National Center on Birth Defects and Developmental Disabilities

The Study to Explore Early Development

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SEED Research Objectives

- Assess etiologic risk factors for ASD
  - Focus on
    - Genetics
    - Non-genetic exposures in pregnancy
- Characterize ASD phenotypic subtypes
- Assess health of children with ASD and other developmental disabilities

SEED Methods

Case-control study – designed to enroll demographically diverse population of children from various U.S. areas

3 groups of children and their mothers are invited

- **ASD Group**

  identified from clinics and schools that conduct developmental exams on children residing in defined population area for each site

- **Comparison Group 1 – Other Developmental Delays (DD)**

  identified from same sources as ASD gp

- **Comparison Group 2 – Population Controls (POP)**

  sampled from birth records at each site

SEED Methods

- Birth cohorts:
  - *SEED 1:   2003-2006*
  - *SEED 2:   2008-2011*
  - *SEED 3:   2014-2017*

- Children 30-68 months of age during data collection

SEED Methods

Rigorous case classification methods

- At enrollment, children have presumptive classification – ASD, DD, POP

- **All** children screened for autism symptoms -- *Social Communication Questionnaire* (SCQ)

- Children with high SCQ score or a previous ASD diagnosis considered **possible ASD cases**

- Possible ASD cases undergo confirmatory assessments -- *ADOS and ADI-R (Autism Diagnostic Observation Schedule, Autism Diagnostic Interview-Revised)*

- Children meeting SEED study criteria on ADOS and ADI-R classified as cases

SEED Methods, Data Collection

Study Instrument	SEED 1
Social Communication Questionnaire	X
Maternal Telephone Interview *Family socio-demographics, maternal reproductive health & pregnancy exposures*	X
Self-administered Forms *Family and child health and child behaviors and development*	X *(12)*
In Person Child Developmental Assessment *All -- Mullen Scales of Early Learning* *Possible ASD cases –ADOS, ADI-R, Vineland Adaptive Behavioral Scales*	X
Buccal and Blood Samples *Collected from child, mother, and father if available*	X
Dysmorphology Exam	X
Diet and Stool Diaries	X
Medical Record Abstractions *Maternal prenatal care, labor & delivery, and child neonatal, pediatric records*	X

SEED Methods, Data Collection

Study Instrument	SEED 1	SEED 2
Social Communication Questionnaire	X	X
Maternal Telephone Interview *Family socio-demographics, maternal reproductive health & pregnancy exposures*	X	X
Self-administered Forms *Family and child health and child behaviors and development*	X *(12)*	X *(6)*
Maternal and Child Residential History Form		X
In Person Child Developmental Assessment *All -- Mullen Scales of Early Learning* *Possible ASD cases –ADOS, ADI-R, Vineland Adaptive Behavioral Scales*	X	X
Saliva and Blood Samples *Collected from child, mother, and father if available*	X	X
~~Dysmorphology Exam~~	X	
Child Measurements *Weight, height, head circumference*		X
~~Diet and Stool Diaries~~	X	
Medical Record Abstractions *Maternal prenatal care, labor & delivery, and child neonatal, pediatric records*	X	X

SEED Methods, Data Collection

Study Instrument	SEED 1	SEED 2	SEED 3
Social Communication Questionnaire	X	X	**X**
Maternal Telephone Interview *Family socio-demographics, maternal reproductive health & pregnancy exposures*	X	X	**X**
Self-administered Forms *Family and child health and child behaviors and development*	X *(12)*	X *(6)*	**X *(6)***
Maternal and Child Residential History Form		X	**X**
In Person Child Developmental Assessment *All -- Mullen Scales of Early Learning* *Possible ASD cases —ADOS, ADI-R, Vineland Adaptive Behavioral Scales*	X	X	**X**
Saliva and Blood Samples *Collected from child, mother, and father if available*	X	X	**X**
~~Dysmorphology Exam~~	X		
Child Measurements *Weight, height, head circumference*		X	**X**
~~Diet and Stool Diaries~~	X		
~~Medical Record Abstractions~~ *~~Maternal prenatal care, labor & delivery, and child neonatal, pediatric records~~*	X	X	

SEED Sample Summary

Final Study Classification	ASD	DD	POP	Total
SEED 1	707	1270	1223	3200
SEED 2	773	1060	1066	2899
Total	1480	2330	2289	6099

SEED Analyses

- **SEED 1** -- analyses ongoing
  - >40 papers completed (17 published or In Press)
  - >40 analyses in progress
- **SEED 2** – analytic files recently finalized, many new analyses with expanded sample size being planned
- **SEED 3** – data collection began in August

SEED Teen

SEED Teen Research Objectives

To assess and compare adolescents with ASD, with other DDs, and adolescents in the general population (POP)

- Developmental trajectory from preschool age to adolescence

- Health and functioning

- Healthcare utilization and needs

- Education attainment and needs

- Family impacts

SEED Teen Overview

- First phase is a follow-up of children enrolled in SEED 1 case-control study

- 4 sites included: *GA, MD, NC, PA*

- Data collection will occur when children ~14-15 years of age

- Sample size estimates of eligible children

ASD	DD	POP	Total
381	542	487	1410

SEED Teen Data Collection

Mother or other primary caregiver asked to complete

- 2 questionnaires
  - *Social Responsiveness Scale* – standardized instrument that was also included in the case-control study
  - *SEED Teen Health and Development Survey* -- developed by SEED Teen investigators
  - Total time to complete ~1 hour

- Supplemental consent form to share genetic data from biosamples obtained previously with NIH repositories

Highlights of SEED Analyses and Findings

ASD Risk Factors Studies

- *Autism Spectrum Disorder and Birth Spacing*– *Laura Schieve, PhD*

- *Maternal Infection and Fever during Pregnancy and Risk of Autism Spectrum Disorder* – *presented by M. Danielle Fallin, PhD on behalf of Lisa Croen, PhD*

ASD Genetic Associations

- *Peripheral Blood DNA Methylation and ASD –* *M. Danielle Fallin, PhD*

ASD and Child Health Effects

- *Gastrointestinal Symptoms in 2 – 5 Year Old Children*– *Ann Reynolds, MD*

Characteristics of Children with ASD

- *A Novel Protocol for Characterizing Dysmorphology to Enhance the Phenotypic Classification of ASD* -- *Stuart Shapira, MD, PhD*