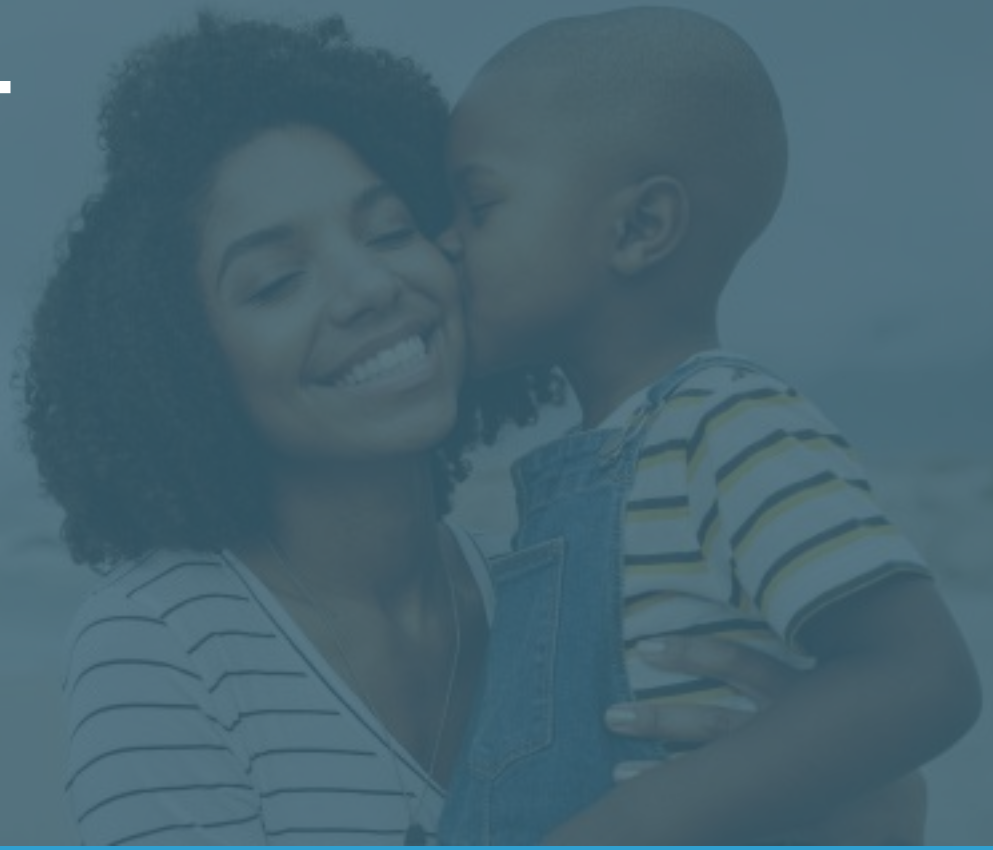
IMPAACT Network Overview

January 2021



IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Mission

IMPAACT is a global collaboration of researchers, community representatives, and other partners that aims to significantly decrease HIV and HIV-associated infections and to decrease mortality and morbidity due to HIV and HIV-associated infections and co-morbidities among infants, children, adolescents, and pregnant and postpartum women.

Research Agenda

- Advance ART of pregnant and postpartum women with HIV, aiming to optimize maternal and child health outcomes, and accelerate the evaluation (PK, safety, antiviral efficacy), licensure and optimal use of **potent and durable ARVs** for pregnant women and infants, children and adolescents with HIV.
- Evaluate the potential for **ART-free remission** through therapeutic interventions aimed at prevention, clearance and post-treatment control of HIV reservoirs in infants, children and adolescents with HIV.

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Research Agenda

- Evaluate novel approaches for **tuberculosis** prevention, diagnosis and treatment in pregnant and postpartum women and infants, children and adolescents with and without HIV that will lead to optimal dosing and regimens, licensing and improved treatment outcomes.
- Determine optimal and feasible methods for the prevention and management of **complications and co-infections** of HIV and its treatment in infants, children, adolescents and pregnant and postpartum women.

