



# NIMH Priorities and Plans: Women's Health Research

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Director, NIMH

September 13, 2017



National Institute  
of Mental Health

# Objectives

- About the NIMH
- Research Priorities
- Women's Health Research
- Science Highlights
- Large Studies, Resources, and Repositories

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# About the NIMH



- The National Institute of Mental Health (NIMH) is the lead federal agency for research on mental illnesses.
- NIMH supports more than 3,000 research grants and contracts at universities and other institutions across the country and overseas.
- NIMH intramural research programs support approximately 600 scientists working on the NIH campuses.



# NIMH Strategic Plan for Research



## **Objective 1:**

**Define the mechanisms of complex behaviors**

## **Objective 2:**

**Chart mental illness trajectories to determine when, where, and how to intervene**

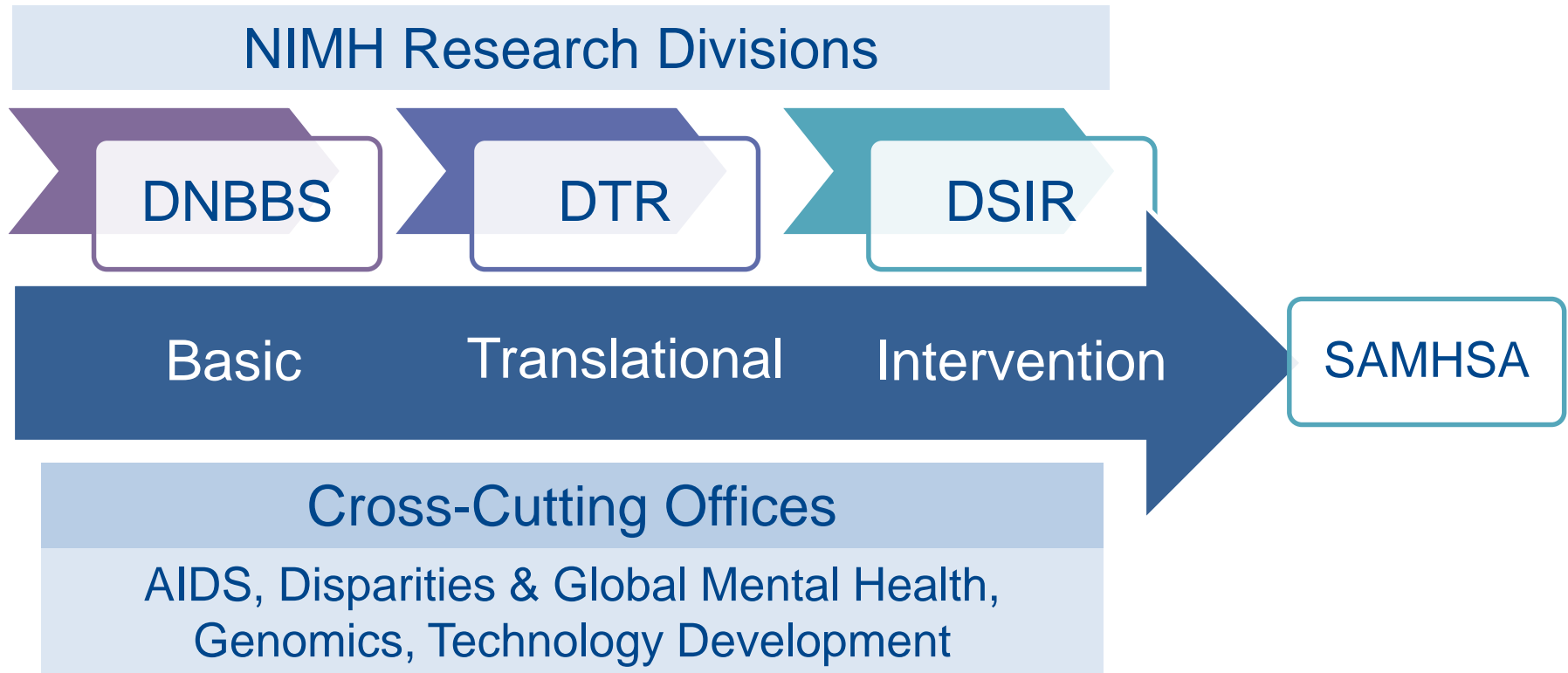
## **Objective 3:**

**Strive for prevention and cures**

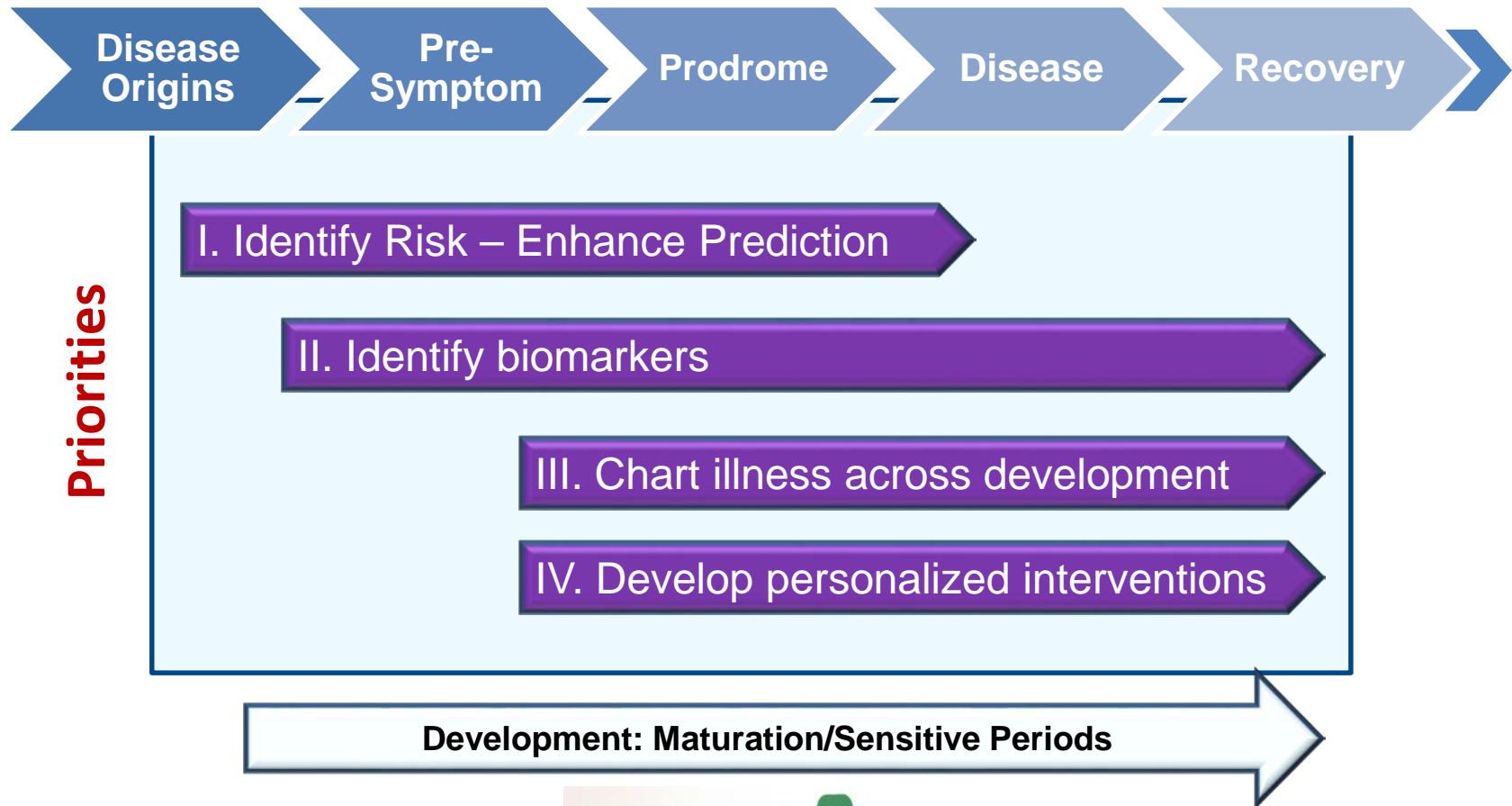
## **Objective 4:**

**Strengthen the public health impact of NIMH-supported research**

# From Basic Research to Implementation



# From Disease Origin to Recovery



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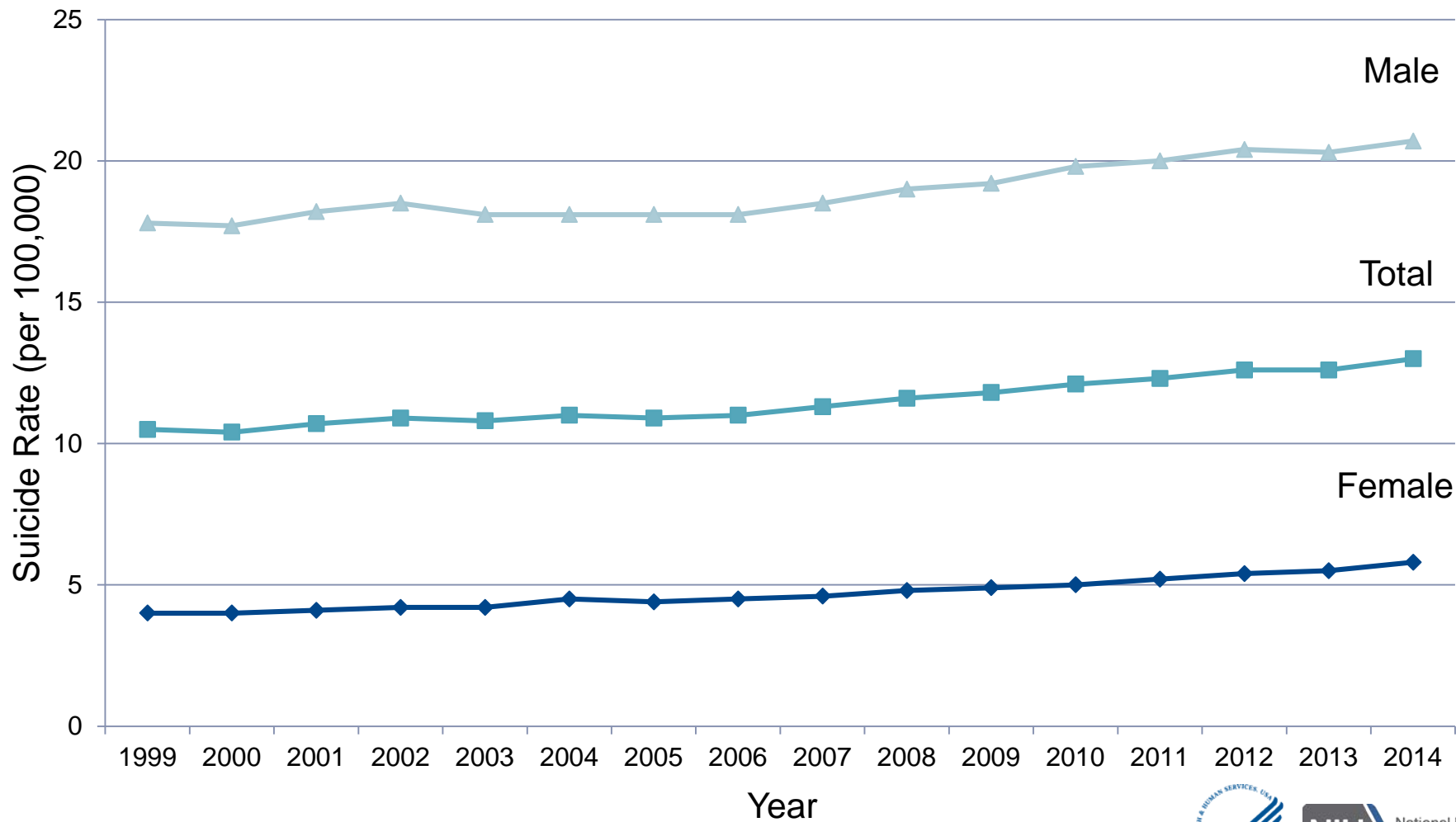
# Research Priorities

- **Short-term Goals: Suicide Prevention**
  - Identify implementable evidence-based practices and knowledge gaps
- **Medium-term Goals: Neural Circuits**
  - Develop technologies to interrogate neural circuits, and ultimately improve the understanding and treatment of mental health disorders
- **Long-term Goals: Computational Psychiatry**
  - Develop computational perspectives and approaches to improve the understanding and treatment of mental health disorders



# Short-term Goal: Suicide Prevention

Age-Adjusted Suicide Rates in the United States (1999-2014)



Data courtesy of CDC



# NIMH Suicide Workshop

## Mechanisms Underlying Suicide Risk: Integrating RDoC to Inform Novel and Personalized Intervention Research

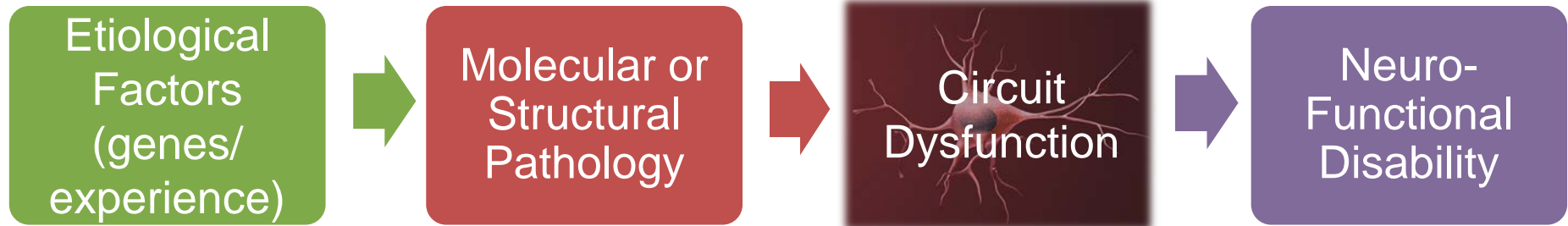
June 2-3, 2016

