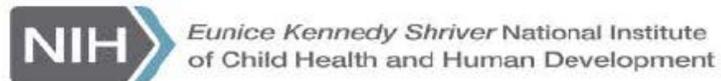


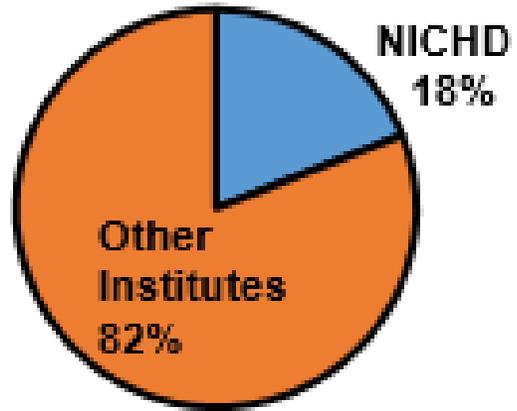
NICHD's Report to the Advisory Committee to the Director

Diana W. Bianchi, M.D.
Director, NICHD
December 14, 2017





What's In a Name?



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





The Docent Approach to NICHD Science

Fertility
Pregnancy



**Neonatal
Health**
Data Sharing

Fertility

- Normal fertility is a biomarker for long-term human health
- Mildest manifestation of single gene disorders is infertility
- NICHD's portfolio encompasses research in contraception, fertility and infertility, gynecologic health and disease
- New concept: Oncofertility
 - Made possible by funding multi-disciplinary team science



Voice of the Patient: Megan Connolly



Megan Connolly speaking at NICHD's September 2017 Council meeting, starting at 1:24:11. <https://videocast.nih.gov/summary.asp?Live=26286&bhcp=1>



the Oncofertility[®] Consortium

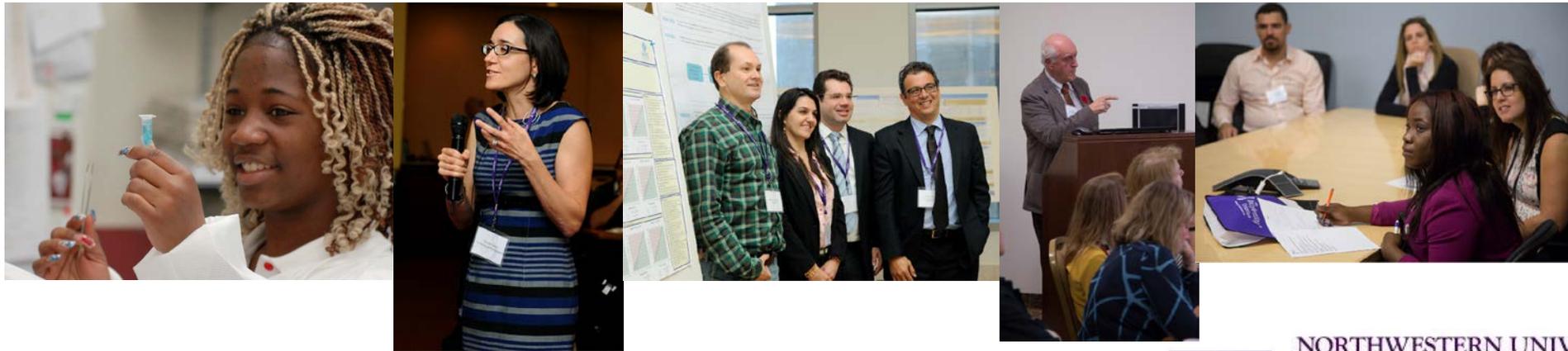
**NATIONAL
PHYSICIANS
COOPERATIVE**



the Oncofertility[®]
Consortium

www.oncofertility.northwestern.edu

**GLOBAL
ONCOFERTILITY
NETWORK**



Funded by NICHD: P50HD076188

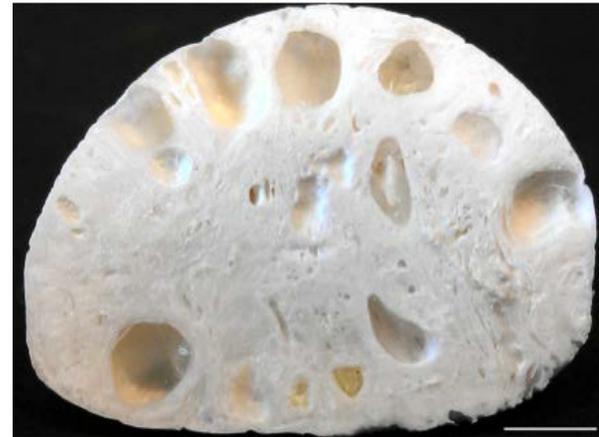
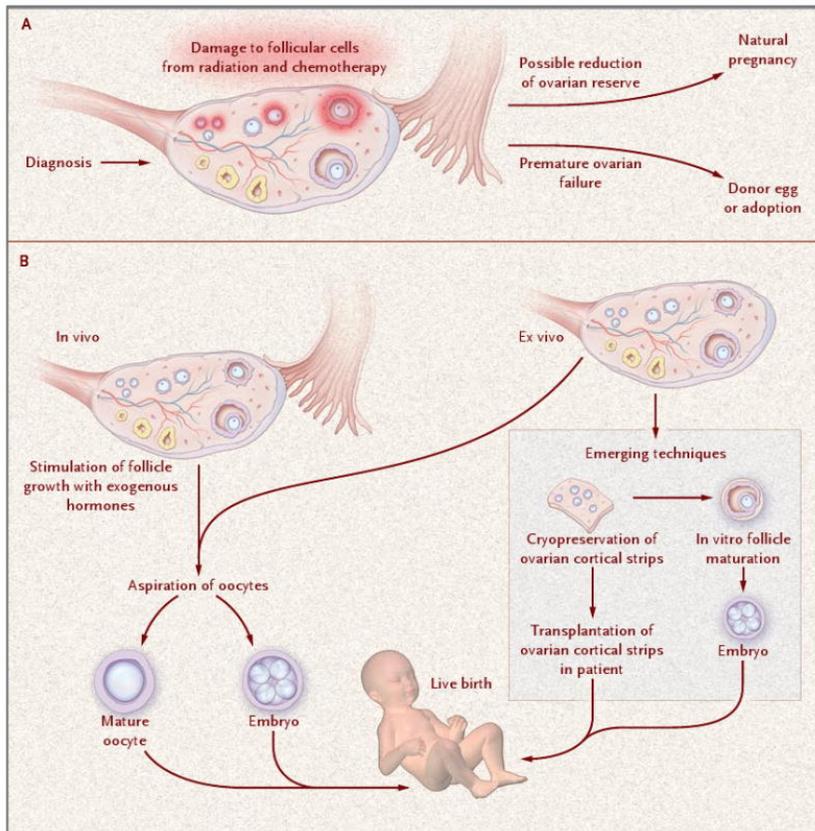


