Meeting of the Interagency Autism Coordinating Committee

January 29, 2013

The National Institutes of Health
The William H. Natcher Conference Center
45 Center Drive, Conference Rooms E1/E2
Bethesda, MD

Conference Call Access:
Phone: (866) 740-1260
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Meeting of the IACC

Morning Agenda

10:00 AM **Call to Order and Opening Remarks**
Thomas Insel, M.D., Chair, IACC

10:05 **Science Update**
Thomas Insel, M.D., Chair, IACC

10:20 **Round Robin**

Meeting of the IACC

Science Update

Thomas R. Insel, M.D.
Director, National Institute of Mental Health and Chair, IACC
IACC Full Committee Meeting – January 29, 2013

Q1. When should I be concerned?

Current Biology
Volume 22, Issue 4, 21 February 2012, Pages 338–342

Infant Neural Sensitivity to Dynamic Eye Gaze Is Associated with Later Emerging Autism

Mayada Elsabbagh, Evelyne Mercure, Kristelle Hudry, Susie Chandler, Greg Pasco, Tony Charman, Andrew Pickles, Simon Baron-Cohen, Patrick Bolton, Mark H. Johnson, the BASIS Team

2012 Dec 6;5C:10-24

Developmental Cognitive Neuroscience

Atypical lateralization of ERP response to native and non-native speech in infants at risk for autism spectrum disorder

Anne M. Seery, Vanessa Vogel-Farley, Helen Tager-Flusberg, Charles A. Nelson

Molecular Psychiatry September 11, 2012

Predicting the diagnosis of autism spectrum disorder using gene pathway analysis

E Skafidas, R Testa, D Zantomio, G Chana, IP Everall and C Pantelis

Q2. How can I understand what is happening?

PNAS

July 31, 2012

Modeling an autism risk factor in mice leads to permanent immune dysregulation

Elaine Y. Hsiao[1], Sara W. McBride, Janet Chow, Sarkis K. Mazmanian, and Paul H. Patterson

JAMA Psychiatry

Original Article | Jan 2013

Microglial Activation in Young Adults With Autism Spectrum Disorder

Katsuaki Suzuki, MD, PhD; Genichi Sugihara, MD, PhD; Yasuomi Ouchi, MD, PhD; Kazuhiko Nakamura, MD, PhD; Masami Futatsubashi, BS; Kiyokazu Takebayashi, MD, PhD; Yujiro Yoshihara, MD, PhD; Kei Omata, PhD; Kaori Matsumoto, MA; Kenji J. Tsuchiya, MD, PhD; Yasuhide Iwata, MD, PhD; Masatsugu Tsujii, MA; Toshirou Sugiyama, MD, PhD; Norio Mori, MD, PhD

Molecular Psychiatry January 22, 2013

Elevated maternal C-reactive protein and autism in a national birth cohort

AS Brown[1,2], A Sourander[1,3,4], S Hinkka-Yli-Salomaki[3,4], IW McKeague[5], J Sundvall[6] and H-M Surcel[7]

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Q3. What caused this to happen and can it be prevented?

Autism After Infection, Febrile Episodes, and Antibiotic Use During Pregnancy: An Exploratory Study

Hjördis Ósk Atladóttir, Tine Brink Henriksen, Diana E. Schendel and Erik T. Parner

Pediatrics 2012;130;e1447; originally published online November 12, 2012

PEDIATRICS

OF THE AMERICAN ACADEMY OF PEDIATRICS

Rare Complete Knockouts in Humans: Population Distribution and Significant Role in Autism Spectrum Disorders

Elaine T. Lim,[1,4,5,6,7] Soumya Raychaudhuri,[4,6,9] Stephan J. Sanders,[10] Christine Stevens,[4] Aniko Sabo,[11] Daniel G. MacArthur,[1,4,6] Benjamin M. Neale,[1,4,5,6] Andrew Kirby,[1,4,6] Douglas M. Ruderfer,[1,3,4,5,6,8,12,14,15] Menachem Fromer,[1,3,4,5,6,8,12,14,15] Monkol Lek,[1,4,6] Li Liu,[18] Jason Flannick,[1,2,4,6] Stephan Ripke,[1,4,5] Uma Nagaswamy,[11] Donna Muzny,[11] Jeffrey G. Reid,[11] Alicia Hawes,[11] Irene Newsham,[11] Yuanqing Wu,[11] Lora Lewis,[11] Huyen Dinh,[11] Shannon Gross,[11] Li-San Wang,[19] Chiao-Feng Lin,[19] Otto Valladares,[19] Stacey B. Gabriel,[4] Mark dePristo,[4] David M. Altshuler,[1,2,4,6] Shaun M. Purcell,[1,3,4,5,6,8,12,14,15] NHLBI Exome Sequencing Project, Matthew W. State,[10] Eric Boerwinkle,[11,21] Joseph D. Buxbaum,[13,14,15,16,17] Edwin H. Cook,[22] Richard A. Gibbs,[11] Gerard D. Schellenberg,[20] James S. Sutcliffe,[23] Bernie Devlin,[24] Kathryn Roeder,[18] and Mark J. Daly[1,4,5,6,*]

Jan 23, 2013

JAMA Psychiatry

Original Article | Jan 2013

Traffic-Related Air Pollution, Particulate Matter, and Autism

Heather E. Volk, PhD, MPH; Fred Lurmann; Bryan Penfold; Irva Hertz-Picciotto, PhD; Rob McConnell, MD

Q4. Which treatments and interventions will help?