- NIMH hosted a workshop to review current themes in suicide research and to consider how approaches consistent with the Research Domain Criteria (RDoC) framework could provide new insights on the underlying mechanisms of suicide risk
- Discussion topics included gender differences and the timing of early life stress as strong influences in the trajectory of suicide risk over the life course

# NIMH Initiatives for Suicide Prevention

- Applied Research Towards Zero Suicide Healthcare Systems (RFA-MH-16-800)
- Detecting and Preventing Suicide Behavior, Ideation and Self-Harm in Youth in Contact with the Juvenile Justice System (PAR-16-299)
- Addressing Suicide Research Gaps: Aggregating and Mining Existing Data Sets for Secondary Analyses (RFA-MH-18-400)
- Addressing Suicide Research Gaps: Understanding Mortality Outcomes (RFA-MH-18-410)

# Medium-Term Goal: Understanding Neural Circuits



- Understanding brain function and dysfunction
  - Characterize molecular identity, anatomy, and activity patterns in a cell-type specific manner
- Monitor and manipulate circuits for improved function
  - Drive and inhibit circuits with precise behavioral effects

# NIMH Neural Circuits Workshop

## Neural Circuits: Gaps and Opportunities

September 11-12 , 2017

- The overarching goal of the workshop was to identify how NIMH can support the development of technologies to interrogate neural circuits, and ultimately improve the understanding and treatment of mental health disorders

# Long-Term Goal: Computational Psychiatry

Data Mining

Biophysical  
Modeling

Computational  
Modeling

Computational  
Phenotyping



- Test links across multiple levels of analyses (genetic, molecular, cellular, circuit, behavior)
- Formalize behavioral analysis, defining underlying algorithms and facilitating neurobiological and clinical studies
- Provide quantitative assessment of utility of biomarkers
- Lead to an enhanced and integrative nosology

# NIMH Computational Psychiatry Workshop

## Computational Psychiatry: Opportunities and Challenges for the Future

June 26 -27, 2017

- NIMH hosted a workshop to identify how NIMH can support the development of computational perspectives and approaches to improve the understanding and treatment of mental health disorders
- Addressed 4 Areas:
  - Evaluation
  - Computation
  - Psychiatry
  - Basic Fundamental Research