NORTHWESTERN UNIVERSITY
FEINBERG
SCHOOL OF MEDICINE





Improving Fertility Options for Childhood Cancer Survivors



3D printed ovarian scaffold

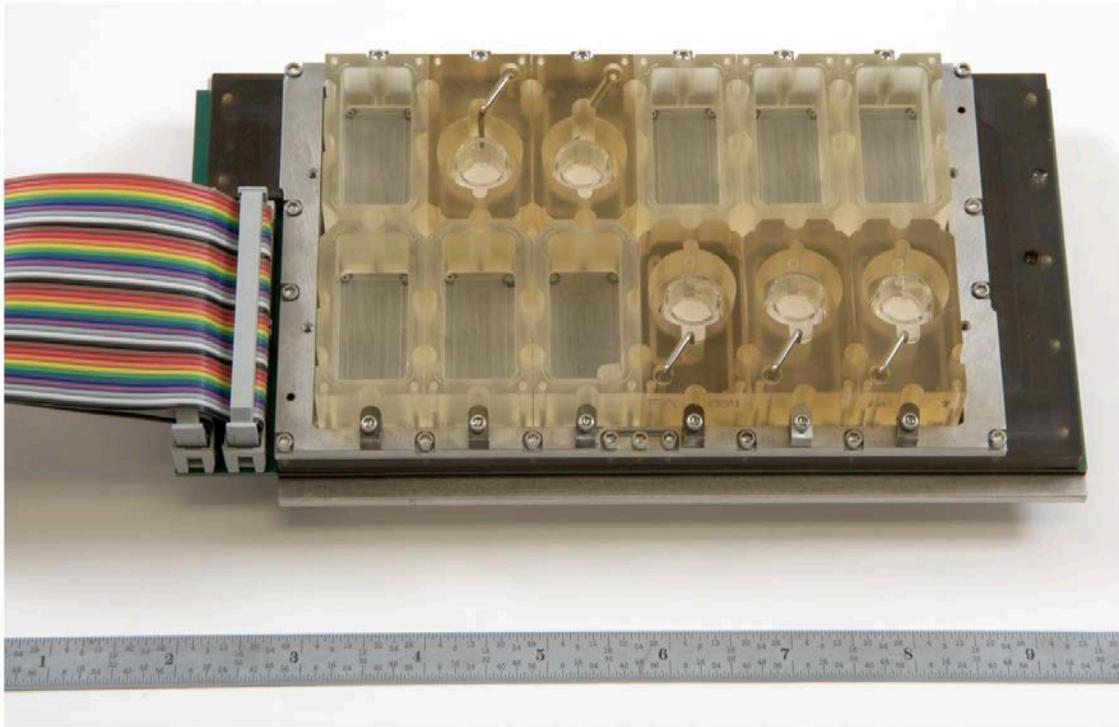


Bioprosthesis ovary restores function *in vivo*

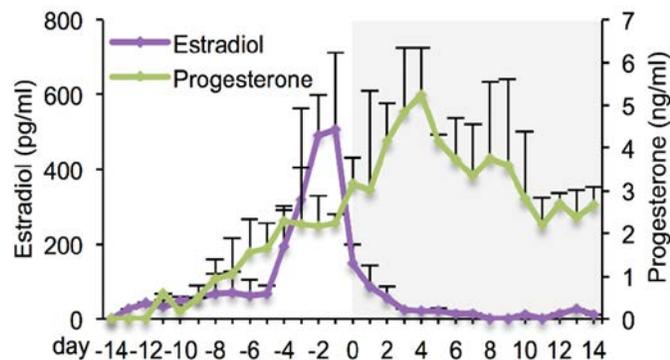
Woodruff lab, Northwestern
HD076188, HD28934,
UH3TR001207



EVATAR: The “Mother” of Microhumans

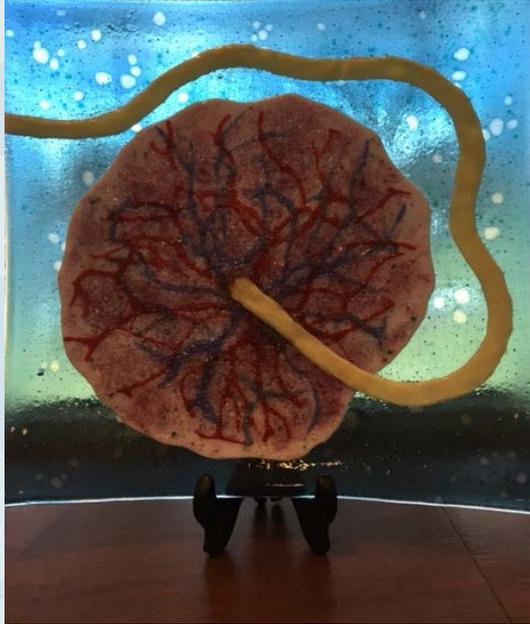


- Enables testing of female tissue function in the presence of cycling hormones
- Contains connected 3D organ models of ovary, fallopian tubes, uterus, cervix and liver (metabolizes hormones)
- Ovaries produce cycling levels of hormones; pumps and channels bring hormones to other organs
- Allows pre-clinical testing of drugs and toxicology studies



Woodruff lab, Northwestern UH3TR001207

Pregnancy



“NICHD’s organ”

- A healthy placenta is essential for normal human development and fetal metabolic programming
- The Human Placenta Project was launched in 2014 to develop novel safe, real-time technologies for assessment of placental development/function
- Current investment of more than \$51M across 9 FOAs: imaging, 'omics, microbiome, epigenetics, exosome analysis
- A global effort: Many PIs from the U.S. but includes researchers in Canada, the UK, and Australia – 32 Awards made since 2015
- Initial successes are beginning to emerge