Science Translational Medicine
AAAS

Effects of STX209 (Arbaclofen) on Neurobehavioral Function in Children and Adults with Fragile X Syndrome: A Randomized, Controlled, Phase 2 Trial

Elizabeth M. Berry-Kravis,[1] David Hessl,[2] Barbara Rathmell,[3] Peter Zarevics,[3] Maryann Cherubini,[3] Karen Walton-Bowen,[3] Yi Mu,[4] Danh V. Nguyen,[4] Joseph Gonzalez-Heydrich,[5] Paul P. Wang,[3]* Randall L. Carpenter,[3] Mark F. Bear,[6] Randi J. Hagerman[7]

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Nonmedical Interventions for Children With ASD:Recommended Guidelines and Further Research Needs

Margaret A. Maglione, Daphna Gans, Lopamudra Das, Justin Timbie, Connie Kasari, For the Technical Expert Panel, and HRSA Autism Intervention Research Behavioral (AIR-B) Network

Pediatrics 2012;130;S169

Q5. Where can I turn for services?

autism

November 2012

Article

Comparing cognitive outcomes among children with autism spectrum disorders receiving community-based early intervention in one of three placements

Nahmias AS, Kase C, Mandell DS.

J Autism Dev Disord. September 2012

Healthcare service use and costs for autism spectrum disorder: a comparison between Medicaid and private insurance.

Wang L, Mandell DS, Lawer L, Cidav Z, Leslie DL.

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Occurrence and Family Impact of Elopement in Children With Autism Spectrum Disorders

Connie Anderson, J. Kiely Law, Amy Daniels, Catherine Rice, David S. Mandell, Louis Hagopian and Paul A. Law 2012;130;870;
originally published online October 8, 2012

Q6. What does the future hold, particularly for adults?

J Am Acad Child Adolesc Psychiatry. 2012 Jun

Developmental Trajectories in Adolescents and Adults With Autism: The Case of Daily Living Skills

Leann E. Smith, Ph.D., Matthew J. Maenner, Ph.D., Marsha Mailick Seltzer, Ph.D.

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

A Systematic Review of Vocational Interventions for Young Adults With Autism Spectrum Disorders

Veenstra-VanderWeele and Zachary Warren

Julie Lounds Taylor, Melissa L. McPheeters, Nila A. Sathe, Dwayne Dove, Jeremy

Pediatrics 2012;130;531; originally published online August 27, 2012

Q7. What other infrastructure and surveillance needs must be met?

J Autism Dev Disord. 2013 Jan

Autism Spectrum Disorder Reclassified: A Second Look at the 1980s Utah/UCLA Autism Epidemiologic Study

Judith S. Miller · Deborah Bilder · Megan Farley · Hilary Coon · Judith Pinborough-Zimmerman · William Jenson · Catherine E. Rice · Eric Fombonne · Carmen B. Pingree · Edward Ritvo · Riva-Ariella Ritvo · William M. McMahon

Meeting of the IACC

Round Robin

Meeting of the IACC

Morning Agenda - Continued

10:50 **CDC Minnesota Somali Project Update**

Amy Hewitt, Ph.D.

University of Minnesota

Marshalyn Yeargin-Allsopp, M.D.

Centers for Disease Control and Prevention

11:20 **Update on Autism Prevalence in Puerto Rico**

Jose Cordero, M.D.

University of Puerto Rico, & Member, IACC

11:35 **Lunch**

Prevalence of Autism in Puerto Rico: Results of the 2011 Survey

José F. Cordero, MD, MPH Annie
Alonso, Psy.D., MSW Hernando
Mattei, PhD
Ilia Torres, MS

January 29, 2012

Graduate School of Public Health
San Juan, PR

RCM
UPR

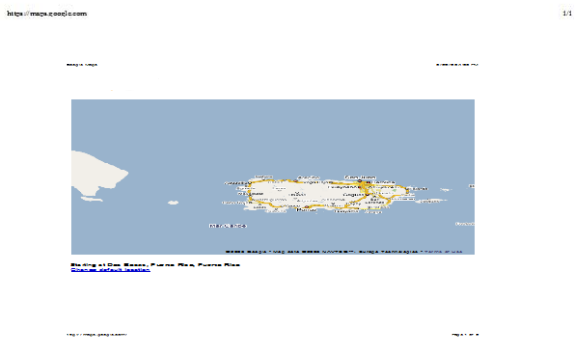
Public Health ***Salud Pública*** ***Santé Publique***

Tópicos

- Background
- SurveyMethodology
- Findings
- Discussion

Where is Puerto Rico?

