Heather Volk
On Behalf of Wendy Klag Center Investigators
The department houses several school-based centers, and has a significant role in many others across the school. These are described below. Centers help bring together faculty, students, and community partners across multiple departments and schools to meet their particular missions in pursuit of improving public mental health.

Center for Prevention of Youth Violence
Center for Prevention & Early Intervention
Moore Center for the Prevention of Child Sexual Abuse
Wendy Klag Center for Autism and Developmental Disabilities
Center for Mental Health and Addiction Policy Research
Center on Aging and Health
• 1 in 38 boys (4 to 1)
• Autism in children costs $61 billion per year in US & $175 billion for adults on the spectrum*
• $50,000-$100,000 per family, depending on age and severity*
• Unmeasured family costs in time, lost wages/career opportunities, relationships

There is no medical detection or cure for autism

www.cdc.gov/ncbddd/autism/data.html
Wendy Klag Center for Autism and Developmental Disabilities

Director: Dani Fallin

Associate Directors:
- Janet DiPietro: Research Initiatives
- Liz Stuart: Statistical Methods
- Li-Ching Lee: Global Epidemiology
- Heather Volk: Environmental Epidemiology

Administrator & Communications: Michelle Landrum

Project Coordinator: Jamie Dahm Kaczaniuk

Scientific Advisory Board:
- Maureen Black
- John Constantino
- Lisa Croen
- Gary Goldstein
- David Mandell

Faculty affiliate members

Students

Study-specific staff

WKC Team
WKC Investigators Work On Many National Studies

Surveillance
- Autism and Developmental Disabilities Monitoring (ADDM) Network

Case-Control Studies
- Study to Explore Early Development (SEED)
- Childhood Autism Risks from Genetics and the Environment (CHARGE)

Enriched Risk Cohorts
- Early Autism Risk Longitudinal Investigation (EARLI)
- Markers of Autism Risk in Babies, Learning Early Signs (MARBLES)
- Infant Brain Imaging Study (IBIS)
- Boston Birth Cohort (BBC)

State Records Data
- Early Markers for Autism (EMA) Study

National Registries
- Danish National Data

Large Online Collections
- Simon’s Foundation SPARK Cohort

Large National Collaborations
- Environmental Influences of Child Health Outcomes (ECHO)

Health Systems
- Kaiser Permanente
Special Issue: Global Autism Research

- Published online June 13, 2017
  DOI: 10.1177/1362361317704603

- Volume 21, Issue 5, July 2017
Autism Etiology: Why & How?

Genetics
- Inherited
  - Common SNP
  - Common CNV
  - Rare SNP
  - Rare CNV
- De novo
  - Rare SNP
  - Rare CNV

Environment
- Parental Characteristics
  - Age
  - Medical Conditions
  - Perinatal/Obstetric
  - Nutrition
- Toxicants
  - Chemical
  - Behavioral
  - Environmental
  - Occupational
  - Pharmaceutical
  - Biological

Gene x Environment
- Statistical and Epidemiologic Interactions
- Exposure modified by genetics
- Genetics modified by exposure
- Genetic and environmental synergism
- Biological Interactions and Molecular Targets
  - Exposure mediated by genetic alterations
  - Gene product contact with exposure
  - Epigenetics

Risk of Autism Spectrum Disorders

Bakulski KM, Singer AB, Fallin MD. 2014. *Frontiers in Autism Research*
SEED is largest population-based US Case-Control Study of ASD (children 2-5 years)

- Genes and Environmental Risks
  - Maternal Interviews
  - Self-administered questionnaires
  - Medical record abstraction
  - Child clinical evaluation and physical exam
    - Developmental evaluation
    - Dysmorphology examination
  - Biosampling:
    - Cheek cells or saliva (parents, child)
    - Blood (parents, child)
    - Hair (child)
    - DNA and DNAmethylation

>2000 ASD cases
>2000 POP controls
Student SEED projects

- Occupational exposures
- Alcohol exposure
- Estrogen exposures
- Screening tool utility by race/ethnicity/SES
- Genetic and dysmorphology insights
- meQTL-based genomic integration
- eQTL-based genomic integration
- DNA methylation signatures of prenatal exposures
- Gene-environment interactions
Table 2. Exposure ORs (95% CIs) for autism, by category of distance from residence to the nearest freeway at time of birth (n = 563).