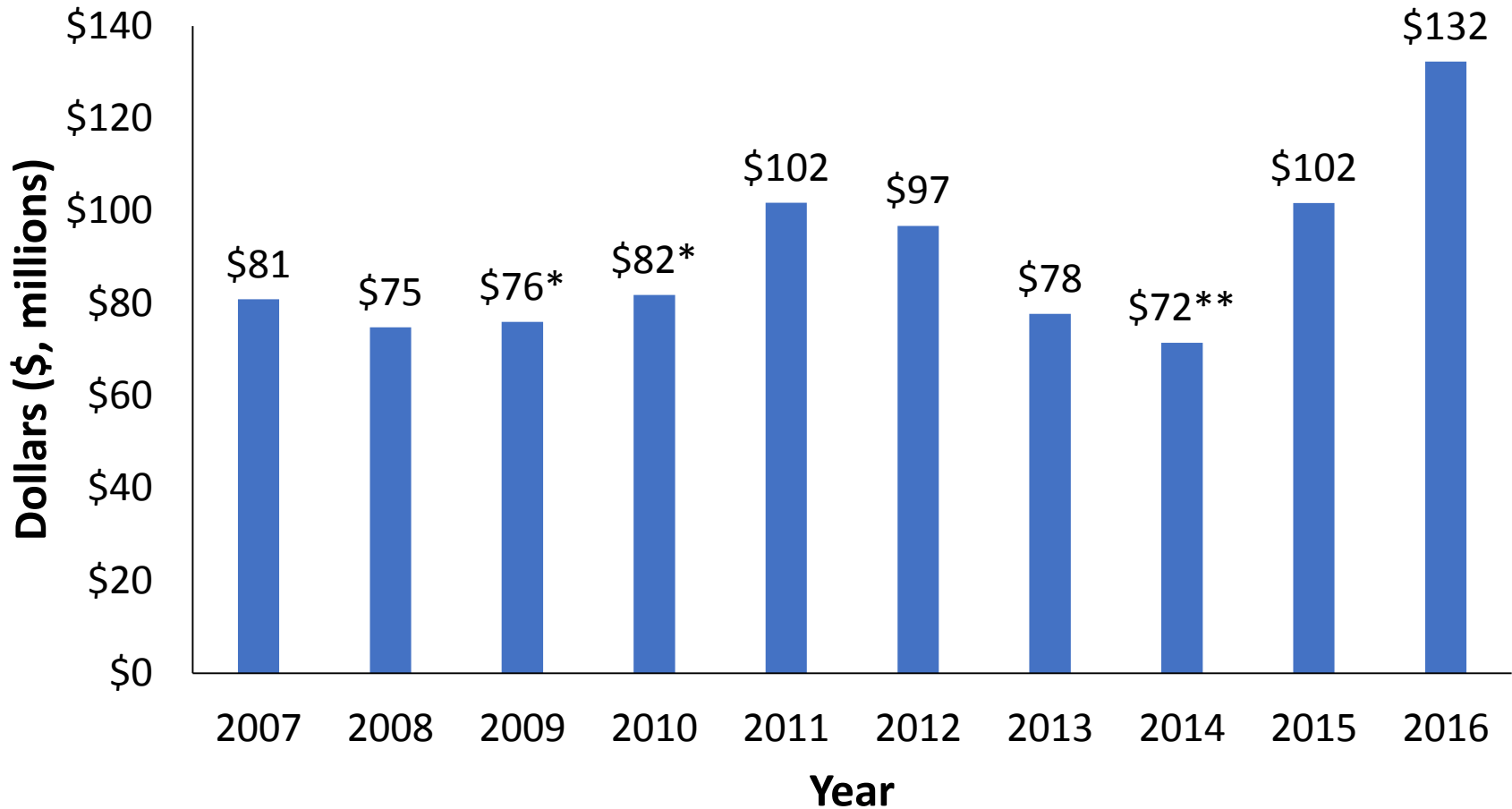




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# NIMH's Spending on Women's Health (2007-2016)



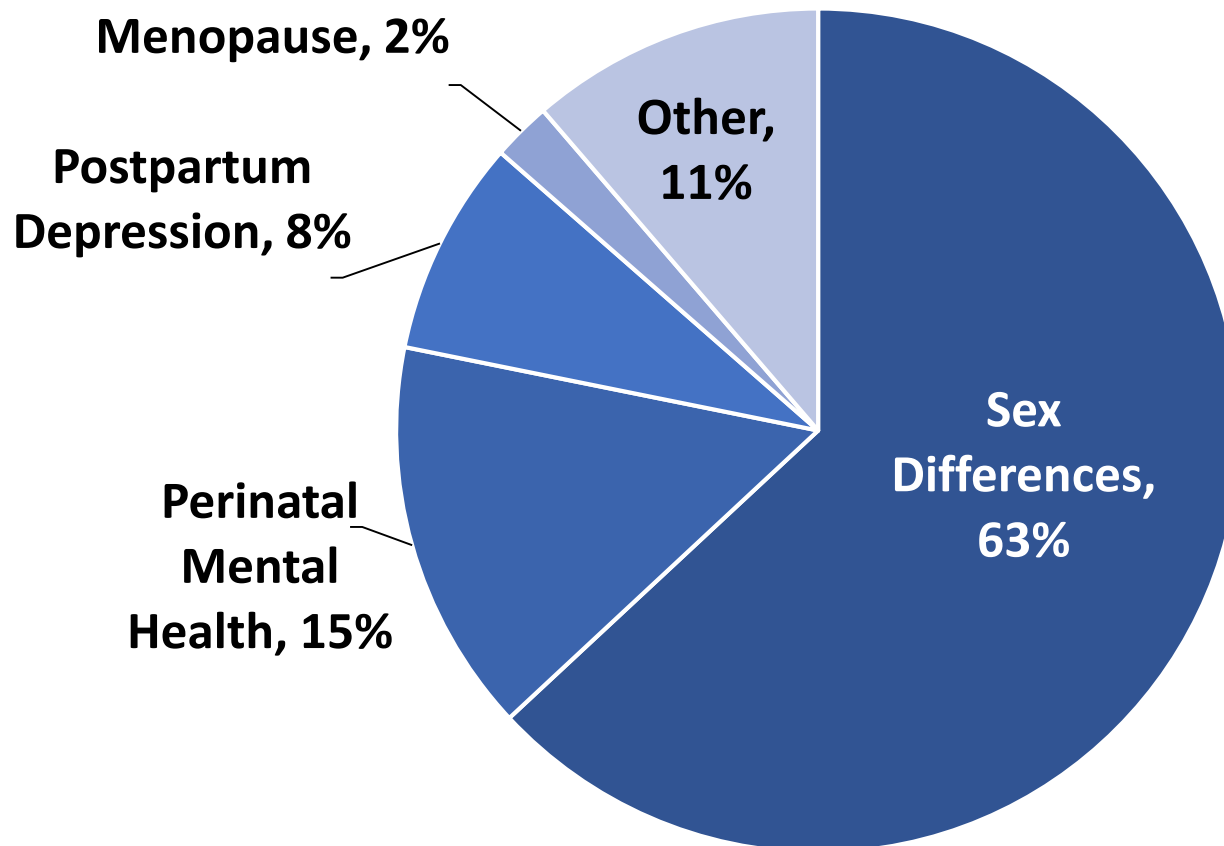
Official dollars determined by PARIS queries reported to NIH Budget

