Autism by the Numbers: The Epidemiology of Autism Spectrum Disorder

UAB Glenwood Endowed Lecture
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Today’s Lecture

• What’s in a number?
  – Global prevalence of autism and change over time

• What we know (and don’t know)
  – Risk factors and the fundamental challenge in autism

• A public health priority
  – How public health has changed (and will continue to change) the autism research and service landscape
What’s in a Number?

US Autism Prevalence
CDC Autism and Developmental Disabilities Monitoring Network

Comprehensive But Not Representative
- 350K+ Children; 11 US Sites
Case Ascertainment
- Health/Education Service Records as Proxy
US Autism Prevalence
CDC Autism and Developmental Disabilities Monitoring Network

Case Ascertainment
- More Sources = Higher Prevalence
- No Record = Missed Case

HHS National Survey of Children's Health

Nationally Representative, but Questionable Diagnostic Validity
- Parent-reported diagnosis – “Has your child ever been diagnosed with an ASD?”
- 1 in 50

Blumberg et al, 2013
**Possible Explanation: Access to Services**

Population

- Low access to services
- Same prevalence

Population

- High access to services

Courtesy of Eric Fombonne

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**Minneapolis Somali ASD Prevalence Project**

- **Overall**: 1 in 48
- **Somali**: 1 in 32
- **White**: 1 in 36
- **Black (non-Somali)**: 1 in 62
- **Hispanic**: 1 in 80

<table>
<thead>
<tr>
<th>Race and ethnicity</th>
<th>Number of children with ASD identified</th>
<th>Prevalence estimate (prevalence per 1,000 children)</th>
<th>95% Confidence interval*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>255 of 12,329</td>
<td>1 in 48 (20.7 per 1,000)</td>
<td>18.3 – 23.4 per 1,000</td>
</tr>
<tr>
<td>Somali</td>
<td>31 of 1,007</td>
<td>1 in 32 (30.8 per 1,000)</td>
<td>21.6 – 43.8 per 1,000</td>
</tr>
<tr>
<td>White</td>
<td>120 of 4,335</td>
<td>1 in 36 (27.7 per 1,000)</td>
<td>23.1 – 33.1 per 1,000</td>
</tr>
<tr>
<td>Black (non-Somali)</td>
<td>53 of 3,312</td>
<td>1 in 62 (16 per 1,000)</td>
<td>12.2 – 20.9 per 1,000</td>
</tr>
<tr>
<td>Hispanic</td>
<td>30 of 2,399</td>
<td>1 in 80 (12.5 per 1,000)</td>
<td>8.7 – 17.9 per 1,000</td>
</tr>
</tbody>
</table>

Note: We are unable to report on Asian/Pacific Islanders and Native Americans due to their low numbers.

* 95% confidence interval is the range in which an estimate is likely to fall.
Are We Underestimating?
CDC Autism and Developmental Disabilities Monitoring Network

Alabama
Tracking Autism Spectrum Disorder and Other Developmental Disabilities in Alabama
What You Need To Know

A Snapshot of Autism Spectrum Disorder In Alabama

How many children were identified with ASD?

- 1 in 175 children (age 3-7) were identified with ASD.

This estimate is lower than the average number of children identified with ASD in all areas of the United States where CDC surveys ASD.

New Jersey
Tracking Autism Spectrum Disorder and Other Developmental Disabilities in New Jersey
What You Need To Know

A Snapshot of Autism Spectrum Disorder In New Jersey

How many children were identified with ASD?

- 1 in 45 children (age 3-7) were identified with ASD. This estimate is lower than the average number of children identified with ASD in all areas of the United States where CDC surveys ASD.

