Safe Passage Study Update
Aberdeen Area Indian Health Service
Perinatal Infant Mortality Review Board (PIMR)

Aberdeen Area Infant Mortality Study
Aberdeen Area Infant Mortality Study (1992-1996)

- 9 tribes and 1 urban area in the Northern Plains participated
- Sample Size
  - 72 deaths
  - 38 of 72 (53%) confirmed as SIDS
- Significant risk factors for SIDS
  - Maternal drinking during periconceptional period: ↑ 6x
  - Maternal binge drinking during the 1st trimester: ↑ 8x
  - Two or more layers of clothing at death: ↑ 6x

Iyasu et al., JAMA 2002
The Rostral and Caudal Domains of the Serotonergic (5-HT) Brainstem System

Rostral Domain (upper brainstem): Cognition and Affective Behavior

Caudal Domain (lower brainstem): Integration & modulation of resp, autonomic control, temp reg, upper airway reflexes
SIDS: Failure of the Serotonin Brainstem “Alarm” System
Resulting in an Inability to Wake Up to Dangerously Low Levels of Oxygen and/or
Dangerously High Levels of Carbon Dioxide During Sleep
Step 1
Life-threatening event
Asphyxia and brain hypoperfusion

Step 2
Failure of arousal
Progressive asphyxia

Step 3
Hypoxic coma

Step 4
Bradycardia and gasping

Step 5
Failure of autoresuscitation resulting in death
Prenatal Alcohol, SIDS, and Stillbirth

Phase I, 2003-2006: Development of hypotheses and protocols; pilot/feasibility studies

Phase II, 2006-2016: Performance of full-scale, hypotheses-driven studies (prospective and retrospective studies planned)

Enrollment complete n= 12,024

Funded by NICHD/NIAAA/NIDCD – U01-HD045935 (Elliott)
PASS Network Organizational Structure

**Clinical Sites**
- Northern Plains, USA
  - Pine Ridge, SD
  - Rapid City, SD
  - Sanford Health, SD
  - Spirit Lake, ND
- Stellenbosch, SA
  - Bishop Lavis

**NIH**
- National Institute of Child Health and Development (NICHD)
- National Institute on Alcohol Abuse and Alcoholism (NIAAA)
- National Institute on Deafness and Other Communication Disorders (NIDCD)

**Steering Committee**

**Analysis Centers**
- Data Coordinating and Analysis Center (DCAC)
  - DM-STAT, Inc.
  - Boston
- Developmental Biology and Pathology Center (DBPC)
  - Children's Hospital
  - Boston
- Physiology Assessment Center (PAC)
  - Columbia University
  - New York

With oversight from the Advisory and Safety Monitoring Board (ASMB)
Multidisciplinary Approach

Environmental Modifiers
- Dose, Pattern, Timing, Smoking, Nutrition, Maternal Disease, Psychosocial Factors

Fetal Alcohol Exposure
- Self-Report, Meconium Biomarkers

Placenta
- Ultrasonography, Pathology, Biochemistry

CNS and ANS
- Fetal/Infant Physiology, Infant EEG and Hearing, Neuropathology

Stillbirth
- Pathology

SIDS
- Pathology

FASD
- Dysmorphology, Neurodevelopment

Genetic Modifiers
- CNVs, Epigenetics
Northern Plains Infrastructure

- **Tribal**
  - Community involvement from study initiation
  - Tribal Resolutions – Oglala Sioux Tribe & Spirit Lake Nation
    - Multiple time points
- **Regulatory**
  - IRB’s: Sanford; Oglala Sioux Tribe Research Review Board; Aberdeen Area Indian Health Service; UND (agreement); Regional Health (agreement);
- **Federal**
  - Certificate of Confidentiality
    - Judge Linda Chezem, NIAAA
- **State**
  - MOA - South Dakota Dept of Social Services
  - MOA – WIC (recruitment)
PASS Partners

Sioux Falls (SD)
- Sanford Health
- Sanford Women’s, Sioux Falls
- LCM Pathologists, Sioux Falls

Pine Ridge (SD)
- Pine Ridge IHS
- Oglala Lakota College, Dept. of Nursing
- WIC

Spirit Lake/Altru (ND)
- Mercy Hospital, Devil’s Lake, ND
- Spirit Lake MCH – IHS, Fort Totten, ND
- Altru Clinic, Devil’s Lake, ND
- University of North Dakota

Rapid City (SD)
- Rapid City Regional Hospital
- Native Women’s Health Center
- USD Sanford School of Medicine
- WIC
- Black Hills Ob-Gyn
- Black Hills Peds
- Rapid City Community Health
- Clinical Lab of the Black Hills
Common Study Protocol

**Prenatal week**
- 6
- ~22
- ~30
- 34+
- **birth**

**Postnatal month**
- 1
- 12

**Recruitment**
- 12,000 pregnant women

**12,000 pregnant women**
- Exposure Hx
- Fetal/Infant Physio
- 3D & Doppler U/S
- Psychosocial
- SES, Maternal Saliva
- Nutrition
- Autopsy, Neuropath, Classification

**EMBEDDED STUDY**
- Cord Blood
- Meconium
- Dysmorphology
- Chart Abstraction
- Neurodevelopment
- Placental Path
- Cord Blood, Meconium

**All subjects**

**Embedded only**

**Fetal demise**

**Infant demise**

**SANFORD RESEARCH**
Compliance:

- On average, **a given woman** came in for **82.8%** of all scheduled prenatal, delivery, newborn, and postnatal contacts.
- Consent for DNA for research: **98.5%**
- Consent for placental tissues for research: **94.3%**
- Consent for photographs of infant face: **99.3%**
- Withdrawal of overall study consent: **3%**
- Pregnancy outcome ascertainment rate: **97.6%**
Future Steps

• Last baby anticipated birth Aug. 2015
  – Become unblinded to stillbirth data
  – Primary analysis complete by Jan. 2016

• Last 1 year visit completed Aug. 2016
  – Become unblinded to SIDS data
  – Primary analysis complete by Jan. 2017

• Numerous other secondary findings in process
What it’s been like managing the study(s) in Pine Ridge

Cultural Competency; Understanding the Customary beliefs and social norms
Challenges

• Spiritual beliefs, teachings and understanding
• Transportation
Successes

- Transparency
- Respect
- Transportation
Vision for the Future

• The same but different “Culture is one group of people preferred way of meeting their basic human needs” - Carol Iron Rope Herrera (2014)

• TEAMWORK
Funding Acknowledgements

• PASS: NICHD/NIAAA/NIDCD – U01-HD045935 (Elliott)
Pilamaya (thank you)!