Multidisciplinary Science

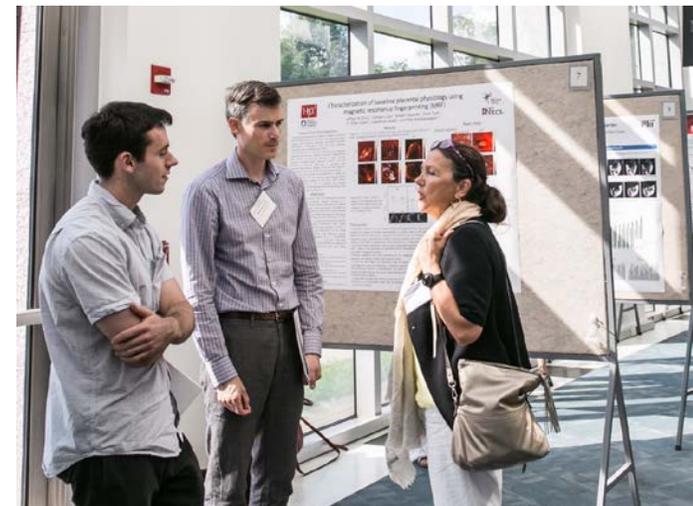


4th Annual Human Placenta Project Meeting



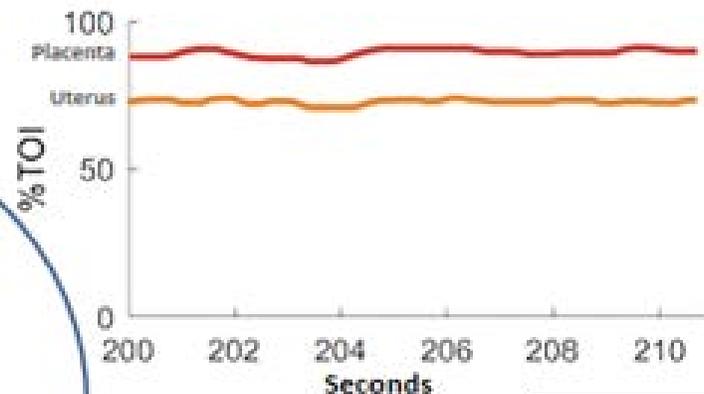
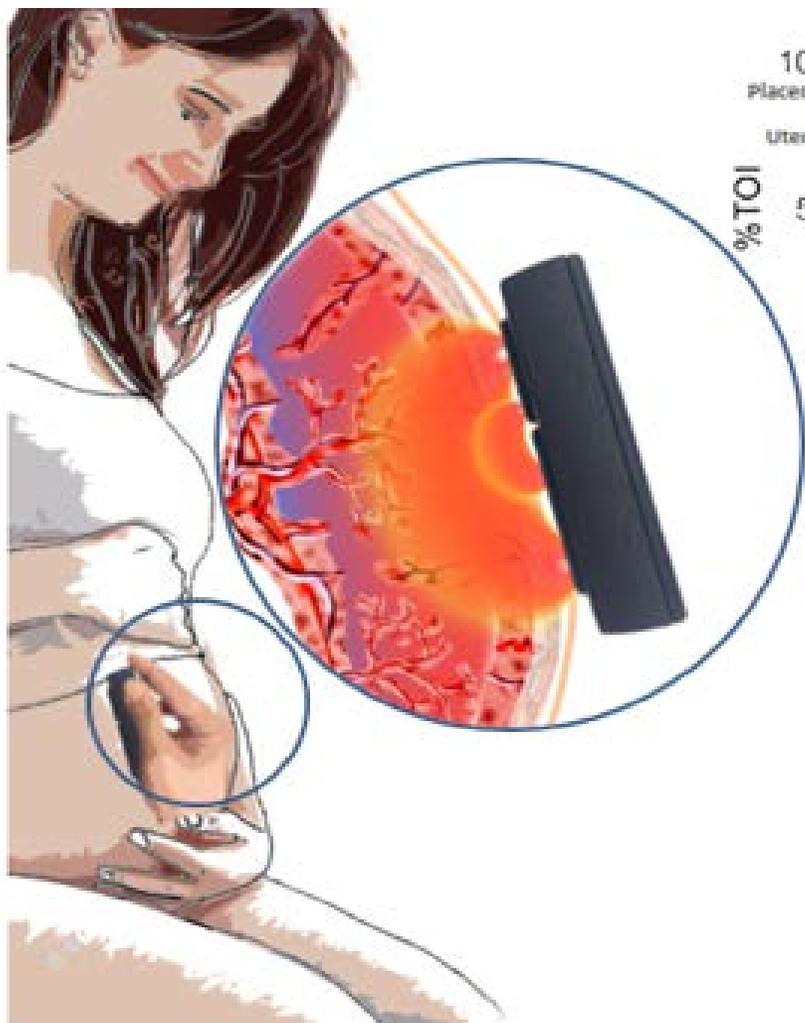
July 24-25, 2017