\* Includes ARRA funding

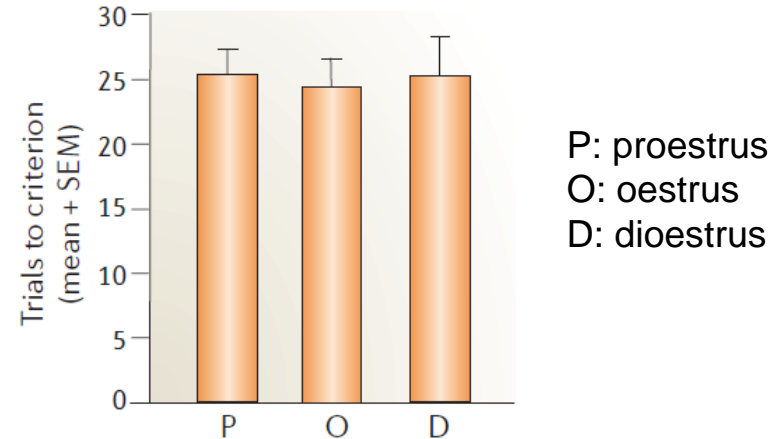
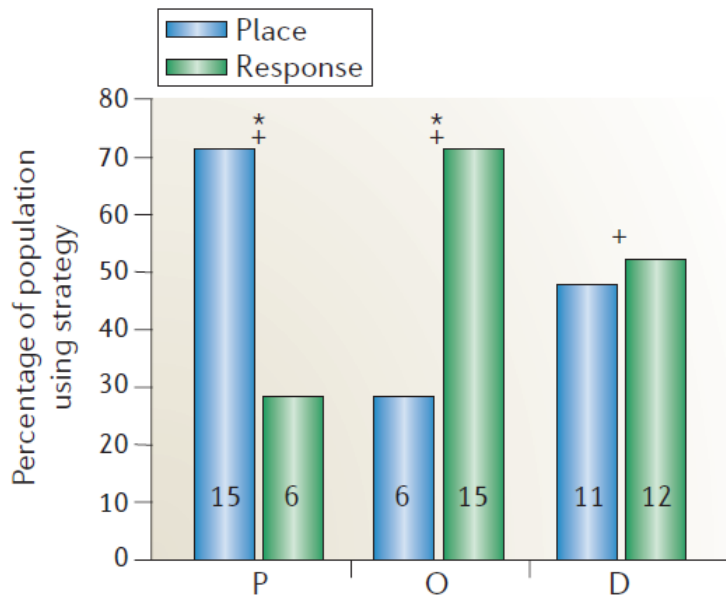
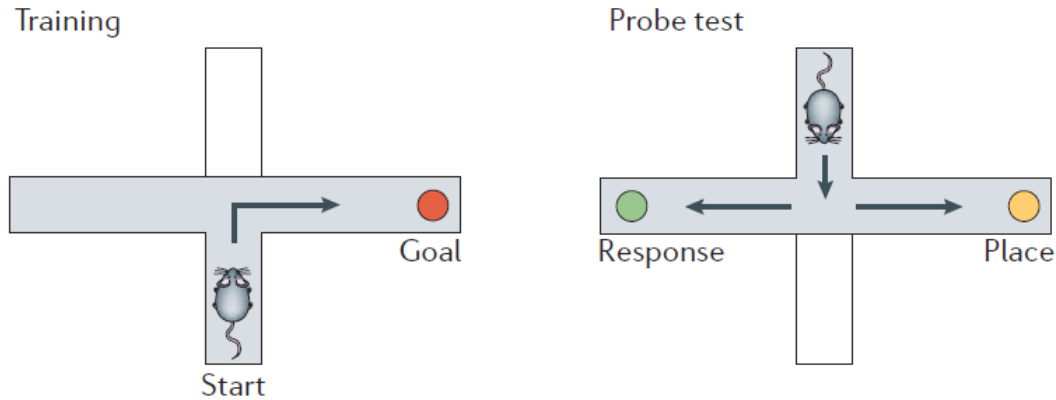
\*\* Does not include AIDS dollars



# NIMH's Women's Health Portfolio (2016)



# Sex as a Biological Variable



P: proestrus  
O: oestrus  
D: dioestrus

# NIMH Women's Mental Health Research Program, Office for Research on Disparities and Global Mental Health

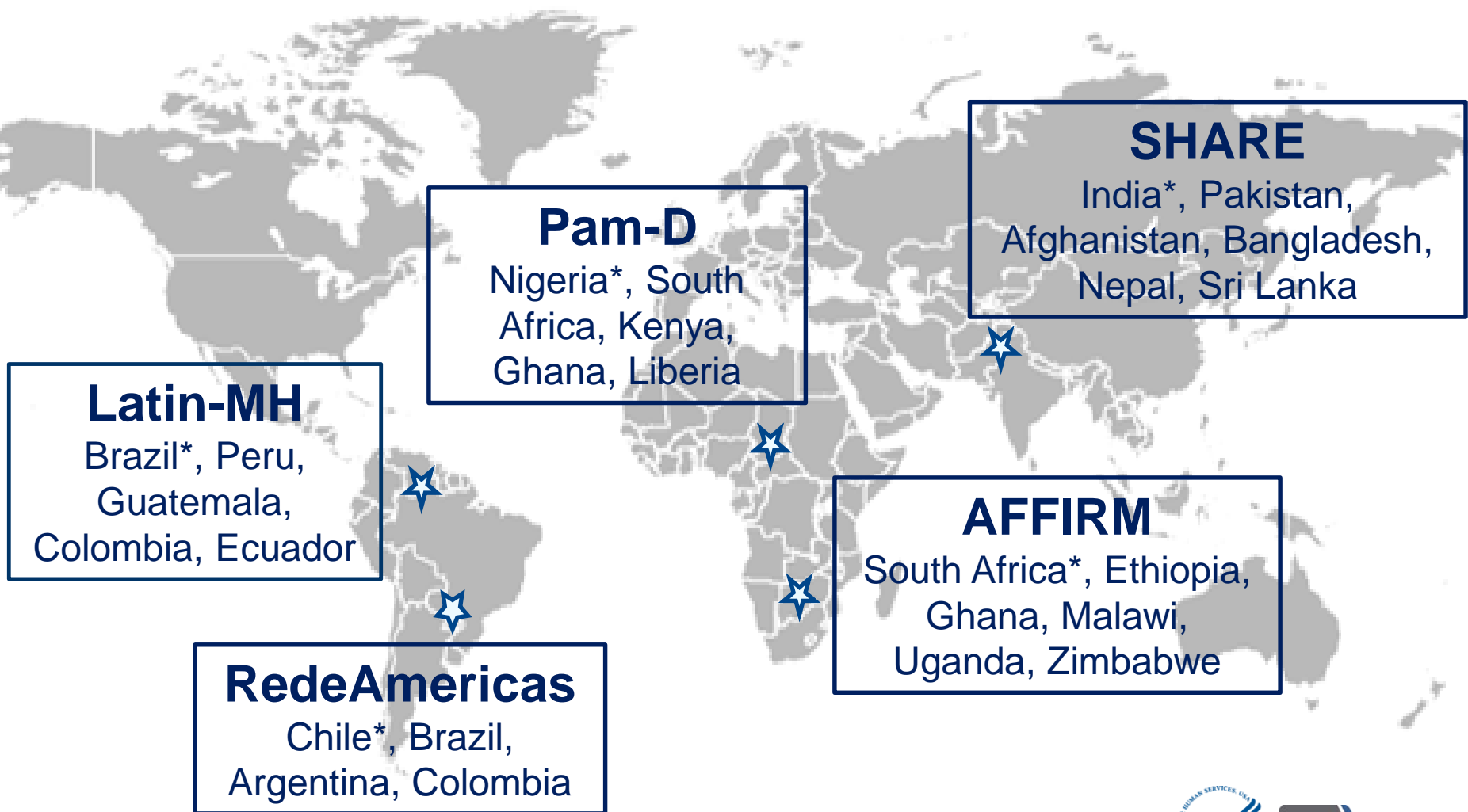
- Coordinates with the NIMH scientific Divisions to promote research on women's mental health and to encourage the examination of sex and gender differences in NIMH funded research
- Works closely with the NIH Office for Research on Women's Health and other NIH Institutes and Centers to facilitate joint funding opportunities
- Serves as a liaison to other federal agencies and external stakeholders on research issues relevant to women's mental health



# Women's Mental Health and Sexual and Gender Minority Mental Health FOAs

- Notice of Information: NIMH High-Priority Areas for Research on Women's Mental Health During Pregnancy and the Postpartum Period
- Research on the Health of Women of Underrepresented, Understudied and Underreported (U3) Populations (PA-17-101)
- Administrative Supplement for Research on Sex/Gender Influences (PA-17-078)
- Administrative Supplements for Research on Sexual and Gender Minority Populations (PA-17-098)
- The Health of Sexual and Gender Minority (SGM) Populations (R01, R03, and R21) (PA-15-261, PA-15-262, and PA-15-263)