- Puerto Rico is an island in the Caribbean that since 1898 have been under the sphere of the United States
- In 2010 its population was nearly 3.7 million
- In 2010 there were about 40,000 births



Autism: Challenges in Puerto Rico

- There were no survey or surveillance data to estimate the prevalence of autism in Puerto Rico
  - Available data sources
  - Children with autism registered through Special Education, Department of Education
  - Survey of Children with Special Health Care Needs

Objetives

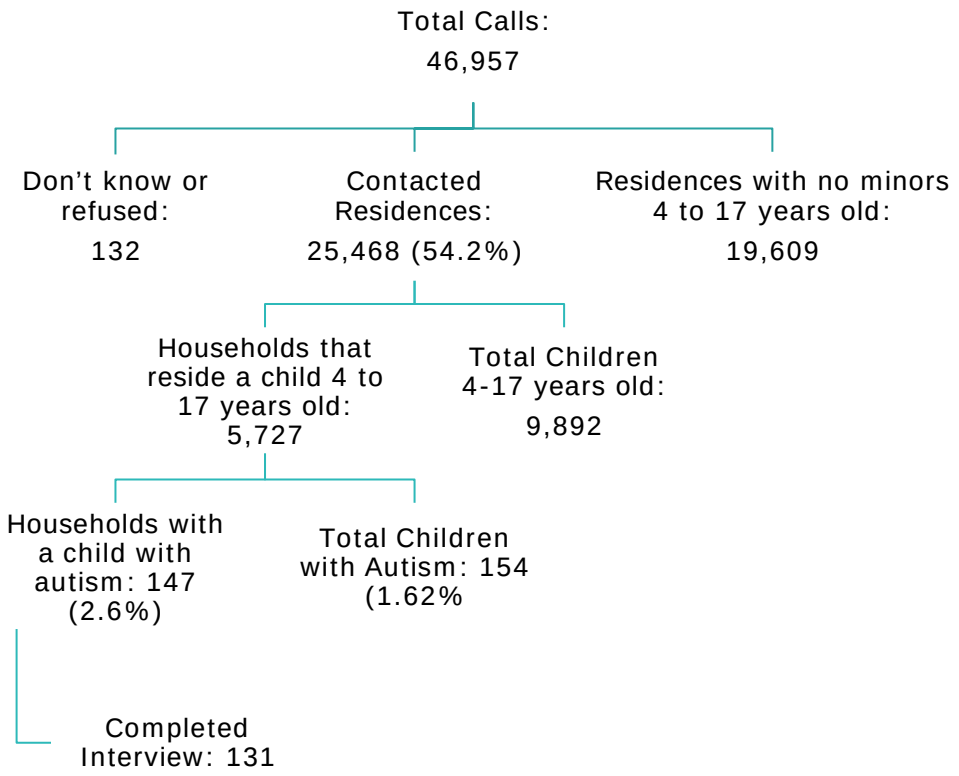
- Estimate the prevalence of autism in 2011 among children aged 4 to 17 years
- Evaluate their need for health, education, and social services needs (data not presented)