<table>
<thead>
<tr>
<th>Exposure category</th>
<th>n (cases/controls)</th>
<th>Crude</th>
<th>Adjusted&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 309 m from freeway (closest 10%)</td>
<td>38/19</td>
<td>1.86 (1.04–3.45)</td>
<td>1.86 (1.03–3.45)</td>
</tr>
<tr>
<td>309–647 m from freeway (10th to 25th percentile)</td>
<td>43/41</td>
<td>0.98 (0.60–1.59)</td>
<td>0.96 (0.58–1.56)</td>
</tr>
<tr>
<td>647–1,419 m from freeway (25th to 50th percentile)</td>
<td>77/63</td>
<td>1.14 (0.76–1.71)</td>
<td>1.11 (0.73–1.67)</td>
</tr>
</tbody>
</table>

Table 2. Odds of ASD for 606 children based on continuous pollutant exposure by periconceptional folic acid intake<sup>a</sup>

<table>
<thead>
<tr>
<th>Air pollutant</th>
<th>Month 1 FA (&lt; or ≥ 800 µg)</th>
<th>Odds ratio (95% CI)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Unadjusted</td>
<td>Adjusted&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>NRP Low</td>
<td></td>
<td>1.87 (1.09, 3.19)</td>
<td>1.57 (0.92, 2.70)</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>0.98 (0.63, 1.51)</td>
<td>0.92 (0.59, 1.45)</td>
</tr>
<tr>
<td>Interaction p</td>
<td></td>
<td>0.066</td>
<td>0.137</td>
</tr>
</tbody>
</table>

<sup>a</sup> Hispanic vs. white, black/Asian/other vs. age degree or higher vs. some high school, ≤ 35 years, and maternal smoking during pregnancy and no smoking during pregnancy.

Goodrich et al., 2018
Enriched Risk Cohort Studies

Figure 6. EARLI Network core protocol data collection schedule
A researcher measures a family’s living room before gathering a dust sample, paying close attention to areas where pregnant mother sits.

At right, a researcher processes a placental sample, which may provide clues to the fetal environment.
Epigenetics:
The study of heritable and reversible cellular information other than the DNA sequence itself

DNA methylation (DNAm)

Histone tail modifications
- acetylation
- methylation
- phosphorylation

Epigenetic machinery

Chromatin structure
- loops
- compaction

ncRNAs

MMBD2
Epigenetics: Chemical Modifications of DNA that Control Expression of Genes

Gene “switched on”
- Active (open) chromatin
- Unmethylated cytosines (white circles)
- Acetylated histones

Gene “switched off”
- Silent (condensed) chromatin
- Methylated cytosines (red circles)
- Deacetylated histones

Transcription possible

↓ Methylation & ↑ H acetylation = ↑ Expression

Transcription impeded

↑ Methylation & ↓ H acetylation = ↓ Expression

Epigenetics control the flow of DNA-> RNA-> Protein

↓ Methylation & ↑ H acetylation = ↑ Expression

↑ Methylation & ↓ H acetylation = ↓ Expression
Role of DNA methylation in ASDs

- Prenatal
- Birth
- Lifespan
- Post-mortem
Role of DNA methylation in ASDs

Prenatal | Birth | Lifespan | Post-mortem

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Role of DNA methylation in ASDs
Paternal sperm DNA methylation associated with early signs of autism risk in an autism-enriched cohort

Jason I Feinberg,1,2 Kelly M Bakulski,1,2,3 Andrew E Jaffe,4,11 Rakel Tryggvadottir,7 Shannon C Brown,1,2 Lynn R Goldman,9,6 Lisa A Croen,7 Irv Hertz-Picciotto,8 Craig J Newshaffer,9,10 M Daniele Fallin1,11,* and Andrew P Feinberg2,12,*

Candidate differentially methylated regions (DMRs) (n=4) in paternal semen that are associated with offspring 12-month AOSI scores, an indicator of autism risk.
Brain Development in Autism: Infant Siblings

UNC researchers unlock new clues in fight against autism

Low-Risk Infant with Normal MRI; ASD-negative at 24M

High-Risk Infant with Increased Extra-Axial CSF; Diagnosed with ASD at 24M
Boston Birth Cohort

Enrollment Summary
8,500 mother-infant pairs (~2,500 preterm)

Demographics
Inner city, minority (65% blacks, 25% Hisp) in Boston

Timepoints
Enrolled at Birth, 24-72 hours after delivery
F/U at pediatric primary care visits

Data Collected
Prenatal and Perinatal EMR Data
Clinical Measurements including Growth and Development at F/U
Epidemiological questionnaires

Biospecimens:
Maternal and Cord Blood, Placenta Tissue;
Venous Blood at F/U
The Association of Maternal Obesity and Diabetes With Autism and Other Developmental Disabilities

