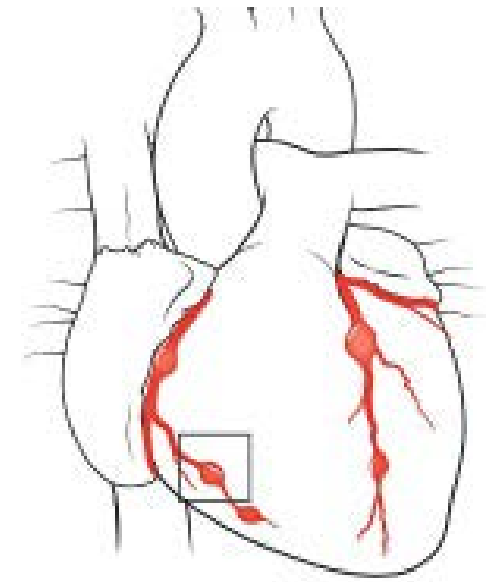
CDC-funded study will seek factors that increase vulnerability to the novel coronavirus

BOSTON CHILDREN'S HOSPITAL



MIS-C Clinical Presentation

- Fever ($\geq 38.0^{\circ}\text{C}$ for ≥ 24 hours)
- Laboratory evidence of inflammation
- Clinically severe illness requiring hospitalization, with multisystem (≥ 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
- Positive for current or recent SARS-CoV-2 infection or COVID-19 exposure within prior 4 weeks
- Observed variations
 - Full blown MIS-C (critically ill, in ICU)
 - Milder version of MIS-C (hospitalized, but not in ICU)
 - Significant respiratory involvement
 - Classic Kawasaki disease



Research Platform to Understand MIS-C

AT-RISK PEDIATRIC COVID-19 COHORT
(PREVAIL)

Goal: Large cohort to advance understanding of pediatric SARS-CoV-2 spectrum of illness

LONG-TERM FOLLOW UP
Goal: Ascertain outcomes, treatment effects, and long term, multisystem complications of MIS-C

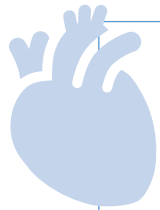
MIS-C COHORT PLATFORM
Goal: Comprehensive understanding of phenotypes, natural history, outcomes, pathobiology of MIS-C

Streamlined common data protocol, collection, robust cloud-based data sharing

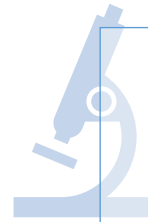


MIS-C COHORT PLATFORM

Goal: Comprehensive understanding of phenotypes, natural history, outcomes, and pathobiology



Longitudinal follow-up
(e.g., echo core lab)



Adaptive design trials
and trial prep (PK/PD
studies)



Deep phenotyping:
WGS, RNA seq,
Antibody profiling, etc.



Data platform to
support access and
computation



Data Coordinating
Center to aggregate
data



Leveraging and linking
existing cohorts and
networks



Pediatric Trials Network

- Purpose: Gather information on pharmacokinetics and safety of several drugs not typically used in children to define appropriate dosing of these drugs for COVID-19
- Incorporated opportunistic study of six drugs into an existing protocol:
 - Includes antiviral and anti-inflammatory drugs (e.g., Azithromycin, Chloroquine, Hydroxychloroquine, Lopinavir/Ritonavir, Ribavirin, and Tocilizumab)
 - Can add more products as they are implemented into care of children
- Partnered with nearly 50 study sites across the country to collect blood samples to
 - Characterize pharmacokinetics of these drugs across the pediatric age range
 - Collect information on drug safety and clinical course (e.g., date(s) of positive testing; duration and type of respiratory support; duration of hospitalization; mortality)
 - Develop partnerships with PIs around the country who are exploring the safety and efficacy of hydroxychloroquine and/or azithromycin



AT-RISK PEDIATRIC COVID-19 COHORT (PREVAIL)

Goal: Large cohort to advance understanding of pediatric SARS-CoV-2 spectrum of illness