Grantee updates, poster session and demos





Wireless Compact Wearable Device for Continuous Placental Oxygenation Monitoring



- **Continuous**
- **Non-invasive**
- **High Clinical Impact Potential**

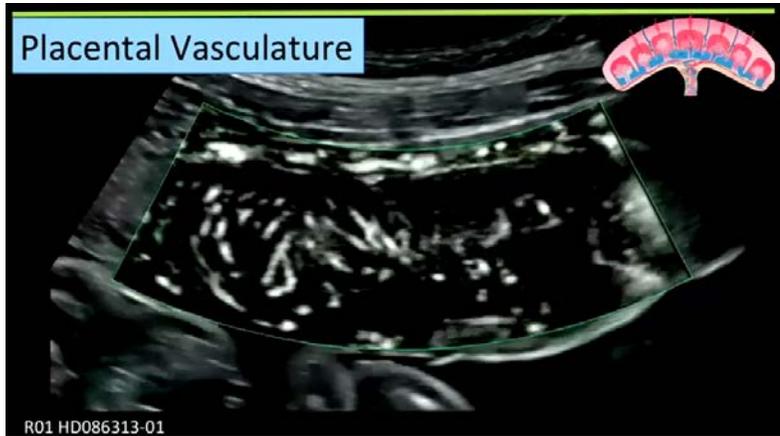


Laboratory of Dr.
Amir Gandjbakhche

Clinical
Collaborations
with

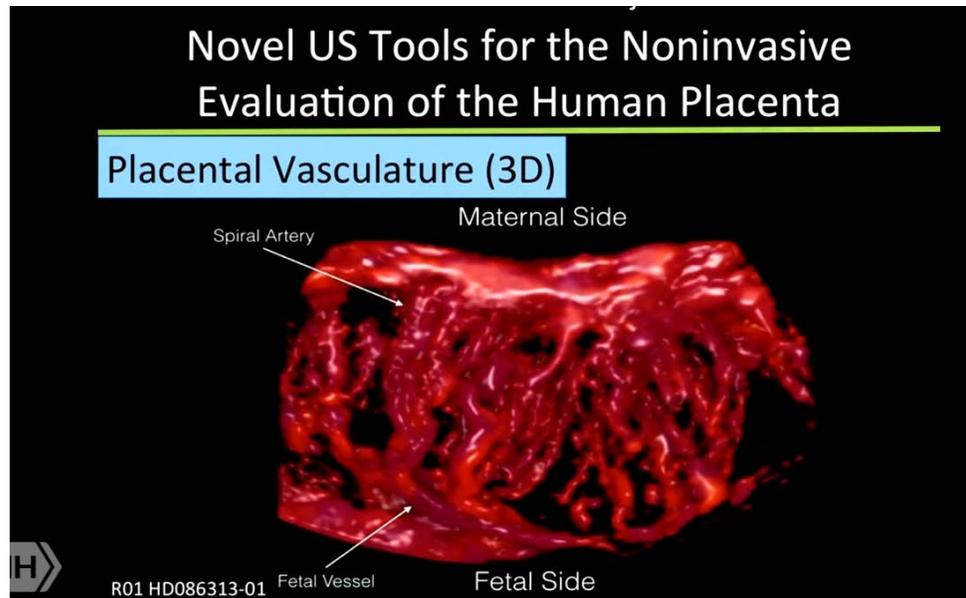
Wayne
State/Hutzel
Hospital and

Walter Reed
National Medical
Center



Anatomy: Microvascular Imaging

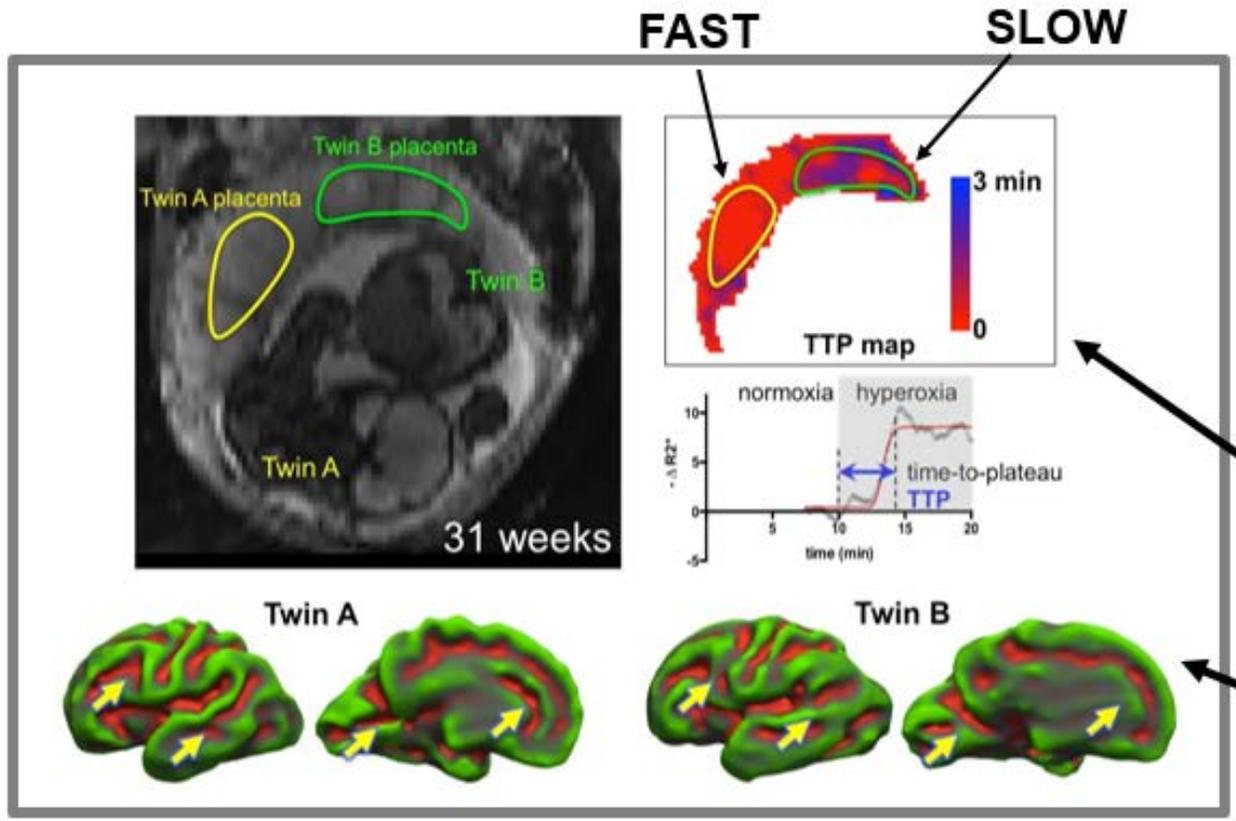
- 15-16 weeks gestation – can visualize both fetal and maternal circulation
- Can count spiral arteries, fetal arterioles, and do quantitation with doppler techniques
- Generate a vascular index – the degree of vascularity for a given region of the placenta



Allows assessment of the overall health of the placenta

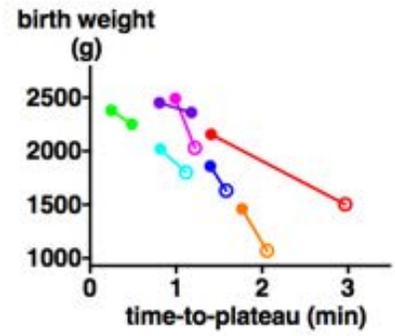
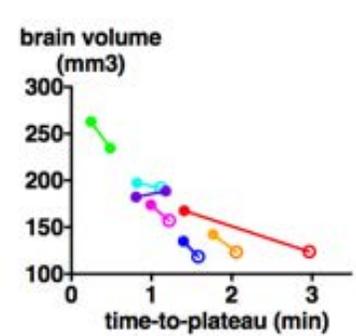
Alfred Abuhamad, EVMS - HPP Grantee

Applying Cutting-Edge MRI Technologies to Placental Assessment



Connecting placental function to outcomes

- Monochorionic diamniotic twins
 - Same placenta, separate amniotic sacs
- Unequal placental delivery of oxygen
- Differences in brain formation
- Differences in brain volume and birth weight



Ellen Grant, Harvard Medical School - HPP Grantee



Ira Flatow, Host

science FRIDAY

June 23, 2017



SEGMENT | 17:32

Getting To Know The Placenta

Researchers look to the mysterious organ for a new way of monitoring fetal health during pregnancy.