# Collaborative Hubs for International Mental Health Research

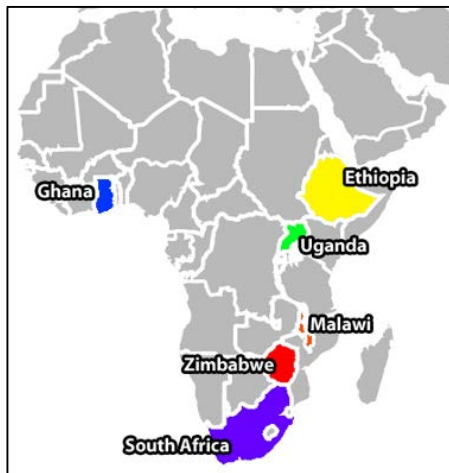


# Global Research on Maternal Depression



- **South Asian Hub for Advocacy, Research and Education (SHARE)**

- Developed an innovative approach for the delivery of an established psychological treatment that reduces the burden of depression in mothers in South Asia



- **Africa Focus on Intervention Research for Mental Health (AFFIRM)**

- Tested the effectiveness of a task sharing model to provide counselling for depressed pregnant women by non-specialist health workers in a primary care setting in South Africa



# NIMH Intramural Research Program: Behavioral Endocrinology Branch

- Peter Schmidt, M.D., Chief
- Studying how changes in reproductive hormones trigger mood disorders, why these hormones trigger mood disturbances only in some women, and how the pathogenic mechanisms underlying these disorders translate into novel therapies or novel uses of existing therapies
  - Postpartum Depression
  - Premenstrual Dysphoric Disorder (PMDD, a severe premenstrual syndrome)
  - Perimenopausal Depression
- Examining the role of growth and pubertal development in normal brain development, in collaboration with NICHD investigators



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# Science Highlight: Sex Differences in Neuronal Cell Loss

*Neuroscience*

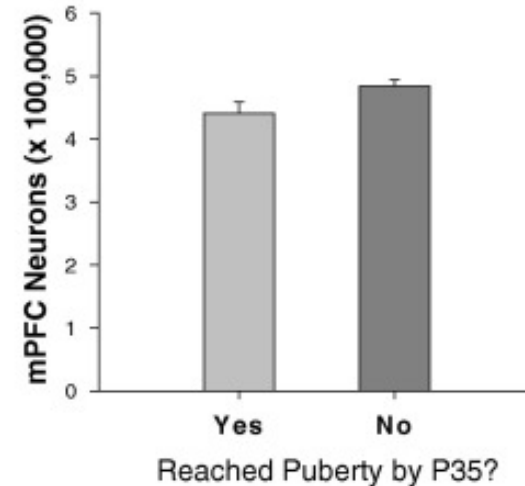
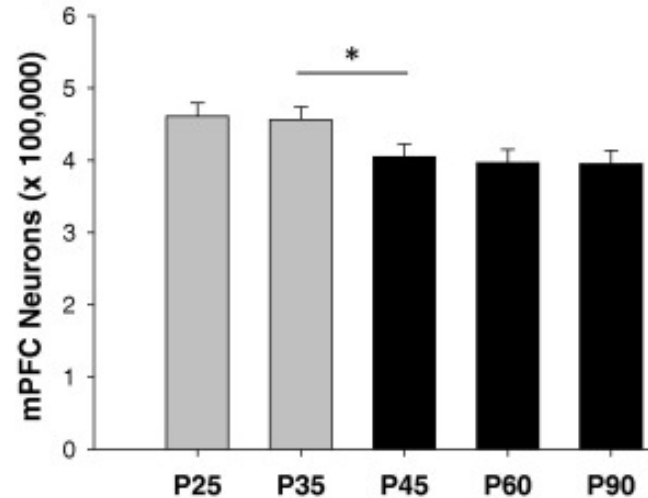
**THE TIMING OF NEURONAL LOSS ACROSS ADOLESCENCE  
IN THE MEDIAL PREFRONTAL CORTEX OF MALE AND FEMALE RATS**

**J. WILLING \* AND J. M. JURASKA**

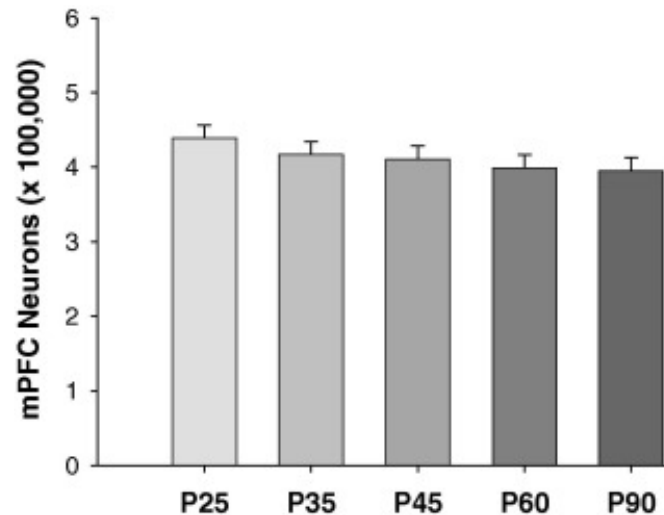
2015

# Animal Models Reveal Puberty-associated Patterns of Cell Loss

Female rats lost neurons in the medial prefrontal cortex between postnatal days 35 and 45



Males did not lose a significant number of neurons from preadolescence to adulthood



# Science Highlight: Sex-Differences in Oxytocin Expression

## Archival Report

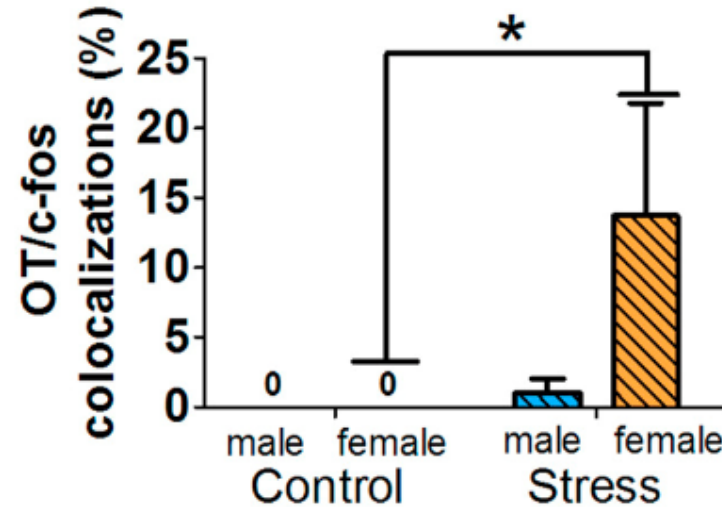
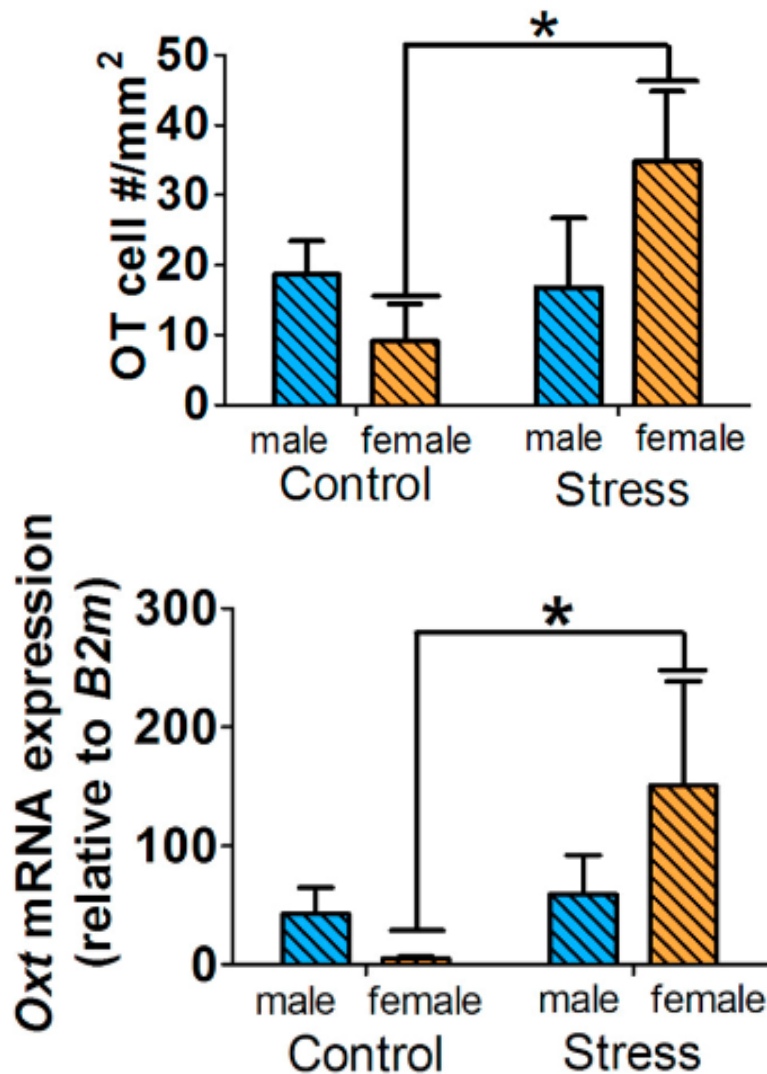
Biological  
Psychiatry