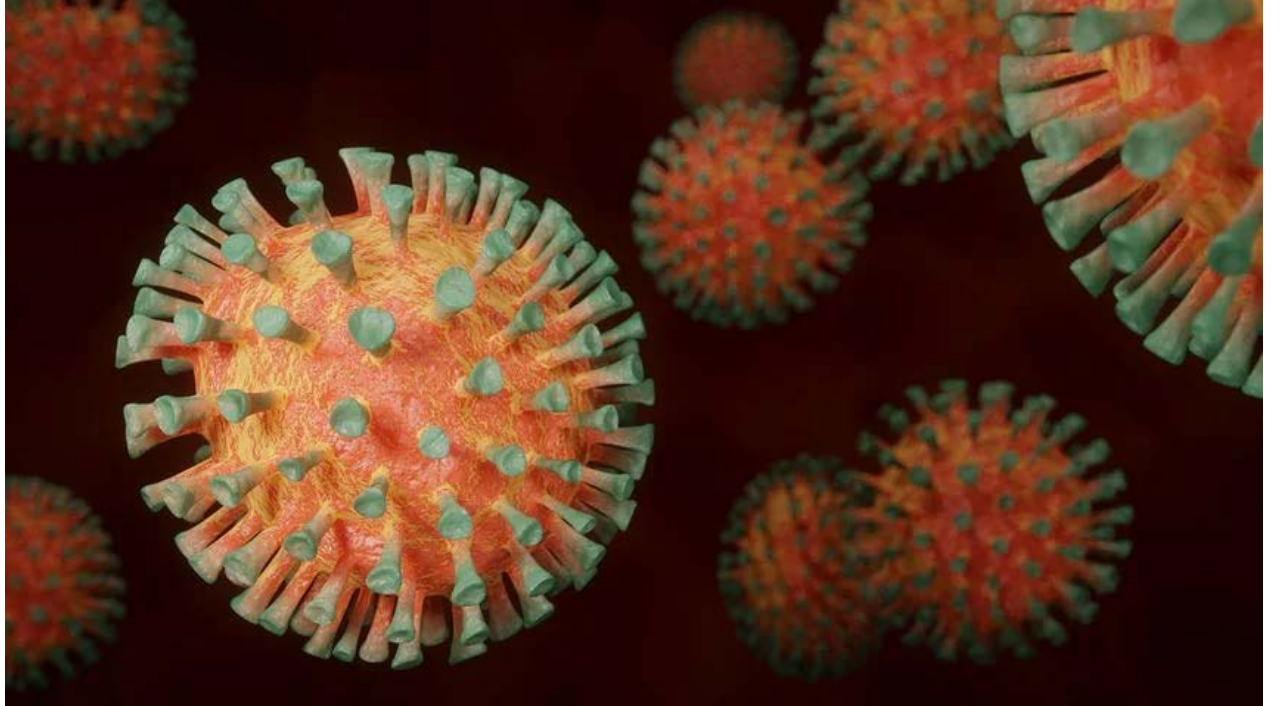
- Up to 10,000 SARS-CoV-2 positive children and adolescents
- Build on existing clinical trial network infrastructures
- Basic genetic and immunophenotyping studies
- Use EHRs, minimal testing and case report forms
- Control group for MIS-C and those who develop severe but typical COVID-19
- Smaller group with COVID-19: deep phenotyping and more extensive clinical data to understand disease manifestations and progression
- Leverage RADx PREVAIL study: develop novel or non-traditional approaches (e.g., diagnostic and prognostic biomarkers) to identify and characterize the spectrum of MIS-C and predict the longitudinal risk of disease severity after SARS-CoV-2 exposure