Direct ASD Assessment
Korean Autism Study

Korean Autism Study
- Total Population Study
- 46K Children

- Mechanisms to Identify Children
  1. Mandatory Educational System
  2. Home Schooling
  3. Disability Registry

- Two Stage Design
  1. Multi-Informant Screening
  2. Confirmative Dx with ADOS & ADI-R

- Prevalence of ASD among kids enrolled in special education classes was 0.75%
  - Similar to US service records prevalence

- When include children from the general classrooms, prevalence was 2.64%
  - Two-thirds of cases previously missed, higher functioning

Kim et al, 2011
Enhanced US Prevalence Study

True Differences in Prevalence?
Categories of factors that may influence prevalence

Intrinsic Factors
*Internal methodology or measurement factors involved in documenting ASD prevalence*

Rice, Rosanoff, et al 2013
Global Variability in ASD Prevalence

- Previously reported global ASD prevalence ~1%, but most estimates from Western, developed countries
- Variability within same countries
- Recent estimates HIGHLY variable

Elshabagh et al, 2012

WHO Review

- Significant heterogeneity in ASD prevalence across studies
- Association with geographic region
- Wide age range: 0-17
- Variability in severity: Normal IQ 30.0%-85.3%
- Association between year of publication and prevalence

Elshabagh et al, 2011
A True Increase Over Time?
Categories of factors that may influence prevalence

**Intrinsic Factors**
*Internal methodology or measurement factors involved in documenting ASD prevalence*
- Different study methodology, particularly in case ascertainment approach
- “Majority” of variation in between-study prevalence can be explained by methodology

**Extrinsic Factors**
*External factors associated with changes in the way ASD is identified over time*

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Rice, Rosanoff, et al 2013

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123% Increase in 10 Years

*Autism Prevalence Since 2000*
Improved Detection

ADDN, 2014

Changes in Diagnosis

King & Bearman, 2009
Changes in Diagnosis

ASD Prevalence Trends in the USA

Gurney et al, 2003

TABLE 1: Prevalence Estimates DSM-IV Pervasive Developmental Disorder (PDD), Autism Spectrum Disorder (ASD), and DSM-5 Social Communication Disorder (SCD)

<table>
<thead>
<tr>
<th></th>
<th>DSM-IV (95% CI)</th>
<th>DSM-5 (95% CI)</th>
<th>DSM-5 ASD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3.64 (9.4-3.5)</td>
<td>2.58 (9.3-2.4)</td>
<td>2.70 (9.2-2.1)</td>
</tr>
<tr>
<td>CPD</td>
<td>0.49 (0.4-0.5)</td>
<td>0.45 (0.4-0.5)</td>
<td>0.29 (0.2-0.3)</td>
</tr>
<tr>
<td>CPD</td>
<td>0.73 (0.4-0.9)</td>
<td>0.73 (0.5-0.9)</td>
<td>0.73 (0.7-0.9)</td>
</tr>
<tr>
<td>Other ASD-Related</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autism Disorder</td>
<td>1.04 (0.7-1.3)</td>
<td>0.93 (0.6-1.1)</td>
<td>0.93 (0.8-1.1)</td>
</tr>
<tr>
<td>Asperger</td>
<td>0.40 (0.2-0.6)</td>
<td>0.39 (0.2-0.6)</td>
<td>0.39 (0.2-0.6)</td>
</tr>
<tr>
<td>PDD-HLD</td>
<td>0.20 (0.1-0.3)</td>
<td>0.19 (0.1-0.3)</td>
<td>0.19 (0.1-0.3)</td>
</tr>
<tr>
<td>SCD</td>
<td>3.78 (3.4-4.2)</td>
<td>3.51 (3.2-3.8)</td>
<td>3.71 (3.4-4.1)</td>
</tr>
<tr>
<td>Other ASD</td>
<td>0.47 (0.4-0.5)</td>
<td>0.42 (0.3-0.5)</td>
<td>0.39 (0.3-0.4)</td>
</tr>
</tbody>
</table>

Note: CPD = general population sample; PDD = pervasive developmental disorder; SCD = other specified

From a comprehensive and up-to-date database of current understanding.
Improved Awareness

The odds of being diagnosed with ASD increase based on how close the child lives to a previously diagnosed child with autism

King & Bearman, 2010

A True Increase?
Categories of factors that may influence prevalence

Intrinsic Factors
Internal methodology or measurement factors involved in documenting ASD prevalence
- Different study methodology, particularly in case ascertainment approach
- “Majority” of variation in between study prevalence can be explained by methodology

Extrinsic Factors
External factors associated with changes in the way ASD is identified over time
- Shift in diagnostic criteria, increased awareness/recognition
- Only account for 26% and 16% respective increases in prevalence over time

Risk Factors
Possible etiologic factors associated with true increase in ASD within the population

Rice, Rosanoff, et al 2013
Advanced Parental Age

- Maternal & paternal age as independent continuous variables
  – Grether et al, 2009

- Moms: 10 yr increase in age, 38% increase in risk (OR=1.38)
- Dads: 10 yr increase in age, 22% increase in risk (OR=1.22)

Advanced Paternal Age?