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History

- Formed in 2006 (preceded by PACTG)
- Successfully renewed in 2013 and in 2020
- Funded by US National Institutes of Health
  - Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID)
  - *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)
  - National Institute of Mental Health (NIMH)

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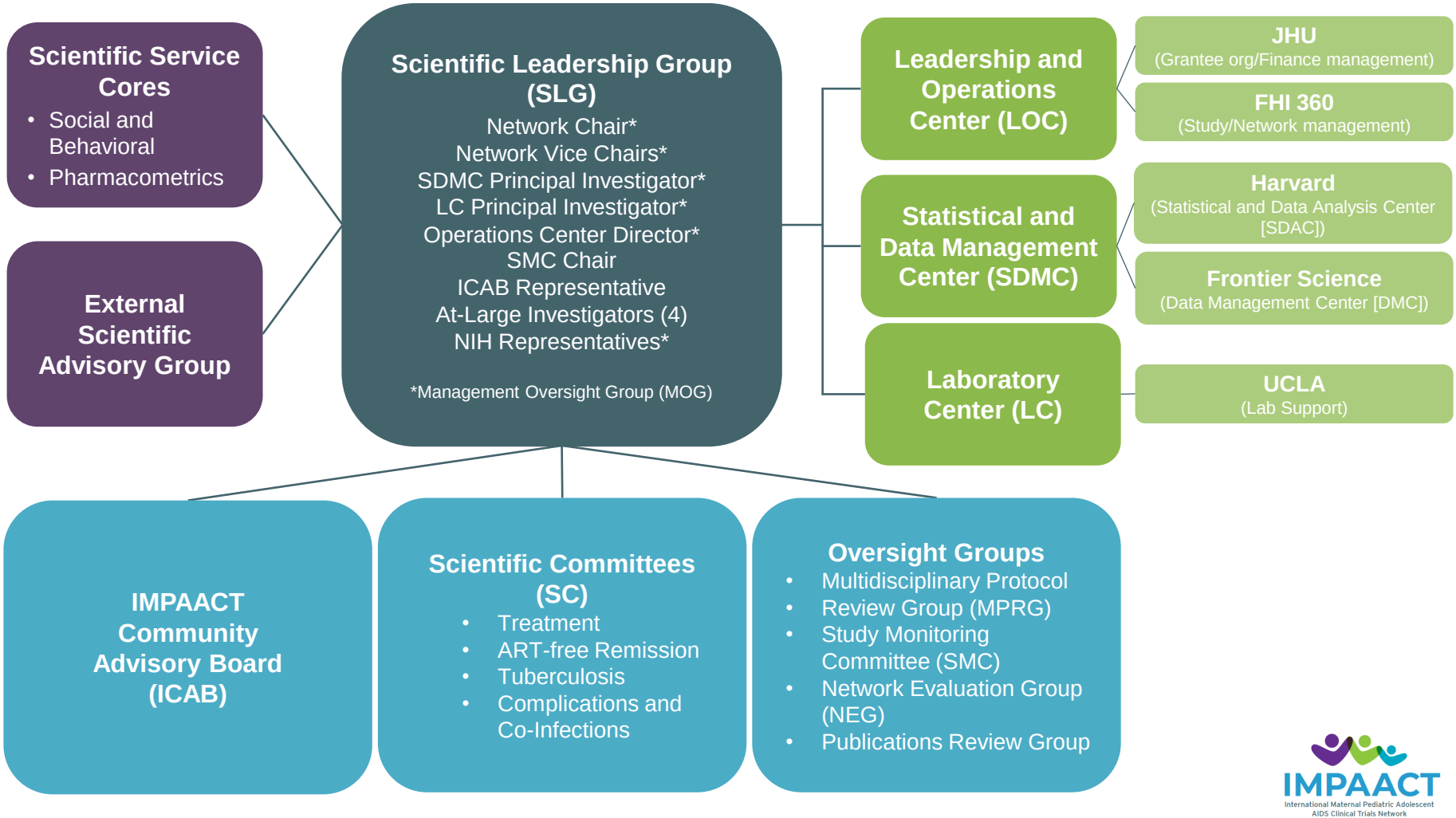
Organization

IMPAACT is comprised of:

- Scientific and management leadership groups
- Clinical research sites where studies are conducted
- Central resources that support study operations, data collection and analysis, and laboratory testing for Network studies



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Clinical Research Sites

45 sites in 12 countries across Africa, Asia, and the Americas

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19 Sites in the United States

plus 7 protocol-specific sites

26 Sites in Africa, Asia and South America

plus 2 protocol-specific sites

	NICHD-supported site
	NIAID-supported site
	Protocol-specific site

Scientific Leadership

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Network Leadership

The Network is under the leadership of the Network Chair, Sharon Nachman, and the Network Vice Chairs, Patricia Flynn and Philippa Musoke.