Methods

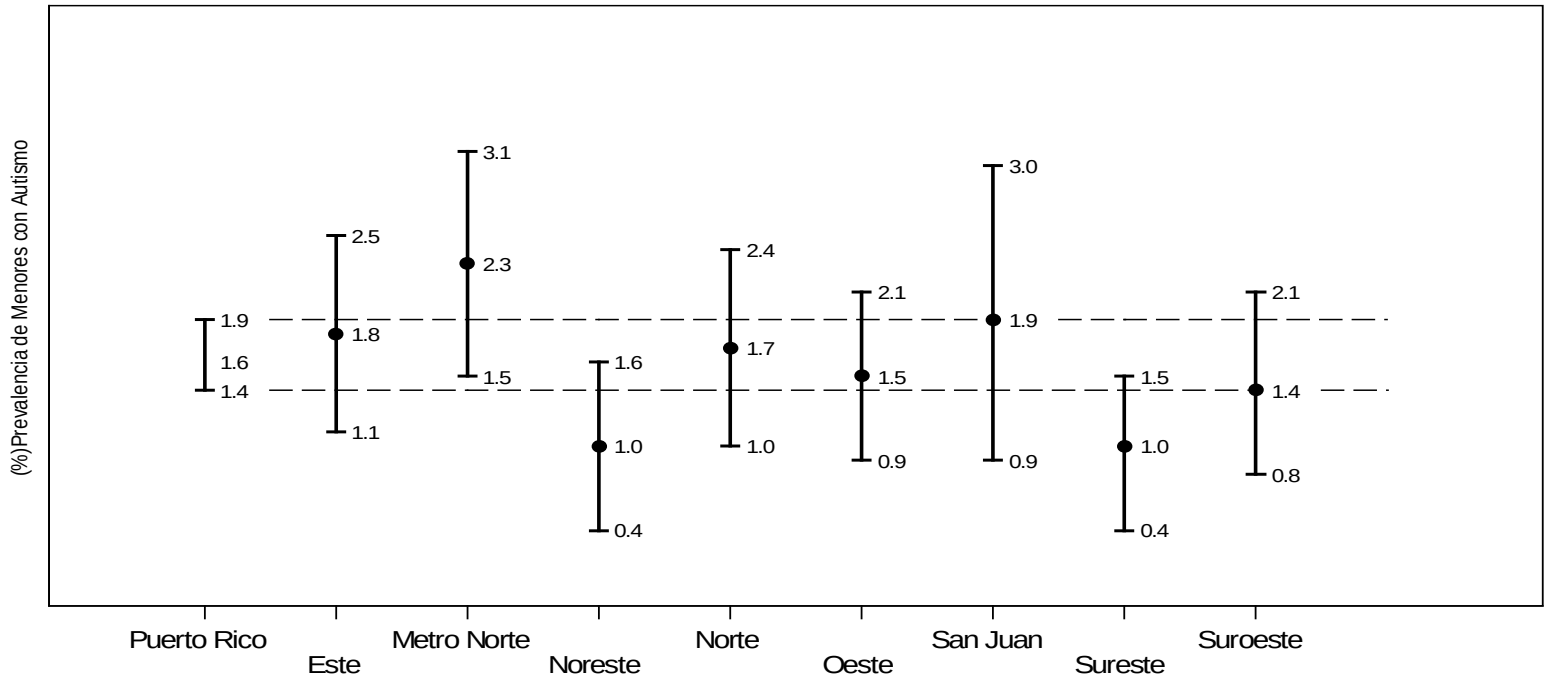
- Telephone survey using random-digit dialing methods among residences with a telephone
- Target population

  Children 4 to 17 years old
- Probability Sample was stratified based on the regions of the Puerto Rico Health Insurance Services Administration

Autism Survey, Call Flow, Puerto Rico, 2011



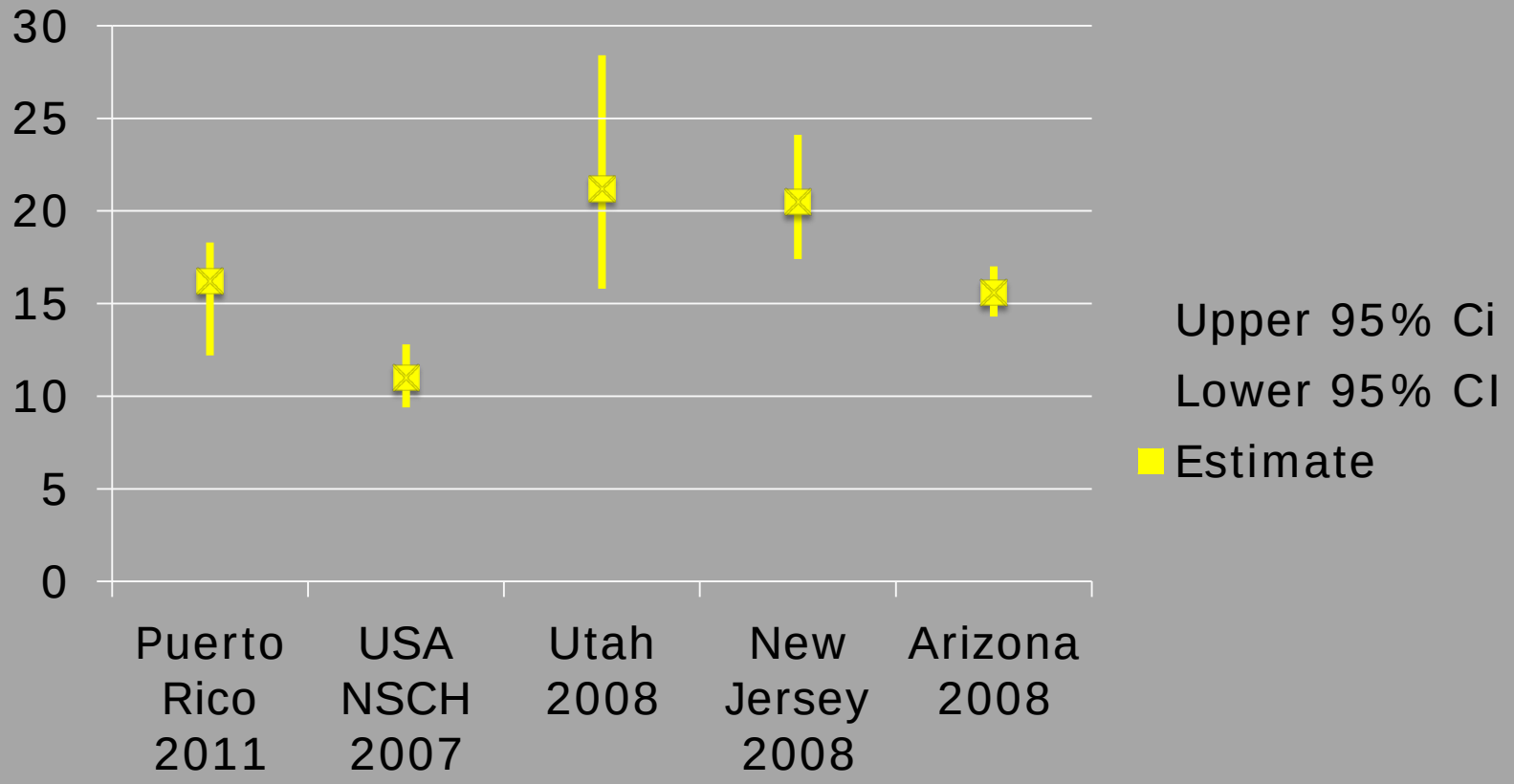
Autism Prevalence by Region, Puerto Rico, 2011