READ MORE

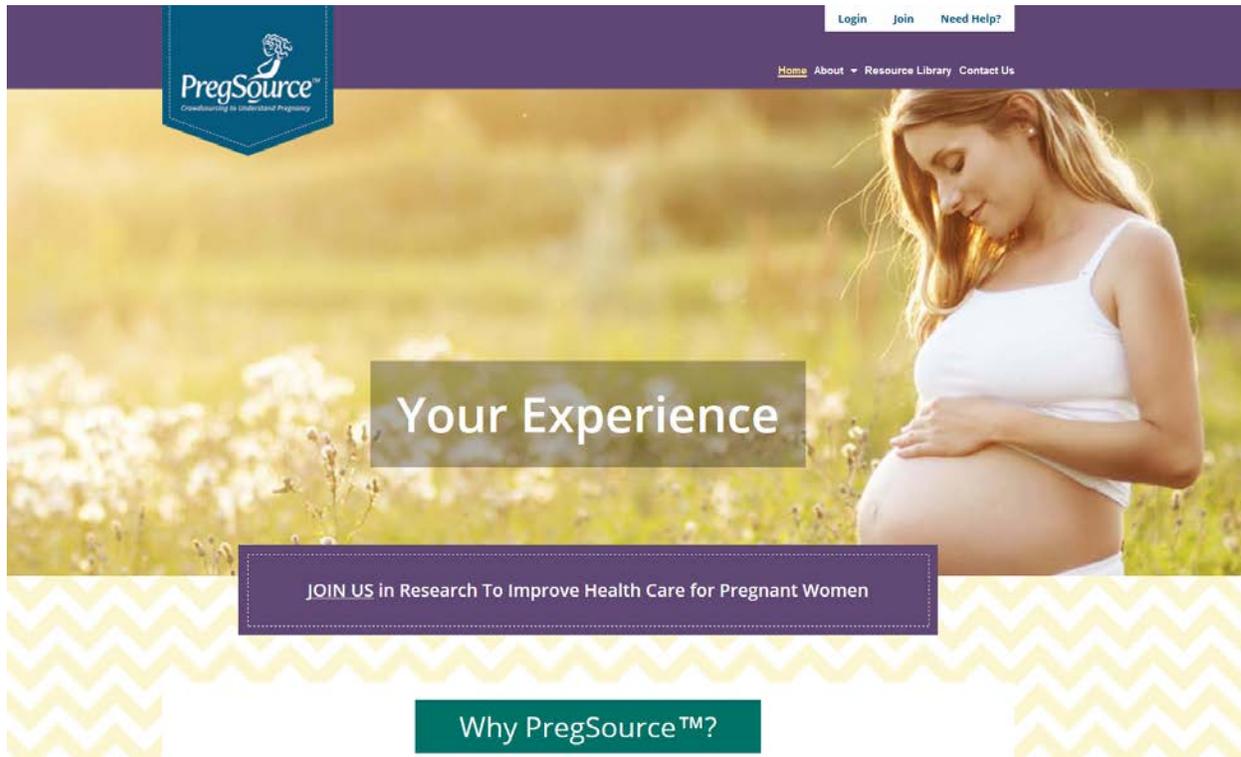
<https://www.sciencefriday.com/segments/getting-to-know-the-placenta/>

r

Using *Crowdsourcing* to Define Typical Pregnancy

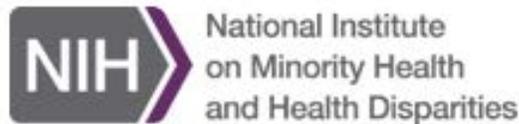
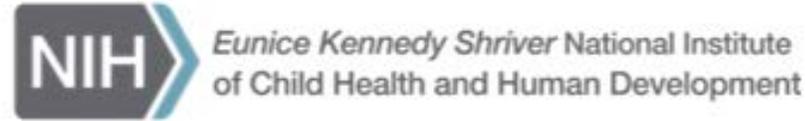


PregSource™ Home Page



- Pregnant women will provide information about their experiences in real-time:
 - Sleep
 - Nausea
 - Exercise
 - Weight
 - Medications
- Answers to these topics will help researchers build a more complete picture of normal pregnancy and develop strategies for improving maternal care

PregSource™ Partners



21st Century Cure Act Update



SEC. 2041. TASK FORCE ON RESEARCH SPECIFIC TO PREGNANT WOMEN AND LACTATING WOMEN.

Specific topics to be addressed:

- Existing Federal efforts and programs to understand the health effects on pregnant and lactating women, and related birth and pediatric outcomes
- Research collaboration potential
- Ethical issues surrounding inclusion of pregnant and lactating women in clinical research
- Effective communication strategies with health care providers and the public
- 2 of 4 meetings have been completed
- Report to HHS due in September 2018