### **Sex-Specific Effects of Stress on Oxytocin Neurons Correspond With Responses to Intranasal Oxytocin**

Michael Q. Steinman, Natalia Duque-Wilckens, Gian D. Greenberg, Rebecca Hao, Katharine L. Campi, Sarah A. Laredo, Abigail Laman-Maharg, Claire E. Manning, Ian E. Doig, Eduardo M. Lopez, Keenan Walch, Karen L. Bales, and Brian C. Trainor

2016

# Oxytocin-sensitive Networks Contribute to Stress-related Sex Differences



In female mice, but not in male mice, social defeat induced a long-lasting increase in the # of OT neurons, OT/c-fos colocalization, and *Oxt* gene expression.

# Science Highlight: Preventing Maternal Depression

**JAMA Psychiatry**

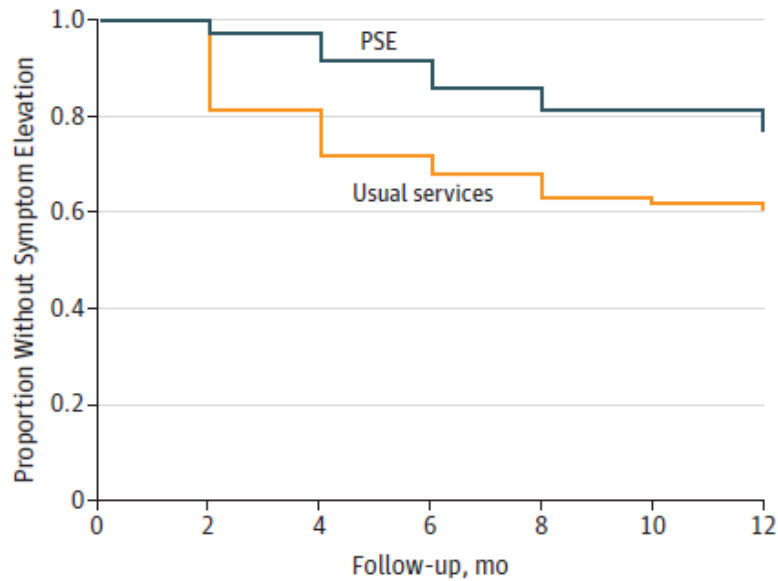
## Efficacy of a Maternal Depression Prevention Strategy in Head Start A Randomized Clinical Trial

Michael Silverstein, MD, MPH; Yaminette Diaz-Linhart, MSW, MPH; Howard Cabral, PhD, MPH; William Beardslee, MD;  
Mark Hegel, PhD; Winta Haile, BA; Jenna Sander, MPH; Gregory Patts, MPH; Emily Feinberg, ScD

2017

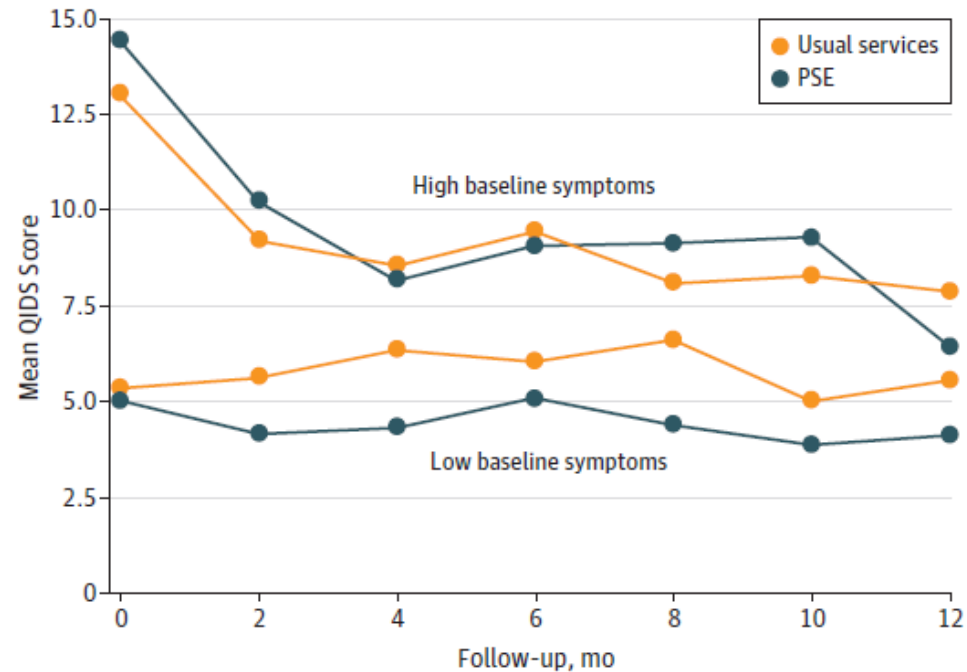
# Science Highlight: Preventing Maternal Depression

Survival analysis



No. at risk	0	2	4	6	8	10	12
Usual services	84	69	60	56	52	50	
PSE	70	67	63	59	56	55	