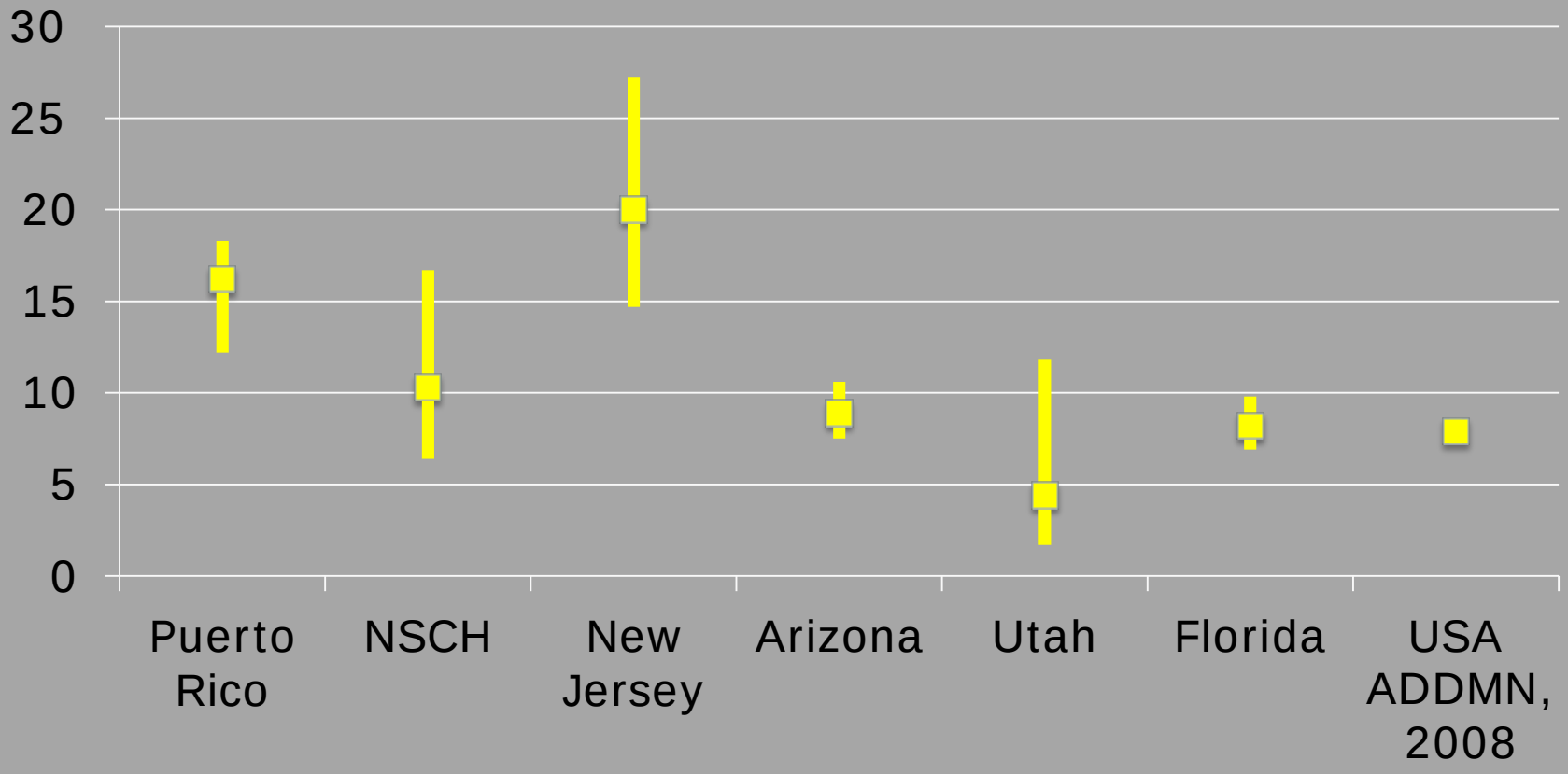
Autism Prevalence and Population Estimates, Puerto Rico , 2011