Mengying Li, MSPH
PhD candidate
PFRH

FIGURE 1
Adjusted HR and 95% CI for ASD associated with maternal obesity and diabetes. The models adjusted for child year of birth, child gender, maternal age, parity, smoking during pregnancy, and preterm birth.
Figure 2. Forest plot comparing the Boston Birth Cohort results to previously reported results. The plot shows effect estimates and 95% confidence intervals for the association between infection or fever (at any point during pregnancy and by trimester) and autism.
Kaiser Permanente Northern California

- Group practice prepaid integrated health program
- 3.5 million patients
- 8,000 physicians
- 21 hospitals
- Fully electronic health record
- Serves ~30% of population in geographic region
Nordic Registries - Denmark

Science 31 March 2000:
Vol. 287 no. 5462 pp. 2398-2399

When an Entire Country Is a Cohort

‘Denmark has gathered more data on its citizens than any other country. Now scientists are pushing to make this vast array of statistics even more useful.’
Parental exposures to occupational asthmagens and risk of autism spectrum disorder in a Danish population-based case-control study

Alison B. Singer, Igor Burstyn, Malene Thygesen, Preben Bo Mortensen, M. Daniele Fallin and Diana E. Schendel

<table>
<thead>
<tr>
<th>Asthmagen Type</th>
<th>% Exposed Controls</th>
<th>% Exposed Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Asthmagen</td>
<td>20.0</td>
<td>18.6</td>
</tr>
<tr>
<td>Any HMW</td>
<td>14.4</td>
<td>13.1</td>
</tr>
<tr>
<td>Animals</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Fish</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Flour</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Plants</td>
<td>&lt;0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Mites</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Enzymes</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Latex</td>
<td>11.3</td>
<td>10.1</td>
</tr>
<tr>
<td>Bioaerosols</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Drugs</td>
<td>1.3</td>
<td>1.2</td>
</tr>
<tr>
<td>Any LMW</td>
<td>10.1</td>
<td>10.6</td>
</tr>
<tr>
<td>Reactive</td>
<td>7.7</td>
<td>7.6</td>
</tr>
<tr>
<td>Isocyanate</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Cleaning</td>
<td>6.2</td>
<td>7.3</td>
</tr>
<tr>
<td>Wood</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Metals</td>
<td>1.1</td>
<td>1.2</td>
</tr>
<tr>
<td>Any Mixed</td>
<td>1.7</td>
<td>1.6</td>
</tr>
<tr>
<td>Metalworking</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Textile</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Agricultural</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Irritant Peaks</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Maternal Adjusted Odds Ratios and 95% CI
Examples of WKC-affiliated Projects

- SEED – Prenatal **anti-depressant use** and interplay with (maternal and child) genetic and epigenetic factors

- EARLI-MARBLES – Prenatal **folic acid supplementation**, and interplay with genetic and epigenetic factors

- EARLI-MARBLES – Prenatal **air pollution** risk, and genetic predisposition, and translation to animal work

- IBIS – Prenatal **air pollution risk** and **early life brain imaging / behavior**

- IBIS – **Genetic and environmental** influences on **school age-outcomes and brain development**

- EARLI-MARBLES – Prenatal **metals exposure** and interplay with genetic and epigenetic factors

- ASD-ER – ECHO cohort - **Prenatal exposures measurable in shed baby teeth**. Now moving into broader data collection related to obesity, airways, health outcomes, neurodevelopment.

- SEED 3 – **new field recruitment**
Environmental influences on Child Health Outcomes (ECHO)

ECHO’S OVERARCHING SCIENTIFIC GOAL:
• Answer crucial questions about the effects of a BROAD range of EARLY environmental influences on child health and development

Outcomes
Obesity
Airways
Pre, Peri, Postnatal
Neurodevelopment
Positive Child Health

ECHO award locations
62 awards
110 PIs
1280 key personnel
44 states, DC, PR
Researchers take on the role of tooth fairy to better understand autism

Scientists study an unexpected source of information about in utero exposure to harmful materials: baby teeth
Join Us!