LONG-TERM FOLLOW UP STUDY

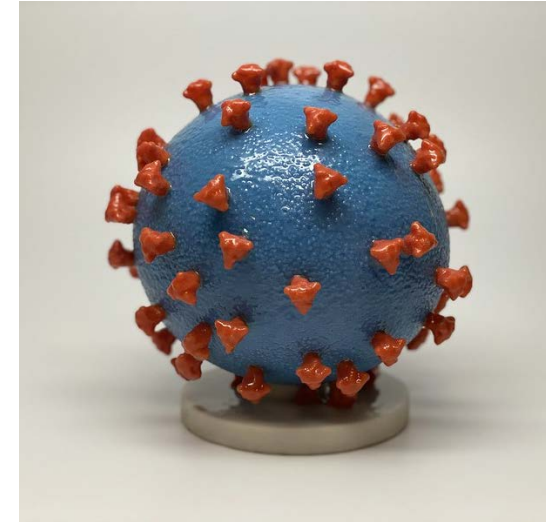
Goals: Ascertain outcomes, treatment effects, and long term, multisystem complications of MIS-C

- Multi-system testing (e.g., cardiac, neurological, GI, respiratory)
- Immunological testing
- Immune response and vaccine considerations



COVID-19 and Pregnancy

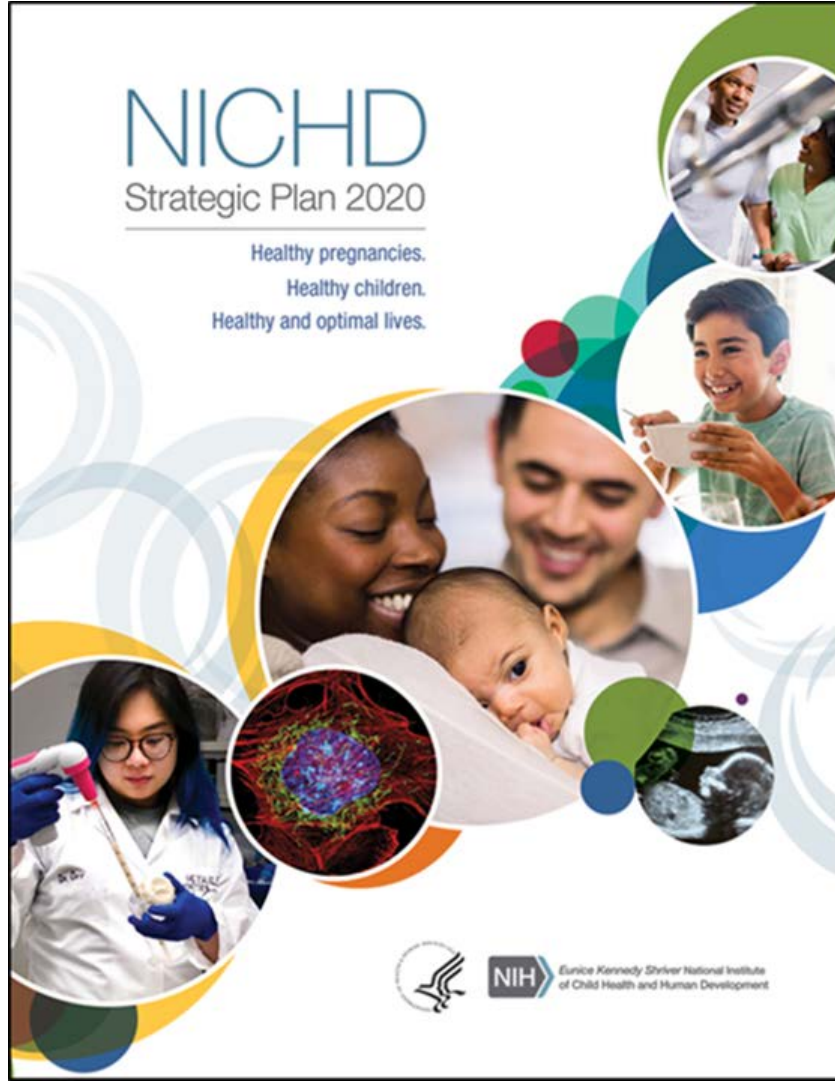
- NICHD's Maternal Fetal Medicines Unit (MFMU) launched a study in May
 - Currently can support enrollment of 21,000 pregnant women over 12 sites
 - Goal is to compare overall antenatal care, maternal health complications, rates of C-sections and maternal mortality in pre- and post- COVID-19 eras
 - Includes natural history study of 1,500 COVID-19+ pregnant women
 - Developed common data elements (CDEs) with other NICHD networks
 - Encouraging other registries adopt these CDEs to aid future meta-analyses
- Discussions occurring with outside organizations for potential collaborations on registry efforts for pregnant women and newborns
- Advocating for inclusion of pregnant women and children in major trans-NIH initiatives such as ACTIV and RADx that involve clinical trials of therapeutic vaccines and rapid testing