- Prevalence
  - 16.2 per 1,000
    - 1 in 62
- Population Estimates
  - 0 to 3 years old: 2,890
  - 4 to 17 years old: 11,743
  - 18 years + (5,062 – 7189)
  - Total (19,965 – 21,822)

Autism Prevalence, PR and Selected US Locations, 2007, 2008, 2011



Autism, Puerto Rico and Hispanics in USA, Selected Locations, 2007, 2008, 2011



Summary

- The prevalence of autism in Puerto Rico for children 4 to 17 years old in 2011 was 1 in 62
- The prevalence of autism in Puerto Rico falls within the range reported for Hispanics in the US
- Differences in prevalence of autism among Hispanic populations in the US should be evaluated.

Gracias
Thank You

Meeting of the IACC

Lunch Break

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Meeting of the IACC

Afternoon Agenda

1:00 PM **Public Comments**

1:30 **Optimal Outcomes in Individuals with a History of Autism**

Deborah Fein, Ph.D.
University of Connecticut

2:00 **Study of Health Outcomes in Children with Autism and their Families**

Anjali Jain, M.D.
The Lewin Group

Craig Newschaffer, Ph.D.
AJ Drexel Autism Institute, Drexel University

Meeting of the IACC

Public Comments

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Meeting of the IACC

Optimal Outcomes in Individuals with a History of Autism

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Optimal Outcome in Children with Autism

Deborah Fein, Ph.D.
Board of Trustees Distinguished Professor
Department of Psychology
Department of Pediatrics
Interagency Autism Coordinating Committee
Jan. 29, 2013

Background (see Helt et al, 2008 review in Neuropsychology Review)

- Most longitudinal studies report 3-25% no longer meet criteria for autism on follow-up
- Most individuals no longer meeting criteria for ASD still show significant impairment in social and/or language functioning (e.g., Piven, 1996; Turner and Stone, 2007)

Lovaas, 1987

- 9/19 in the experimental group (40 hours a week Applied Behavior Analysis - ABA) successfully completed regular first grade in a public school and had an average or better score on IQ tests
- Attempts at replication generally report some children reaching this outcome, but not as many as Lovaas.

- Mundy (1993) pointed out that normal IQ and functioning in regular education is possible in high-functioning autism and does not by itself constitute losing the diagnosis.