Sharon Nachman
Network Chair

SUNY Health Science Center at Stony Brook

Philippa Musoke
International Vice Chair
Makerere University-Johns Hopkins University Research Collaboration

Patricia Flynn
Domestic Vice Chair
St Jude Children's Research Hospital

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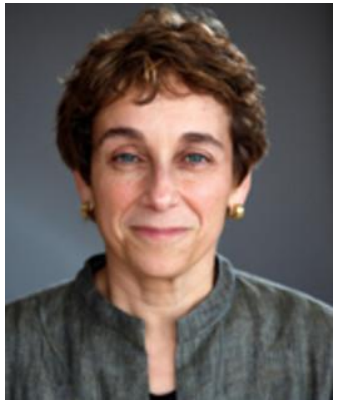
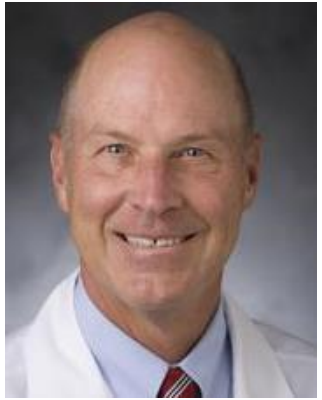
Scientific Leadership

Grace John-Stewart
University of Washington

Steven Douglas
University of Pennsylvania



Elaine Abrams
Columbia University



John Sleasman
Duke University

James McIntyre
Anova Health Institute

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Scientific Leadership Group (SLG)

- Sets the overall scientific agenda of the Network
- Prioritizes studies across the four research areas and the overall network portfolio
- Reviews proposals for new studies based on scientific merit, potential public health impact, and suitability for network implementation
- Fosters collaboration with other networks and partners

Management Oversight Group (MOG)

- Subset of SLG members including the Network chairs and leaders of the Operations Center, Statistical and Data Management Center, and Laboratory Center
- Responsible for
  - Fiscal oversight
  - Regulatory compliance
  - Collaboration agreements
  - Policies and procedures
  - Performance monitoring and evaluation

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Scientific Committees

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HIV Treatment Research Agenda

Pregnant and Postpartum women	Infants (Birth – 1,000 days of life)	Children (1,000 days of life to 13 years)	Adolescents (13-24 years)
Priority 1: Characterize the PK properties and dosing of ARVs and relevant drug-drug interactions (DDIs) among women during pregnancy and lactation, and their infants			
	Priority 2: Evaluate novel prophylaxis regimens for infants born to women with HIV		
	Priority 3: Identify and rapidly evaluate the PK, safety, antiviral efficacy of the most promising ARVs for first line treatment, accelerating licensure for pediatric populations living with HIV. Preventative and/or therapeutic approaches for high-priority diseases		
	Priority 4: Conduct PK and clinical studies necessary to optimize use of current ARVs in achieving virologic suppression among pediatric populations with ARV experience		

Complications and Co-infections

Pregnant and Postpartum women	Infants (Birth – 1,000 days of life)	Children (1,000 days of life to 13 years)	Adolescents (13-24 years)
	Priority 1: Investigate potential neuroprotective and neurotoxic effects of ART to preserve neurocognitive development and mental health in infants, children and adolescents		
Priority 2: Refine and optimize evaluation and treatment of neurocognitive and mental health disorders, particularly executive dysfunction, depression and PTSD			
Priority 3: Evaluate novel preventive and/or therapeutic approaches for high-priority diseases of importance to pediatric HIV-infected/affected populations, including RSV, working with NIAID and other partners			
Priority 4: Evaluate other co-morbidities and complications of importance for pediatric, adolescent and pregnant and postpartum women, with NIH and other partners			