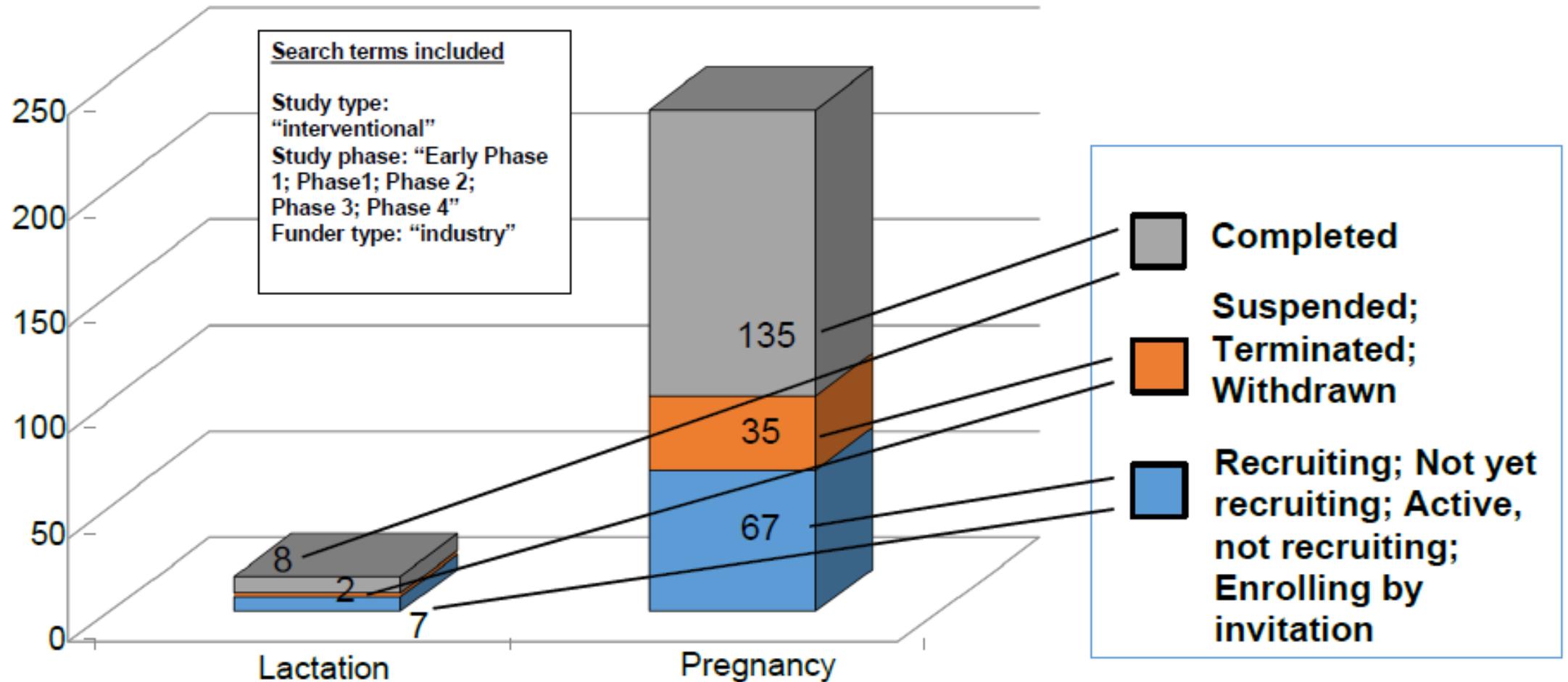


NICHD Pregnancy and Lactation Literature Analysis 2006-2017: Results for Pregnancy

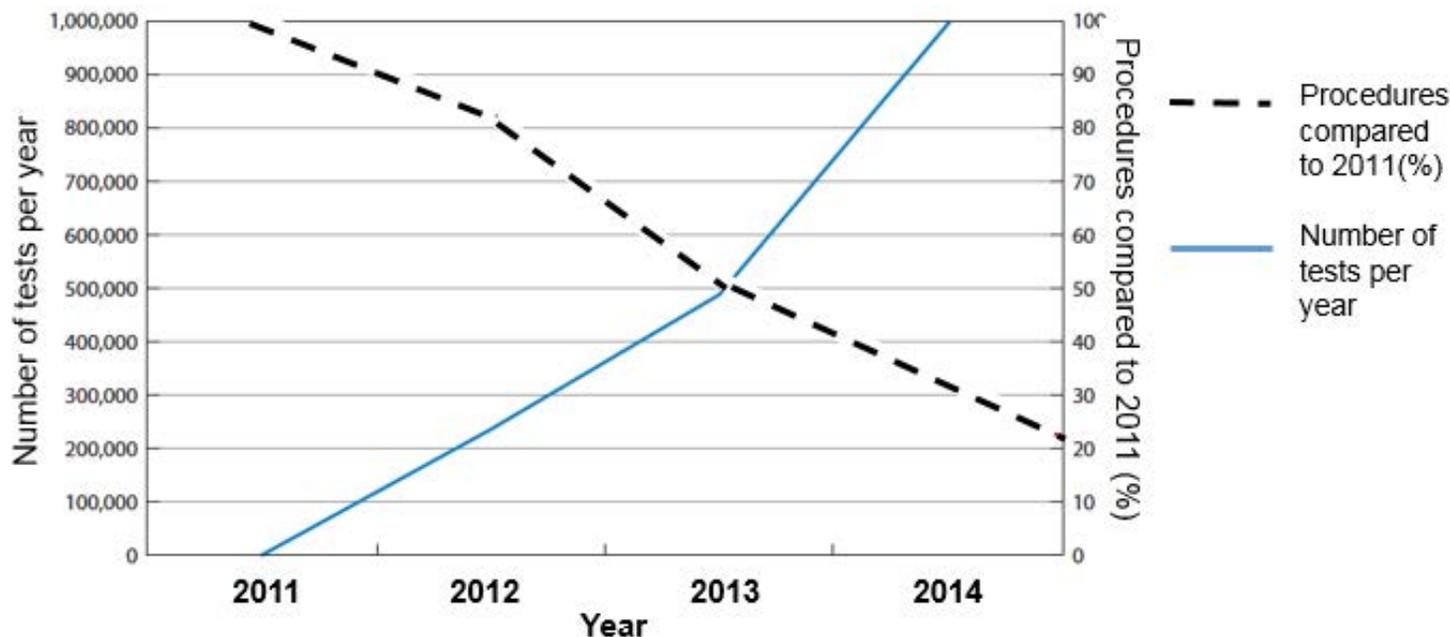
- RCTs rare in almost all areas
- Exceptions:
 - Hypertension
 - Preterm labor
 - Labor pain medication
 - Opioids and tobacco

	Condition	Basic	PK/PD	Pop/DB	RCT
Hypertension	Hypertension	127	9	18	40
Mental Health	Anxiety	16	0	3	2
	Bipolar	1	0	1	0
	Depression	21	4	21	4
	Schizophrenia	11	0	1	0
Pain	Labor Pain	5	0	7	49
	Headache/migraine	0	0	5	1
Preterm labor	Preterm labor	152	21	35	169
Substance Abuse	Alcohol	26	0	0	0
	Cocaine	6	0	1	0
	Meth/amph	10	3	1	0
	Opioids	22	3	9	25
	Tobacco	22	3	16	27