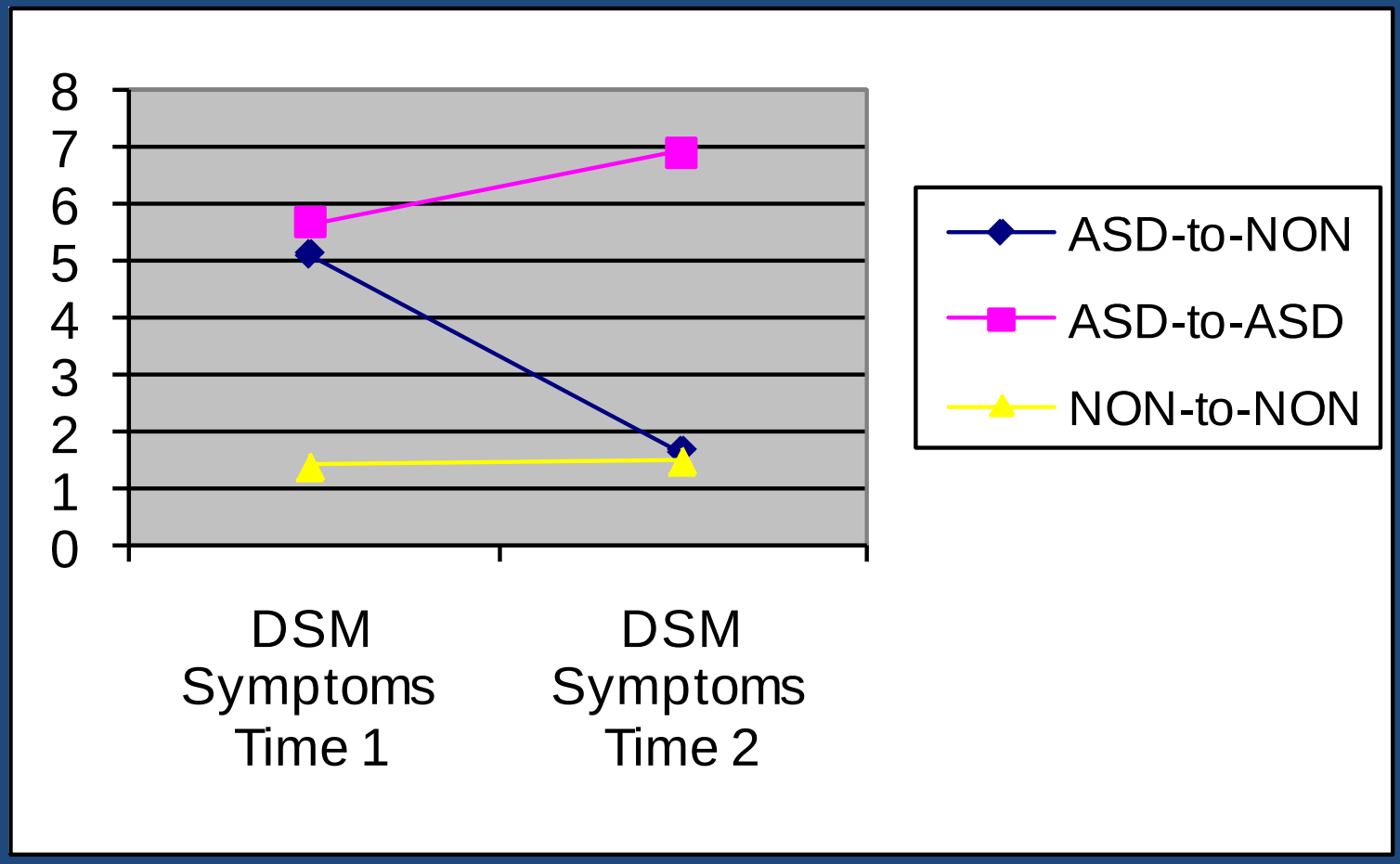
Purpose of our “optimal outcome” studies

- To document the phenomenon in which children with a clear history of ASD no longer meet criteria for ASD, and in whom there are no significant social or language problems
- To explore residual problems that may illuminate core deficits or suggest additional remediation or support needed
- To explore mechanisms of “optimal outcome” by tracking intervention and structural and functional imaging differences