NICHD Strategic Plan Implementation

NICHD Strategic Plan 2020



Focus Areas

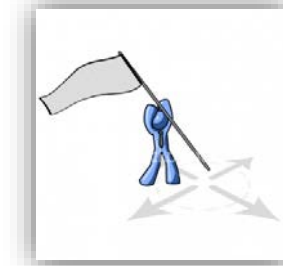
1. Scientific Research Themes



2. Scientific Stewardship



3. Management & Accountability



Strategic Plan Implementation

- Working with NICHD staff to consider how to make progress towards each goal
 - Refreshed extramural branch priorities have been finalized and will be posted soon
- Phased approach enables flexibility and incorporates resource limitations
 - Some objectives are longer-term by nature
- Retaining flexibility to accommodate advances in technology, national health priorities, etc.
- Early endeavors include:
 - Theme 1: Reissued FOA for NICHD's Intellectual and Developmental Disabilities Research Centers
 - Theme 2: Established an intramural Adolescent and Pediatric Gynecology program
 - Theme 3: Maternal Mortality co-morbidities workshop and new trans-NIH initiative under development
 - Theme 4: Navigating Pediatric to Adult Health Care workshop (fall 2020)
 - Theme 5: Implementation plan for Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) (summer 2020)
- Transparency – will regularly report progress to BSC and Council



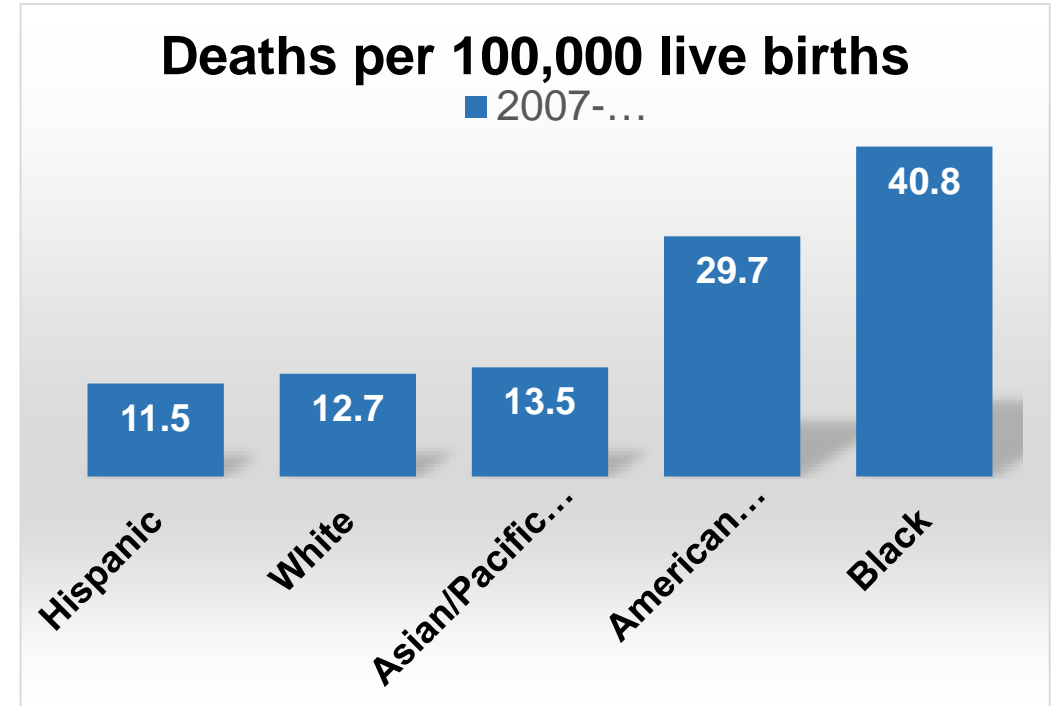


Maternal Mortality

Increased Congressional Interest in Maternal Health



December 11, 2019



Petersen EE, Davis NL, Goodman D, et al. Racial/Ethnic Disparities in Pregnancy-Related Deaths — United States, 2007–2016. MMWR Morb Mortal Wkly Rep 2019;68:762–765.