- No increased risk for moms after adjusting for dads age
- Reichenberg et al, 2006
**Advanced Maternal Age?**

- Sandin et al, 2012 16 studies, moms age as categorical, (e.g. 25-29 ref)
- 35+ vs 25-29, RR = 1.52  
  <20 vs 25-29 RR = 0.76
- Shelton et al, 2010 – “advancing maternal age increased risk for autism monotonically regardless of the paternal age.”

**Air Pollution**

Traffic-Related Air Pollution, Particulate Matter, and Autism

<table>
<thead>
<tr>
<th>Time Period</th>
<th>4th Quarter</th>
<th>1st Quarterly</th>
<th>3rd Quarterly</th>
<th>2nd Quarterly</th>
</tr>
</thead>
<tbody>
<tr>
<td>First time of life</td>
<td>2.67 (1.71-5.62)</td>
<td>2.80 (1.53-5.98)</td>
<td>3.01 (1.79-5.04)</td>
<td>2.99 (1.77-5.12)</td>
</tr>
<tr>
<td>All pregnancy</td>
<td>1.30 (1.03-1.61)</td>
<td>1.53 (1.21-1.95)</td>
<td>1.69 (1.42-2.00)</td>
<td>1.72 (1.44-2.04)</td>
</tr>
<tr>
<td>Adjusted</td>
<td>1.29 (1.02-1.62)</td>
<td>1.51 (1.19-1.89)</td>
<td>1.70 (1.42-2.00)</td>
<td>1.73 (1.45-2.04)</td>
</tr>
<tr>
<td>First trimester</td>
<td>1.96 (1.26-3.02)</td>
<td>2.38 (1.61-3.53)</td>
<td>2.58 (1.93-3.47)</td>
<td>2.62 (2.05-3.37)</td>
</tr>
<tr>
<td>Second trimester</td>
<td>2.07 (1.33-3.20)</td>
<td>2.48 (1.73-3.51)</td>
<td>2.77 (2.24-3.46)</td>
<td>2.83 (2.28-3.55)</td>
</tr>
</tbody>
</table>

Adjusted RR (95% CI)

![Graph](graph.png)

- Figure 2: Association of AOD with air pollutant concentration, tissue specific versus breast specific 95% CI
- B: two-sided p-value, children of the Nurses’ Health Study II n=2192 controls, n=395 cases
Induced Labor

Association of Autism With Induced or Augmented Childbirth in North Carolina Birth Record (1990-1998) and Education Research (1997-2007) Databases

Simone G. Grigoriu, M.D., Rebecca Antshel, Ph.D., David Repacholi, Ph.D., Paul A. Rotan, M.D., and Elena Moebius, M.D.

Table 4. Associations of Induction/Augmentation Treatment Status with Autism Diagnosis by Sex for 3rd to 9th Grade Children

- Induced and not augmented
- Induced and augmented
- Not induced and augmented
- Not induced and not augmented
- Induced only
- Not induced only
- Both sexes
- Males
- Females

Antidepressant (SSRI) Use

Use of Selective Serotonin Reuptake Inhibitors during Pregnancy and Risk of Autism

Anders Hviid, Dr. Med. Sc., Mads Kehlet, M.D., Dr. Med. Sc., and Bjorn Pasterkamp, M.D., Ph.D.