Tuberculosis

Pregnant and Postpartum women	Infants (Birth – 1,000 days of life)	Children (1,000 days of life to 13 years)	Adolescents (13-24 years)
Priority 1: Evaluate the efficacy, PK and safety of new and shorter drug regimens to **prevent** drug-susceptible and drug-resistant TB in HIV-infected and uninfected infants, children, adolescents and pregnant and postpartum women			
Priority 2: Evaluate the efficacy, PK, safety and acceptability of new drug regimens, optimize existing drug dosing and evaluate novel drugs for the **treatment** of drug-susceptible and drug-resistant TB in HIV-infected and uninfected infants, children, adolescents and pregnant and postpartum women			
	Priority 3: Evaluate novel tools for the diagnosis of active TB, correlates of TB treatment in response and markers of disease progression in HIV-infected and uninfected infants, children, adolescents		
Priority 4: Evaluate novel TB vaccines for prevention of TB disease			

ART-free Remission (Cure)

- Evaluate whether very early (within the first 48 hours of life) therapy with more potent ART that blocks virus entry and/or integration, in combination with bNAbs, limits HIV reservoir establishment in infants and leads to ART-free remission
- Evaluate immune-based therapies, including therapeutic HIV vaccines and bNAbs, in children and adolescents with HIV who have displayed long-term suppression on ART and have small, low-diversity HIV reservoirs
- Examine combined initial therapy with ARVs plus immunotherapies, with and without LRAs, in adolescents and young adults with horizontally-acquired HIV to rapidly induce virologic control and potentiate elicitation of a “vaccinal effect” mediated through antigen-antibody immune complexes
- Examine the role of the CNS and T follicular helper CD4+ T cells as sanctuary sites following perinatal HIV infection and develop studies to explore elimination of HIV reservoirs within these anatomic locations
- Identify optimal virologic and immunological biomarkers to detect and quantify HIV reservoirs, and predictors of reservoir size and time to viremic rebound

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Central Resources

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Central Resource Components

Leadership and Operations Center (LOC)

Johns Hopkins University
(Grantee Organization / Network Financial Management)

FHI 360
(Study Development and Implementation, Network Support)

Statistical and Data Management Center (SDMC)

CBAR at Harvard School of Public Health (Statistical support)

Frontier Science Foundation
(Data management support)

Laboratory Center (LC)

University of California, Los Angeles
(Laboratory support)

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Statistical and Data Management Center (SDMC)

HARVARD SCHOOL OF PUBLIC HEALTH

frontier science

- Located at Center for Biostatistics in AIDS Research (CBAR) at the Harvard School of Public Health in Boston, and at Frontier Science Research and Technology Foundation (FSTRF) in Amherst, NY
- Provides statistical leadership and support through all phases of study design, implementation, and reporting of results
- Maintains databases for IMPAACT studies
- Provides training and technical assistance on data collection and data management for IMPAACT studies

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Laboratory Center (LC)

- Located at University of California, Los Angeles
- Identifies and implements state-of-the-art laboratory testing in support of IMPAACT's scientific agenda
- Assists in the development and quality assurance of local laboratory capacity at IMPAACT sites
- Provides technical assistance and support for all laboratory aspects of IMPAACT studies

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Finance and Contracts

- Located at Johns Hopkins School of Medicine
- Administers the IMPAACT grant
- Administers Master Member Agreements (MMA), Protocol Specific Task Orders (PSTO), and Significant Financial Interest (SFI) with each IMPAACT NIAID site and any study-specific sites

Operations Center

- Located at FHI 360, in Durham, North Carolina
- Supports the development, implementation and reporting of all IMPAACT scientific protocols
- Provides a central point of coordination, communications, and support to the IMPAACT Leadership Group and all network committees, protocol teams, and working groups
- Arranges and supports all network meetings and leadership travel

Community Engagement

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Operations Center Community Program

- Coordinates and supports the IMPAACT Network's community participation processes
- Responsible for outlining steps to develop, maintain, support, and encourage the full participation of community representatives in all phases of the research process
- Assists in the development of community education materials and presentations to explain research concepts that support informed consent and increase research literacy

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Site Community Programs

- Typically, a CRS obtains community input into the research process through its Community Advisory Board (CAB).
- CABs build and foster partnerships between researchers and local study communities impacted by HIV/AIDS
- The CRSs support CAB members as they share their community expertise and gain new skills through face-to-face meetings and conference calls.