Maternal Mortality

700-900 maternal deaths: **60% are preventable**

~50,000 near misses

~400,000 women with
co-occurring conditions



~6.3 million
pregnancies
per year
in the U.S.



Leading Causes of Maternal Mortality

During pregnancy

*Other noncardiovascular conditions
 **Other cardiovascular conditions
 Infection

Day of delivery

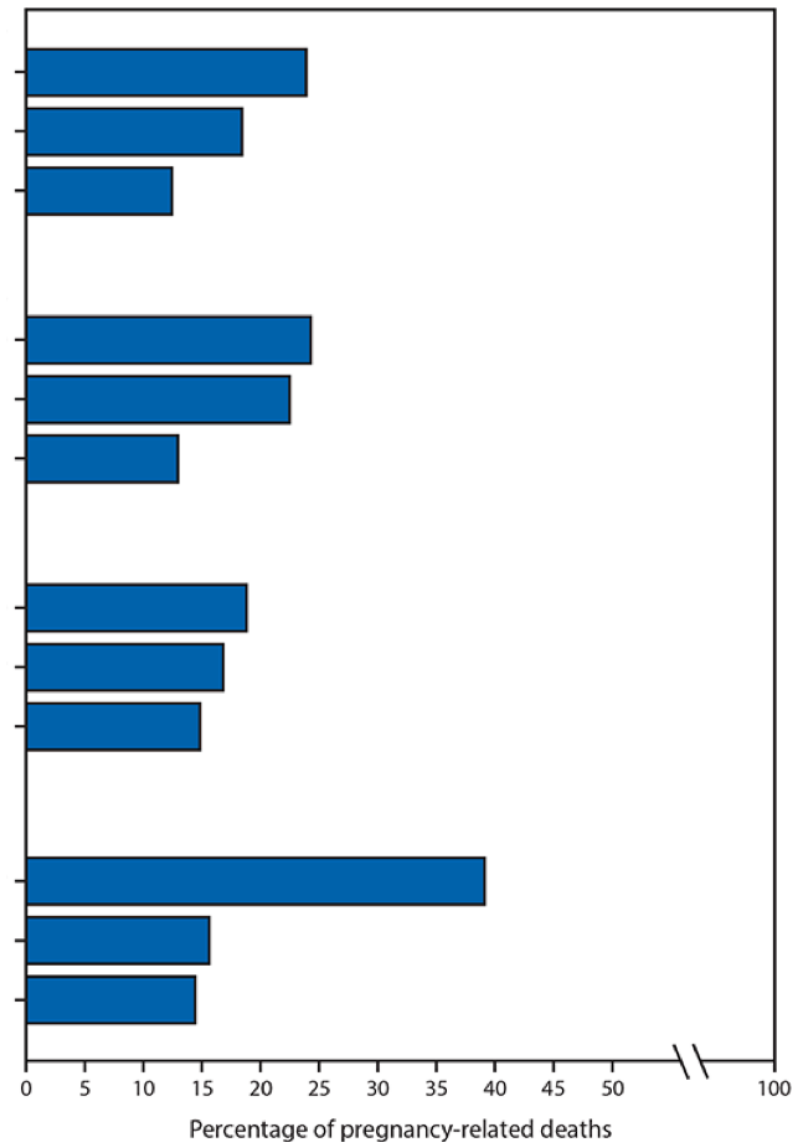
Hemorrhage
 Amniotic fluid embolism
 *Other cardiovascular conditions

1-6 days postpartum

Hemorrhage
 Hypertensive disorders of pregnancy
 Infection

43-365 days postpartum

Cardiomyopathy
 *Other noncardiovascular conditions
 **Other cardiovascular conditions



*Other than noncardiovascular conditions listed (hemorrhage, infection, etc.)