Symptom scores

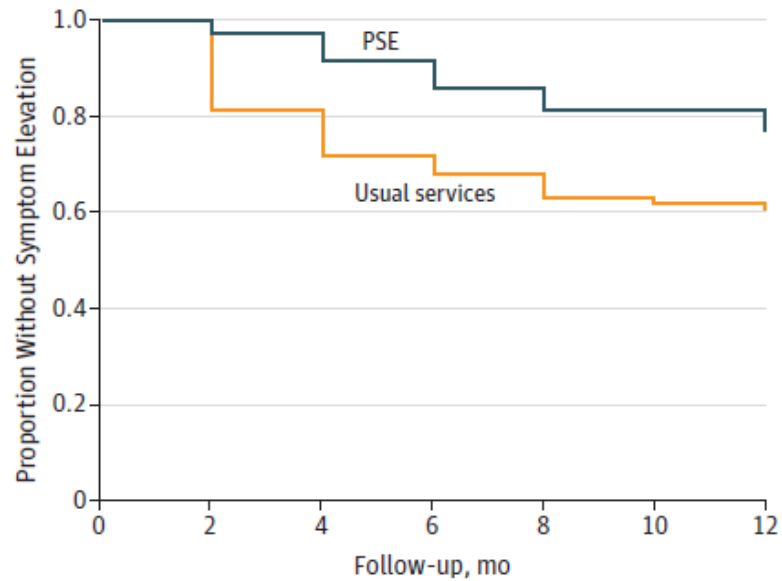


PSE = problem-solving intervention



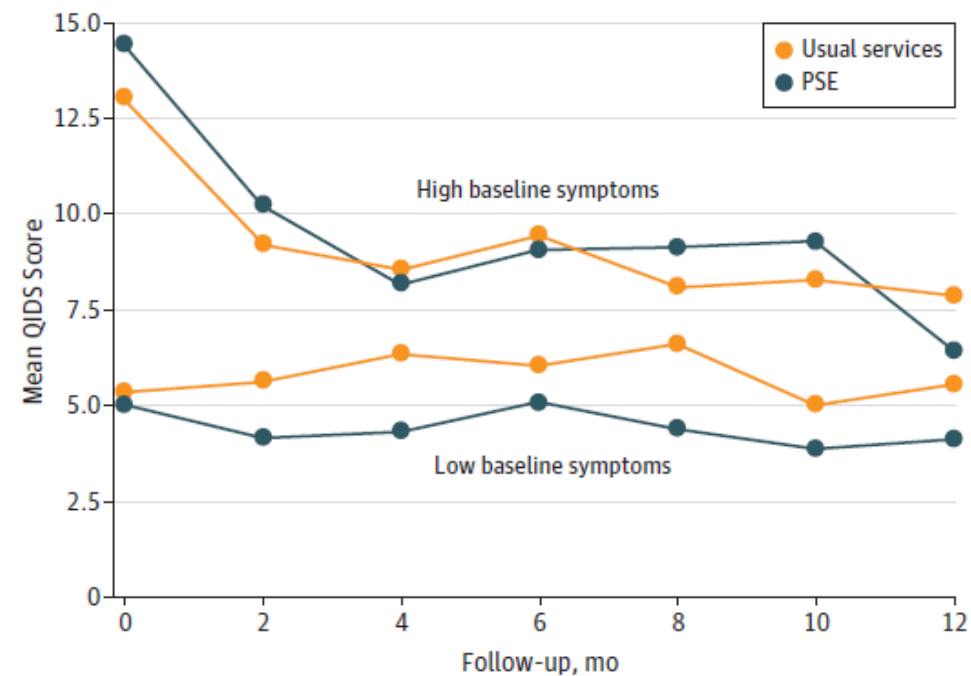
# Science Highlight: Preventing Maternal Depression

**A** Survival analysis



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**B** Symptom scores



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# Science Highlight: Emerging Technologies

## The New York Times

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HEALTH

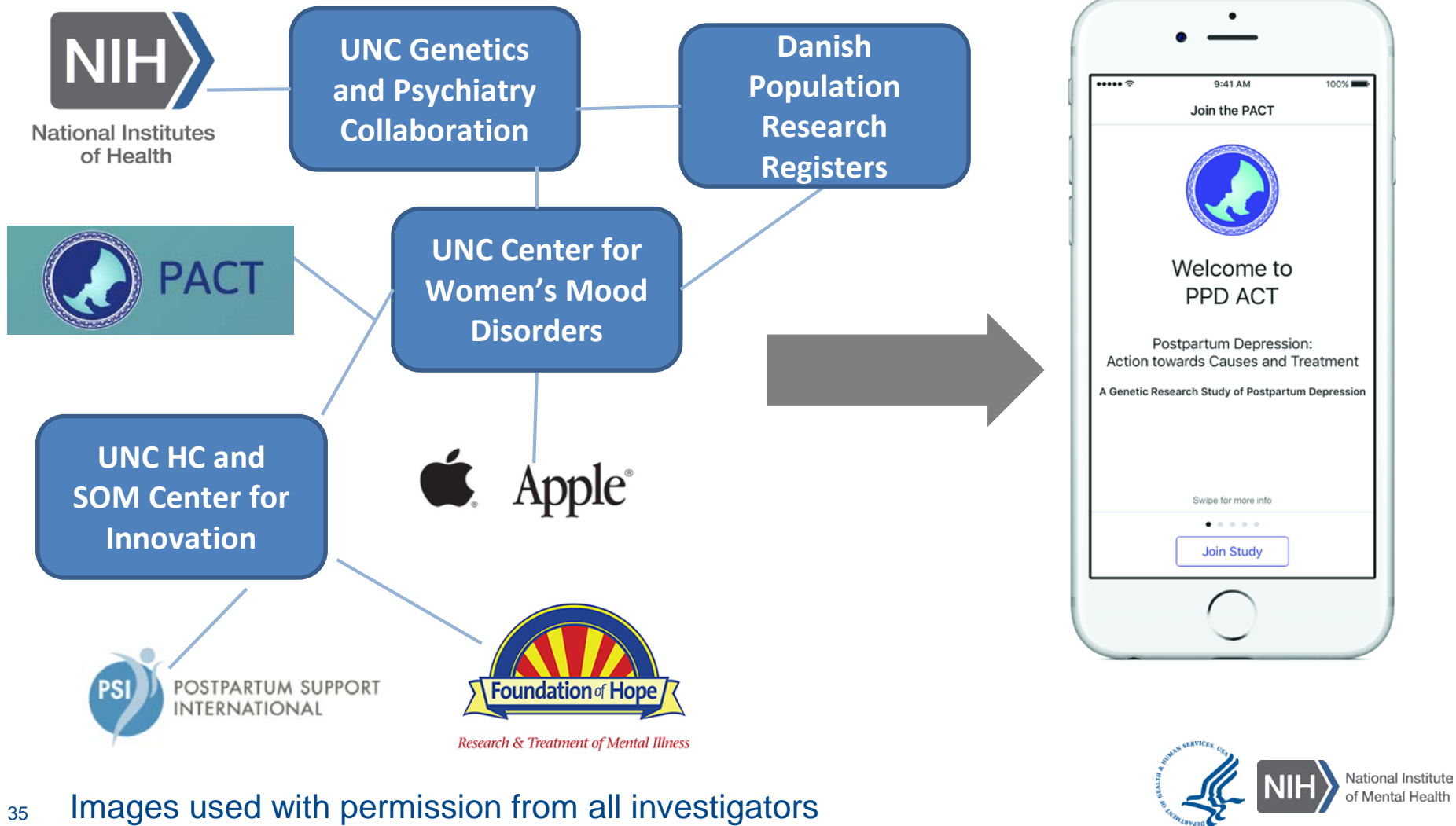
### *Hunting the Genetic Signs of Postpartum Depression With an iPhone App*

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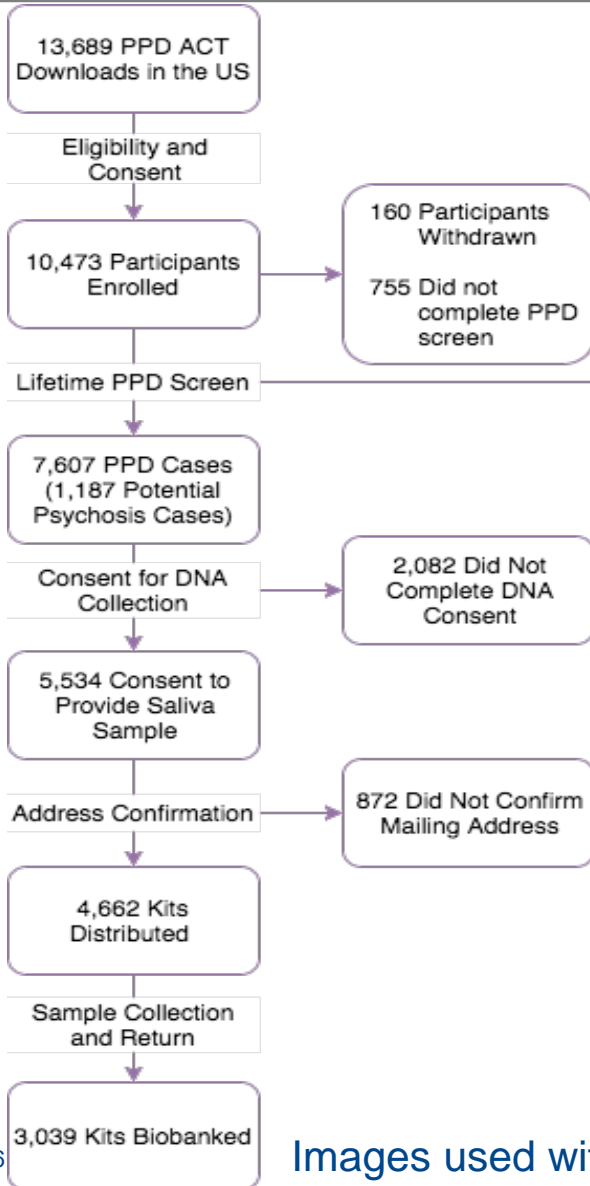
By PAM BELLUCK MARCH 21, 2016