IMPAACT Community Advisory Board (ICAB)

- Two representatives from each IMPAACT site participate in the ICAB
  - 1 Community educator / community liaison
  - 1 CAB representative
- ICAB members provide input to protocol teams, by reviewing protocols in development, adapting sample consent forms for local use, and developing other study-related materials.

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ICAB Representatives on Scientific Committees

- Including community members at all stages and levels of the research process helps build trust and mutual understanding.
- Members of the ICAB Leadership Group also participate in IMPAACT scientific committees as voting members.
- ICAB representatives on scientific committees review and provide feedback on all new concepts and protocols that are in development.

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Scientific Advisory Groups

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Scientific Service Cores

- Social and Behavioral Core
  - Ensures that IMPAACT studies are designed and implemented with appropriate consideration of **social-behavioral factors** that may influence outcomes of interest or success of the study

- Pharmacokinetic Core
  - Develops **pharmacokinetic (PK) and pharmacodynamic (PD) models**
  - Applies statistical methods to optimize study design
  - Performs PK/PD analyses of IMPAACT study data

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External Scientific Advisory Group

- Consists of experts in the Network's research priority areas who are free of conflicts of interest and will conduct a **review of the Network's current and planned scientific agenda** at least every three years, including identifying any gaps and providing recommendations for prioritization and future directions

- The group will be directly advisory to the SLG

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Oversight Groups

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Oversight Groups

Multidisciplinary Protocol Review Group (MPRG)

- Ensures IMPAACT protocols are scientifically rigorous, accurate, consistent, complete, and standardized to the extent possible

Study Monitoring Committee(s) (SMC)

- Monitors participant safety, progress and quality of studies and makes recommendations related to study continuation, cohort progression and dose escalation/dose selection

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Oversight Groups

Network Evaluation Group

- Ensures that the performance of all components of the Network are evaluated
- On behalf of the MOG, oversees periodic evaluations of the key Network components

Publications Review Group

- Reviews all abstracts and manuscripts reporting on Network studies and relevant investigations to ensure high quality products and scientific rigor

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Manual of Procedures

https://www.impaactnetwork.org/resources/manual-procedures

This Manual of Procedures (MOP) describes the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network structure; operating policies; roles and responsibilities of entities and individuals within the IMPAACT Network; protocol development and approval processes; site selection; process; standardized study operations procedures; data and specimen collection and processing procedures; and quality management, monitoring and evaluation of trials conducted by IMPAACT. The IMPAACT MOP is to be used as a reference document for current IMPAACT policies and procedures. Clinical Trial Units are expected to maintain a hard copy of the current IMPAACT MOP at all clinical research sites.

The IMPAACT Network MOP does not replace the study-specific MOP that may be developed for specific IMPAACT studies. The study-specific MOP contains detailed guidance on study implementation. All study procedures within IMPAACT must be conducted in accordance with the study protocol, the study-specific MOP (if applicable), and this Network MOP. In the event that there are inconsistencies between these documents, the precedence that must be followed is:

- If this Network MOP is inconsistent with the study-specific MOP, the study-specific MOP must be followed.
- If the study-specific MOP is inconsistent with the study protocol, the protocol must be followed.

IMPAACT members are encouraged to contact the relevant individuals within the Network with procedural questions. For study-specific questions related to proper implementation, data collection, and laboratory concerns for a study protocol, contact the IMPAACT Operations Center Clinical Trials Specialist (CTS), the study-specific statistician and data manager, and the IMPAACT Laboratory Center (ILC) Quality Assurance/Quality Control Group.

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) is provided by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH), all components of the National Institutes of Health (NIH), under Award Numbers UM1AI068632-15 (IMPAACT LOC), UM1AI068616-15 (IMPAACT SDMC) and UM1AI106716-09 (IMPAACT LC), and by NICHD contract number HHSN275201800001I. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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THANKS!

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