** Other than cardiomyopathy and hypertensive disorders



Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) Initiative

- Trans-NIH initiative that is in development
- Encompasses both foundational biology as well as social and biobehavioral research
- Community partners will be key voices to assess needs and to implement interventions



NOSI for Administrative Supplements for NIH Grants to Add or Expand Research Focused on Maternal Mortality

- Released May 5; **Due June 23, 2020**
- Applications aligned with one or more of these goals:
 - **Incorporate community partnerships and participation** in domestic MM and pregnancy-related and pregnancy-associated morbidity research **to resolve health disparities and attain equity in maternal health.**
 - Expand **research on the leading causes** of MM and pregnancy-related and pregnancy-associated morbidity in the U.S. **to strengthen evidence-based care and prevention strategies** and improve outcomes.
 - Develop an **integrated understanding of** pregnancy-related and pregnancy-associated morbidity and MM **causes**, including underlying comorbidities, **and mechanisms to identify preventable risk factors and develop early effective interventions.**





**Down Syndrome and INCLUDE
(INvestigating Co-occurring conditions across
the Lifespan to Understand Down syndromE)**

Clinical Trials in Down Syndrome

INCLUDE project workshop

(INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome)

- Virtual workshop held May 7-8, 2020
- Focused on clinical trials for co-occurring conditions across the lifespan
- Conditions discussed included heart defects, sleep apnea, Alzheimer's disease, leukemia, infectious diseases, among others
- Included a panel of self-advocates, parents, other advocates, and physicians to discuss considerations for participation in clinical trials
- Does triplication of interferon genes on chromosome 21 predispose to complications of COVID-19 infection?





NICHD Staff Updates

Mary Dasso, Ph.D.

Acting Scientific Director, NICHD Division of Intramural Research

- Named Acting SD in February 2020
- Marshall Scholar at the University of Cambridge, earning a Ph.D. in Biochemistry
- Damon Runyon Fellow at the University of California at San Diego, where she began to study cell cycle regulation
- Came to NICHD in 1992, receiving tenure in 2000
- Head, Section on Cell Cycle Regulation
 - Dr. Dasso's lab studies mechanisms of chromosome segregation
- In 2015, she became the Associate Scientific Director for Budget and Administration



Una Grewal, Ph.D., M.P.H.

Acting Director, Division of Intramural Population Health Research

- Named Acting Director in February 2020
- Earned her MPH and PhD degrees in epidemiology at the University of Michigan School of Public Health
- Joined the DIPHR Epidemiology Branch as a staff scientist in September 2007
- Research focuses on fetal growth and pregnancy outcomes (e.g., labor and delivery, gravid disorders, intrauterine growth restriction, birth defects), especially in relation to maternal nutrition
- Appointed DIPHR Deputy Director in 2013



Leadership Positions: Searches Underway

- **Director, National Center for Medical Rehabilitation Research (NCMRR)**
 - Final interview/selection process underway
- **NICHD Scientific Director**
 - Applications closed June 5, 2020
 - Robust response
 - Search Committee will interview highly qualified applicants and check references
 - List of best candidates presented to NICHD Director for interview and selection
- **Director, Division of Population Health Research (DIPHR)**
 - [Job advertisement open](#) –Applications due July 3, 2020; will remain open until a selection is made
 - Selection process same as for Scientific Director



We're Hiring!

- Senior Policy Advisor for Clinical Research
- Branch Chief
 - Pregnancy and Perinatology Branch, DER
- Program Officers
 - Child Development and Behavior Branch
 - Intellectual and Developmental Disabilities Branch
 - Obstetric and Pediatric Pharmacology and Therapeutics Branch
 - Pediatric Trauma and Critical Illness Branch
 - Pregnancy and Perinatology Branch
- More info at <https://www.nichd.nih.gov/about/jobs>





Questions?