RESULTS: Overall, prevalence of prenatal SSRI exposure was lowest in the third trimester (17.9% vs 20.0% in the second trimester; odds ratio [OR] 0.81; 95% confidence interval [CI], 0.67-1.00). The strongest association was observed with preterm delivery (OR, 1.22; 95% CI, 1.03-1.44) and was stronger in the third trimester (OR, 1.39; 95% CI, 1.12-1.73). Findings were similar among mothers with an anxiety or mood disorder history.
Folic Acid

JAMA The Journal of the American Medical Association

Association Between Maternal Use of Folic Acid Supplements and Risk of Autism Spectrum Disorders in Children

Pill Buett, MD, MPH; Christine Roch; MD; Michael J. Brownstein, PhD; Margareth Haugen, PhD; Mary Honek, MD; Deborah Hsieh, MD; Seth Kelin Lee, MD; W. Ian Luxenberg, MD; Per Magnus, MB, PhD; Terje Reischlum-Christensen, MD, PhD; Byrne Sofield, MD; George D. Davey Smith, MD, DSc; Anne Ger Jørgensen, PhD; Ezra Besser, MD, MPH; Camilla Blidenberg, MD, PhD

Table 2. Risk of Autistic Disorder According to Maternal Folic Acid Use

<table>
<thead>
<tr>
<th>Folic Acid Use</th>
<th>Total</th>
<th>Autistic Disorder</th>
<th>Unadjusted</th>
<th>OR (95% CI)</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>24,134 (38.5)</td>
<td>50 (0.21)</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>61,242 (71.7)</td>
<td>64 (0.11)</td>
<td>0.51 (0.35-0.73)</td>
<td>2.81 (0.84-9.08)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: OR, odds ratio
*Adjusted for year of birth, maternal education level, and parity. For maternal education, missing data were included as a separate category in the logistic regression model.

Risk Factor Summary

- Parental Age – OR = 1.5 CONVERGENCE
  - Maternal vs Paternal – INCONCLUSIVE
- Air Pollution – OR = 2.0 REPLICATION
- Induced Labor – OR = 1.35 – INCONCLUSIVE
- Antidepressant Use – INCONCLUSIVE
- Folic Acid - OR = 0.61 CONVERGENCE

- Older parents at increased risk for developmental issues
- Pre and peri-natal folic acid supplements protective
- Pregnancy seems to be critical exposure window
- RISK ≠ CAUSE
Genes and Environment

- Sibling recurrence risk – 10-20%
- Known genetic risk factor in ~50% of cases
- Heritability of autism estimated 50%
- Complex interaction between genes and environment

The Fundamental Challenge

- Complex
- Biological Spectrum Disorder
- Mild to Severe
- Social / Communication Challenges
- Behaviors
- Medical Co-Morbidities
- Lifelong
- HETEROGENEITY
ASD: What’s in a Name?

- Heterogeneity
  - No two individuals are exactly alike phenotypically
  - Treatments are not equally effective
  - Different underlying biology, etiology

- Current DSM diagnoses group vastly different individuals, heterogeneous syndromes with different underlying pathophysiological mechanisms into broad categories, single disorders

- Limits interpretation of research findings on prevalence, risk factors, and treatments

- Underlying pathways will lead to more personalized treatments

What We Know Works

Detection:
- Autism can be reliably diagnosed by 2 years of age
- Screening can begin as early as 12 months

Intervention:
- Intensive behavioral intervention is effective
- Early intervention can significantly improve long-term outcomes
- Guidelines for the medical treatment of comorbid conditions

Adult Services:
- Transition support
- Post-secondary education, employment, residential
THE COST OF AUTISM
ALONG WITH THE RISE IN AUTISM PREVALENCE COMES THE INCREASE IN COST TO SOCIETY.

Breakdown of Costs by Category

MANDELL ET AL., IN PRESS
Public Health Offers Solutions

- Health Services Research
  - Disparities and access to services
- Dissemination and Implementation
  - Training of professionals, para-professionals
  - Parent/teacher-mediated interventions
  - Tele-health and e-learning
  - Community-based
- International Epidemiology
  - Open-source diagnostic tools
  - Comparative studies provide clues about etiology
  - Unique research resources (e.g. registries)
  - Community engagement, cultural considerations
We Have Work to Do…

Estimated Autism Prevalence and NIH Funding for Autism Research

AUTISM SPEAKS™

Thank you!

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