Status of Industry-Sponsored Interventional Trials in the US



Reproductive Genomics: Partnership with NHGRI



Hui and Bianchi, *Ann Rev Med* 2017; 68: 459-472

© American College of Medical Genetics and Genomics

REVIEW | Genetics in Medicine

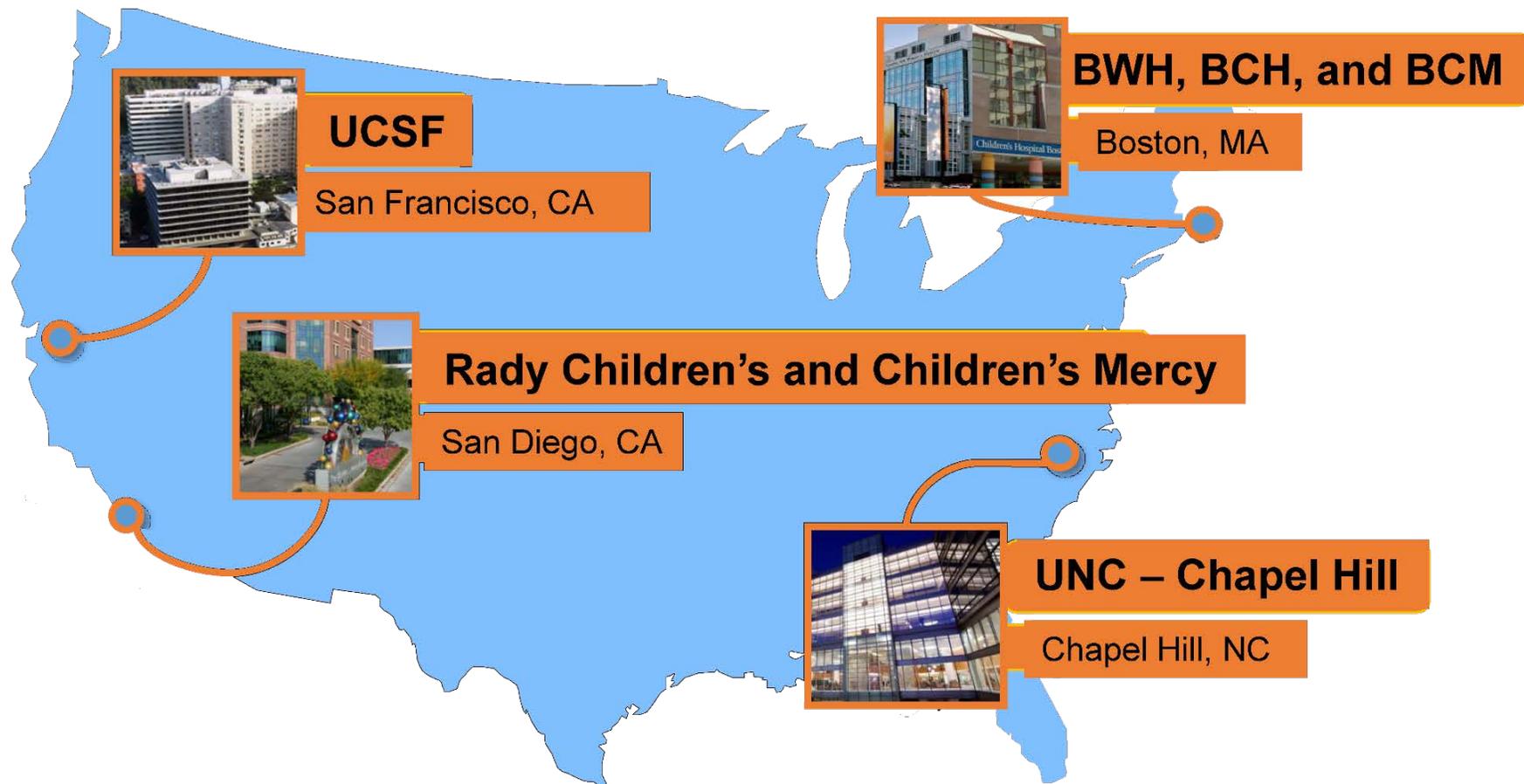
Spring 2018 workshop on Genomic Medicine for Reproductive, Prenatal and Neonatal Health

Cherchez la femme: maternal incidental findings can explain discordant prenatal cell-free DNA sequencing results

Diana W. **Bianchi**, MD

Newborn Sequencing In Genomic medicine and public Health (NSIGHT)

Neonatal Health



Newborn Sequencing Questions



For disorders currently screened for in newborns, how can genomic sequencing **replicate or augment** known newborn screening results?

What knowledge about **conditions not currently screened** for in newborns could genomic sequencing of newborns provide?

What additional clinical information could be learned from genomic sequencing relevant to the **clinical care of newborns**?

N SIGHT Findings to Date



BIOMEDICINE

Baby genome screening needs more time to gestate

Unenthused parents and missed diseases mar pilot efforts

Kaiser J. *Science*. Oct 28 2016;
354: 398-399

- Exome sequencing currently cannot replicate known newborn biochemical screening results – **of 182 exomes, 12.3% false negatives**
- However, WES is useful to augment newborn screening – **can identify mutated gene(s)**
- Recruitment much lower than anticipated based on survey data – **46% reported “very”, or “extremely” interested in newborn genomic testing**
- Initially, only 7% enrollment – **24 of 345 sick NICU infants, and 138 of 2062 healthy babies**
 - Noted logistical concerns on 1st approach
 - After GC meeting, privacy, unclear results, and insurance discrimination concerns noted

Rapid DNA Sequencing in Critically Ill Newborns



- NICU sequencing leads to diagnoses and changes in clinical management
 - **20 out of 35 (57%) infants diagnosed**
 - **13 out of 20 (65%) diagnoses impacted acute clinical management** such as: change in medication, palliative care, or reproductive genetic counseling

Rapid whole-genome sequencing identifies a novel homozygous NPC1 variant associated with Niemann-Pick type C1 disease in a 7-week-old male with cholestasis

Amber Hildreth,^{1,2} Kristen Wigby,³ Shimul Chowdhury,¹ Shareef Nahas,¹ Jaime Barea,³ Paulina Ordonez,^{2,4} Sergey Batalov,¹ David Dimmock,¹ Stephen Kingsmore,¹ and on behalf of the RCIGM Investigators

¹Rady Children's Institute of Genomic Medicine, San Diego, California 92123, USA; ²Department of Pediatrics, Division of Gastroenterology, University of California San Diego, La Jolla, California 92093, USA; ³Department of Pediatrics, Division of Medical Genetics, University of California San Diego, La Jolla, California 92093, USA; ⁴Sanford Consortium of Regenerative Medicine, La Jolla, California 92037, USA

Willig et al.
Lancet Respir Med 2015;
3: 377-387

Data Sharing

<http://dash.nichd.nih.gov>

Study Topics Represented in DASH
(Number of studies in parentheses;
some studies with overlapping topics)

Autism Spectrum Disorder (1)
Children's Bone Health and Calcium (1)
Diabetes (1)
Early Learning (1)
High Risk Pregnancy (2)
HIV/AIDS (29)
Infant Care and Infant Health (3)
Infant Mortality (1)
Labor and Delivery (2)
Neuroscience (1)
Necrotizing Enterocolitis (1)
Pharmacology (2)
Preconception Care and Prenatal Care (1)
Preeclampsia and Eclampsia (2)
Pregnancy (9)
Pregnancy Loss (1)
Preterm Labor and Birth (6)
Rehabilitation Medicine (1)
Stillbirth (1)
Stroke (1)
Sudden Infant Death Syndrome (1)
Women's Health (1)

- Centralized resource for researchers to store and access de-identified data from studies supported by NICHD
- Can help investigators meet NIH's data sharing requirements for their own studies and find others' study data for secondary analyses
- Aims to accelerate scientific findings and improve human health
- Launched in August 2015 and governed by the NICHD DASH Committee



53 Studies Available



22 Study Topics



11.3K+ Users



68 Data Requests

Questions? Contact supportdash@mail.nih.gov.