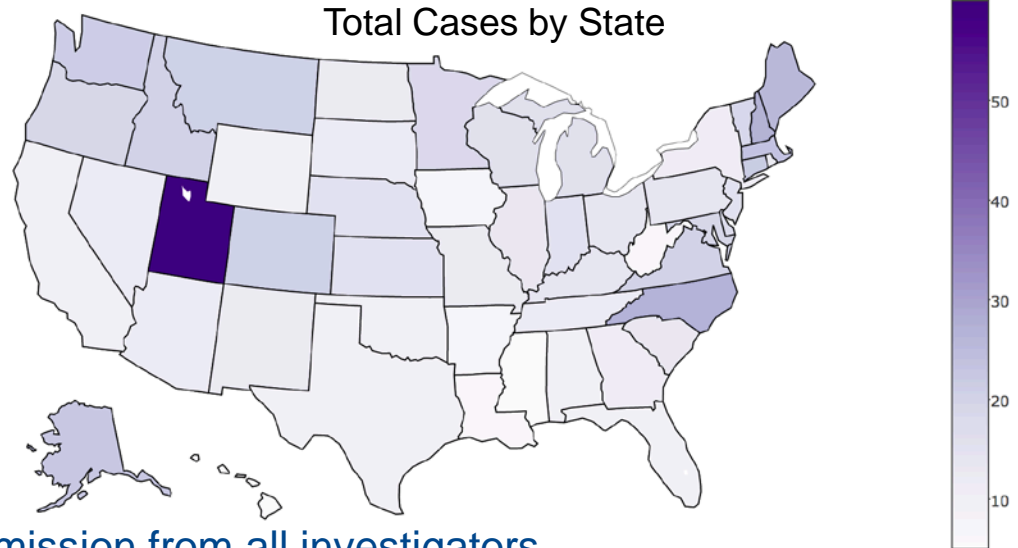
# Power of Team Science to Investigate the Causes of Postpartum Mood Disorders



# Data as of April 2017



- 349 EPDS < 13
- 241 Child born > 6 wks early
- 157 Diagnosed with life-threatening illness after childbirth
- 293 Child died or had life-threatening illness after birth
- 568 Symptom onset prior to pregnancy
- 617 Symptom onset > 3 months postpartum
- 387 Symptom duration < 2 weeks



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# Large Cohort Studies: *All of Us* Research Program

- Key element of the Precision Medicine Initiative (PMI)
  - Launched in FY 2016, now beta testing
  - Aims to enroll over 1 million participants
  - Mission: Accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us



# Large Cohort Studies: ECHO

- Environmental influences on Child Health Outcomes (ECHO)
  - **Cohort:** Aim to include ~50,000 children from diverse racial, geographic, and SES backgrounds
  - **Scientific Goal:** Answer crucial questions about effects of a range of early environmental exposures on child health and development
  - **Focus:** Key pediatric outcomes that have a high public impact

PRE-, PERI-  
AND POSTNATAL



UPPER AND  
LOWER AIRWAY



OBESITY



NEURO-  
DEVELOPMENT



National Institute  
of Mental Health

# Large Cohort Studies: ABCD

- Adolescent Brain Cognitive Development (ABCD) Study
  - Longitudinal study of ~10,000 children from ages 9-10 through early adulthood to assess factors that influence individual brain development trajectories and functional outcomes
  - Aim to fill the gap in research about how childhood experiences affect brain, social, emotional, and academic development
  - Federal collaborators, including NIH (NIDA, NIAAA, NCI, NICHD, NIMH, NIMHD, NINDS, OD), CDC, and DOJ, and private partners





# Big Data – NIMH Data Archive (NDA)

- National Database for Autism Research (NDAR)
  - Trans-NIH initiative sharing research data and results
  - Data from 355 projects and \$800M ASD research investment
  - 115,000+ participants sharing genomics, imaging, neurophysiology, clinical measures
- National Database of Clinical Trials Related to Mental Illness (NDCT)
- Research Domain Criteria database (RDoCdb)
- Adolescent Brain Cognitive Development (ABCD) Study



# NIMH Repository and Genomics Resource (NIMH-RGR)

- Biospecimen repository at Rutgers University Cell & DNA Repository (RUCDR) with clinical/genetic data housed at Washington Univ. in St. Louis (since 1998)

<https://www.nimhgenetics.org/>

- Stem Cell Center at RUCDR provides iPSC lines for research into the cellular mechanisms and druggable targets of mental illness.

Home Available Data Interviews Publications Tools About Site Map Sign In

## NIMH Repository and Genomics Resource

NIMH Center for Collaborative Genomics Research on Mental Disorders

**LATEST AVAILABLE DATA** Depression - Distribution 4.0 includes data from Study 88. (Pls: Le\_

1-2-3-4-5

Request BioSamples

Data Overview

- DNA Samples by Disorder
- iPSC and Fibroblast Cell Lines
- GWAS Data
- Sequence Data
- List of All Studies

Browse Data

Download Data

Stem Cell Resource

Featured Studies

- Clinical Trials
- Psychiatric GWAS Consortium
- The CAPS Project

Help us improve

**NEW!** NIMH Stem Cell Resource for induced pluripotent stem cells (iPSC) and source cells for iPSC.

The NIMH Center for Collaborative Genomic Studies on Mental Disorders was established through the [NIMH Human Genetics Initiative](#) in 1998 to leverage and increase the value of human genetic samples and data produced through NIMH funded research.

The NIMH Center, now known as NIMH Repository and Genomics Resource (NIMH-RGR) plays a key role in facilitating psychiatric genetic research by providing a collection of over 150,000 well characterized, high quality patient and control samples from a [wide-range of mental disorders](#). Through concerted and collaborative efforts of the Biologic Core ([Rutgers University's RUCDR Infinite Biologics](#)) and Data Management Core ([Washington University in St. Louis](#) and the [University of Southern California's Information Sciences Institute](#)), the Center provides the following services:

- Receive, process and store biomaterials ready for analysis (DNA, cell lines and other products) from various primary sources (e.g., blood or skin biopsy) submitted by NIMH grantees
- Distribute biomaterials to approved investigators ([access biosamples](#))

### What's New

July 17, 2014 - iPSC Dist. 3.0 includes data from Study 132 (Pl: Rapoport).

June 19, 2014 - Autism Dist. 12.0 includes data from Study 44 (Pl: Sutcliffe).

May 28, 2014 - Bipolar Disorder Dist. 8.0 includes data from Study 55 (Pls: Nurnberger, Kastelic, McInnis, Reich, Glowinski).

May 20, 2014 - Depression Dist. 4.0 includes data from Study 88 (Pls: Levinson, Weissman, Potash).

April 21, 2014 - Added DP Dataset 7 (Levinson RNA Sequencing Data from Study 88) to Depression Dist. 3.0.

April 15, 2014 - Phelan-McDermid Syndrome Dist. 1.0 includes data from Study 115 (Pls: Hallmayer, Dolmetsch).

March 31, 2014 - Added AU Dataset 4 (Study 65/TASC GWAS Data) to Autism Dist. 11.0.

March 20, 2014 - iPSC Dist. 2.0 includes data from Study 116 (Pl: Vaccarino).

February 20, 2014 - iPSC Dist. 1.0 includes data from Study 115 (Phelan McDermid Foundation; Pls: Hallmayer, Dolmetsch), Study 117 (Fragile X; Pl: Loring, and Study 125 (22q11DS; Pls: Lachman, Rapoport).

# NIMH's Mission

## MISSION

To transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

[www.nimh.nih.gov](http://www.nimh.nih.gov)

*Research = Hope*



# Upcoming NIMH Event

# AUTISM IN GIRLS AND WOMEN

A PANEL DISCUSSION

TUESDAY, SEPTEMBER 19, 2017 • 1:00 PM - 3:00 PM

NEUROSCIENCE CENTER (NSC) • 6001 EXECUTIVE BLVD • ROOM 7102

Event will also be available live on [videocast.nih.gov](http://videocast.nih.gov)



Zoe Gross



Kevin Pelphrey, Ph.D.



Pamela Ventola, Ph.D.