- **Internship** placements decided twice a year, with deadlines of Sept. 30 and Feb. 1. See ‘For Students’ tab on www.jhsph.edu/WKC.
- **Journal clubs** on the 1st Monday of the month
  - 12:15 - 1p.m., Room W4007
  - Topics and dates on www.jhsph.edu/WKC calendar
- **Other events** such as retreats and symposia
- **Pilot funding** for faculty and students. Applications typically due in March.
- **To join WKC contact list**, email mlandru5@jhu.edu
<table>
<thead>
<tr>
<th>Awardee and Type</th>
<th>Proposal Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gazi Azad (Faculty) Department of Mental Health</td>
<td>Partners in School: Improving Parent-Teacher Communication for Continuity of Care in Children with ASD</td>
</tr>
<tr>
<td>Calliope Holingue (Student) Department of Mental Health</td>
<td>Microbiome Composition and Structure of Children with Autism Spectrum Disorder</td>
</tr>
<tr>
<td>Chris Ladd-Acosta (Faculty) Department of Epidemiology</td>
<td>Prostaglandin E2 (PGE2) and risk for autism spectrum disorder (ASD)</td>
</tr>
<tr>
<td>Heather Volk (Faculty) Department of Mental Health</td>
<td>Measurement of Environmental Exposure Biomarkers in Shed Deciduous Teeth</td>
</tr>
<tr>
<td>Vanya Jones (Faculty) Department of Health Behavior &amp; Society</td>
<td>Childhood Unintentional Injury Safety Practices: What are the experiences of parents of children with Autism Spectrum Disorder</td>
</tr>
<tr>
<td>Dr Robert Gilman (Faculty) Department of International Health</td>
<td>Smell as diagnostic aid for autism in Peru</td>
</tr>
<tr>
<td>Martha Brucato (Student) Dept of Epidemiology</td>
<td>Developing methods utilizing Machine Learning and Latent Class Analysis to Identify children with ASD in administrative health data</td>
</tr>
<tr>
<td>Bo Y. Park (Postdoctoral Fellow) Department of Mental Health</td>
<td>Maternal metabolic syndrome and Autism Spectrum Disorder (ASD) risk</td>
</tr>
<tr>
<td>Li-Ching Lee (Faculty) Department of Epidemiology</td>
<td>Parent-Mediated In-Home Intervention for Children with Autism Spectrum Disorder in Bangladesh</td>
</tr>
<tr>
<td>Kripa Raghavan (Doctoral Student) Department of Pop., Family, and Reproductive Health</td>
<td>Micronutrient Determinants of ASD and Developmental Disabilities in a US Urban Low Income Minority Birth Cohort</td>
</tr>
<tr>
<td>Elise Pas (Faculty) Department of Mental Health</td>
<td>Reducing Behavior Problems among Students with an ASD through Coaching Teachers in a Mixed-Reality Setting</td>
</tr>
<tr>
<td>Alden Gross (Faculty) Department of Biostatistics</td>
<td>Development and validation of a continuous scale of autism severity across ADOS modules</td>
</tr>
<tr>
<td>Allan Andersen (Doctoral student) Department of Mental Health</td>
<td>A survey of cost and effectiveness of parental responses to elopement among children with ASD in the Interactive Autism Network</td>
</tr>
<tr>
<td>Kelly Bakulski (Postdoctoral Fellow) Department of Epidemiology</td>
<td>Heavy metals exposure and autism spectrum disorders in the Early Autism Risk Longitudinal Investigation (EARLI)</td>
</tr>
<tr>
<td>Luke Kalb (Doctoral Student) Department of Mental Health</td>
<td>Effects of Federal Mental Health Parity on Psychiatric Department Use among Privately Insured Children with Autism Spectrum Disorder</td>
</tr>
</tbody>
</table>
Public Health Approaches in
Autism and Developmental Disabilities
330.700.01
Term 3, AY 2017 –2018
Instructors: Dani Fallin & Li-Ching Lee
with guest expert lecturers

Autism spectrum disorder (ASD) is a major public health issue. In this course, students will learn about ASD and measurement issues from an epidemiologic perspective, as well as updates on the prevalence of ASD and how prevalence is estimated. The course also covers etiological research methods and findings to date, and discusses the emerging questions for Public Health including etiology, comorbidity, policy and services.

Course content includes:

- History of ASD and DD diagnoses
- Screening and diagnostic assessments
- Prevalence
- Co-occurring conditions
- Life-course presentation
- Demographic risk factors
- Genetic risk factors
- Environmental risk factors
- Current intervention strategies
- Early detection
- Findings and challenges of global public health efforts
- Medical and education-based services
- Emerging biomarkers
Special event this year

Child and Adolescent Psychiatry presents

Autism Scientific Symposium

Marking 75 Years since Leo Kanner first identified autism.

Tuesday, September 25, 2018
2:30pm - 5:00pm
Hurd Hall - Johns Hopkins Hospital

More information: hopkinsmedicine.org/psychiatry/Leo_Kanner_autism

Event is free and open to the public
Further information on Autism

WKC Website: www.jhsph.edu/wkc


Sesame Street Continues to Teach Us All

- https://www.youtube.com/watch?v=uR0nuBr8xZg