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

DASH Study Submissions

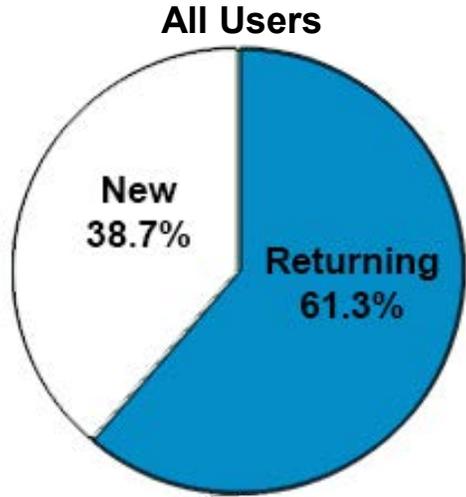


Studies in DASH: Jul '15- Oct '17

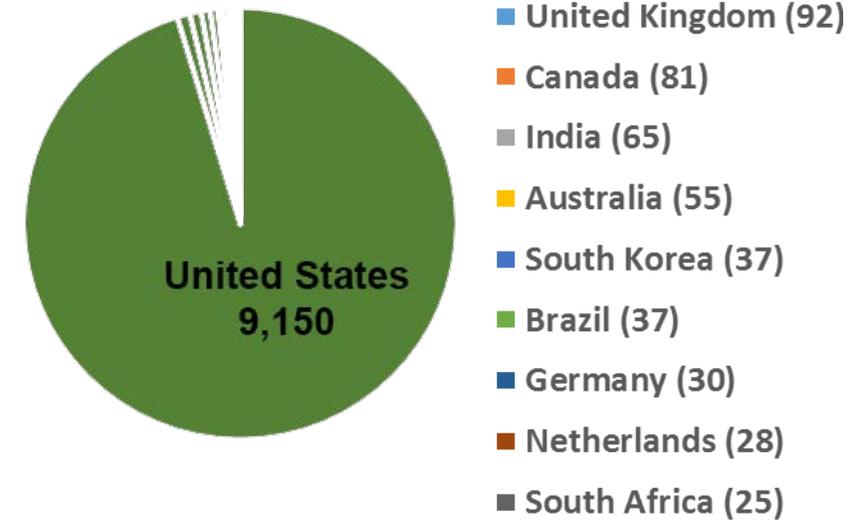
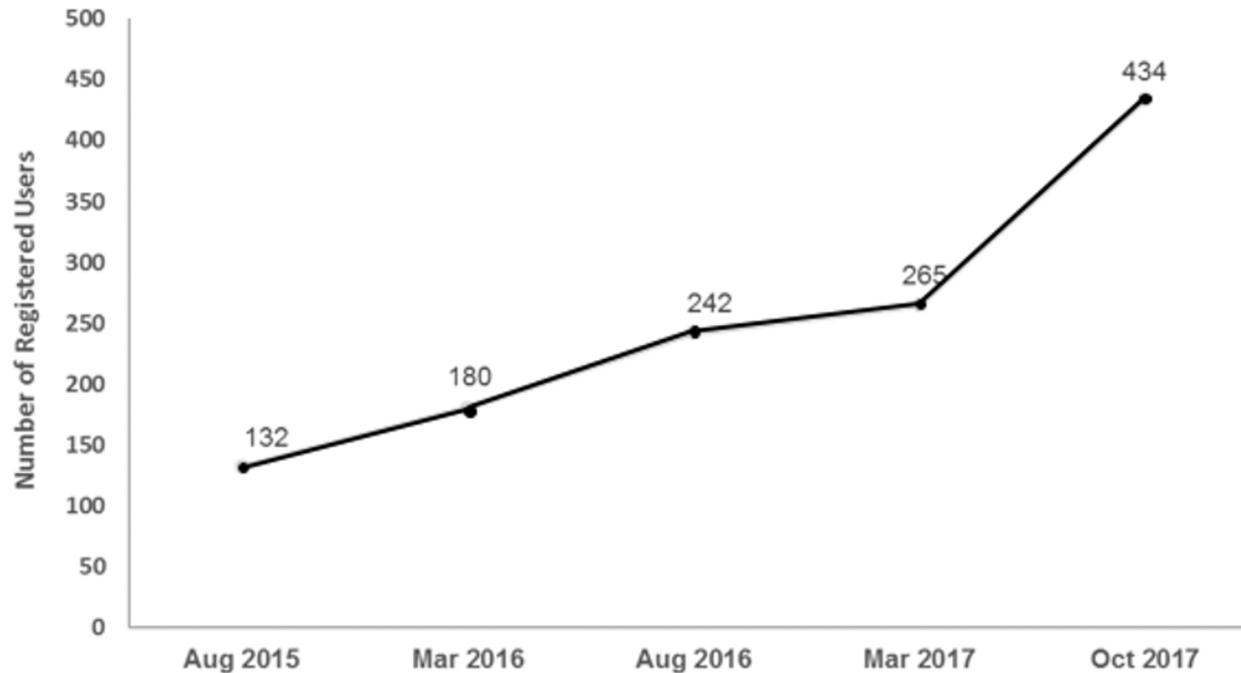


- Average 4.5 studies submitted and released in DASH each quarter, up from 2.5 last year
- *Key Take-away: Obtaining IRB approvals by the PI or the Data Coordinating Center for sharing data in DASH, especially for the 38 multi-site studies, was the single rate limiting factor for timely submission in DASH*

DASH Registered Users



Number of Registered Users in DASH: Aug '15 – Oct '17



10% of users from 105 other countries

Summary



- **NICHD is at the forefront of multi-disciplinary science in reproduction, pregnancy, and neonatal health**
- **The Human Placenta Project is already delivering impactful results**
- **Major gaps in understanding drug effects in pregnancy/lactation**
- **Too early to tell the analytical validity and clinical utility of newborn DNA sequencing**
- **Our vision= to improve lifelong health by understanding human development**



Tara Shafer's presentation at **the 4th Annual Human Placenta Project Meeting**, July 2017 (begins at 1:41:00).

<https://videocast.nih.gov/summary.asp?Live=24783&bhcp=1>.



Questions?