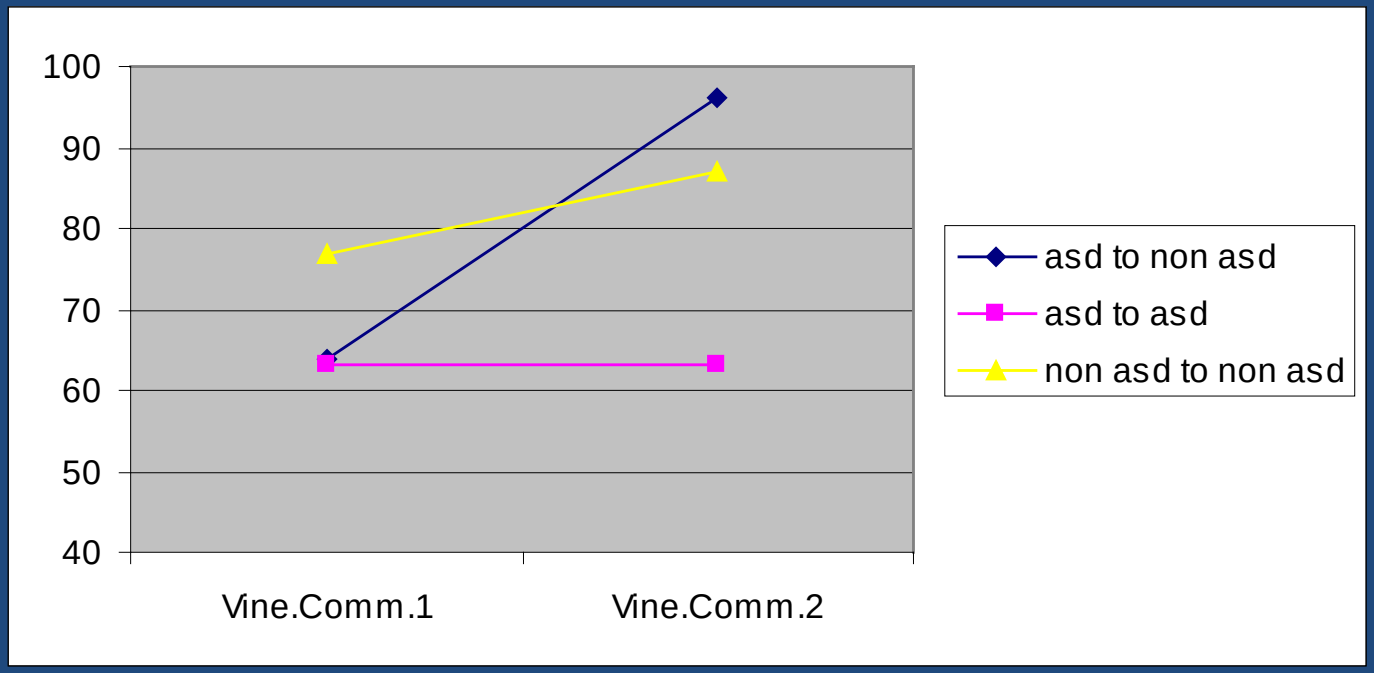
Background

- Sutera, S., et al (2007)
- 73 children dx'd with ASD at age 2 followed to age 4
- 13 (18%) lost dx

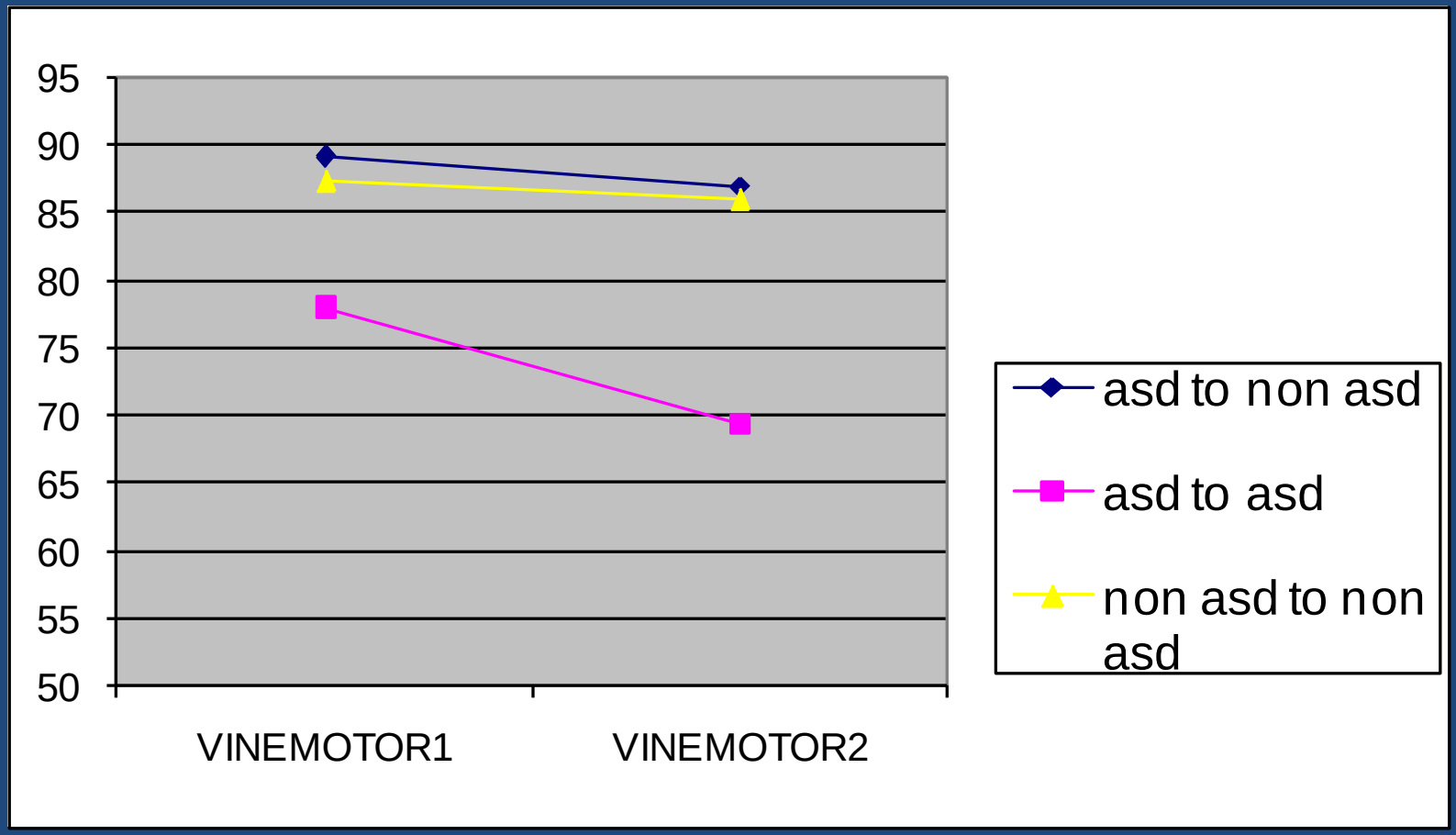
DSM-Symptoms



Vineland Communication



Vineland Motor



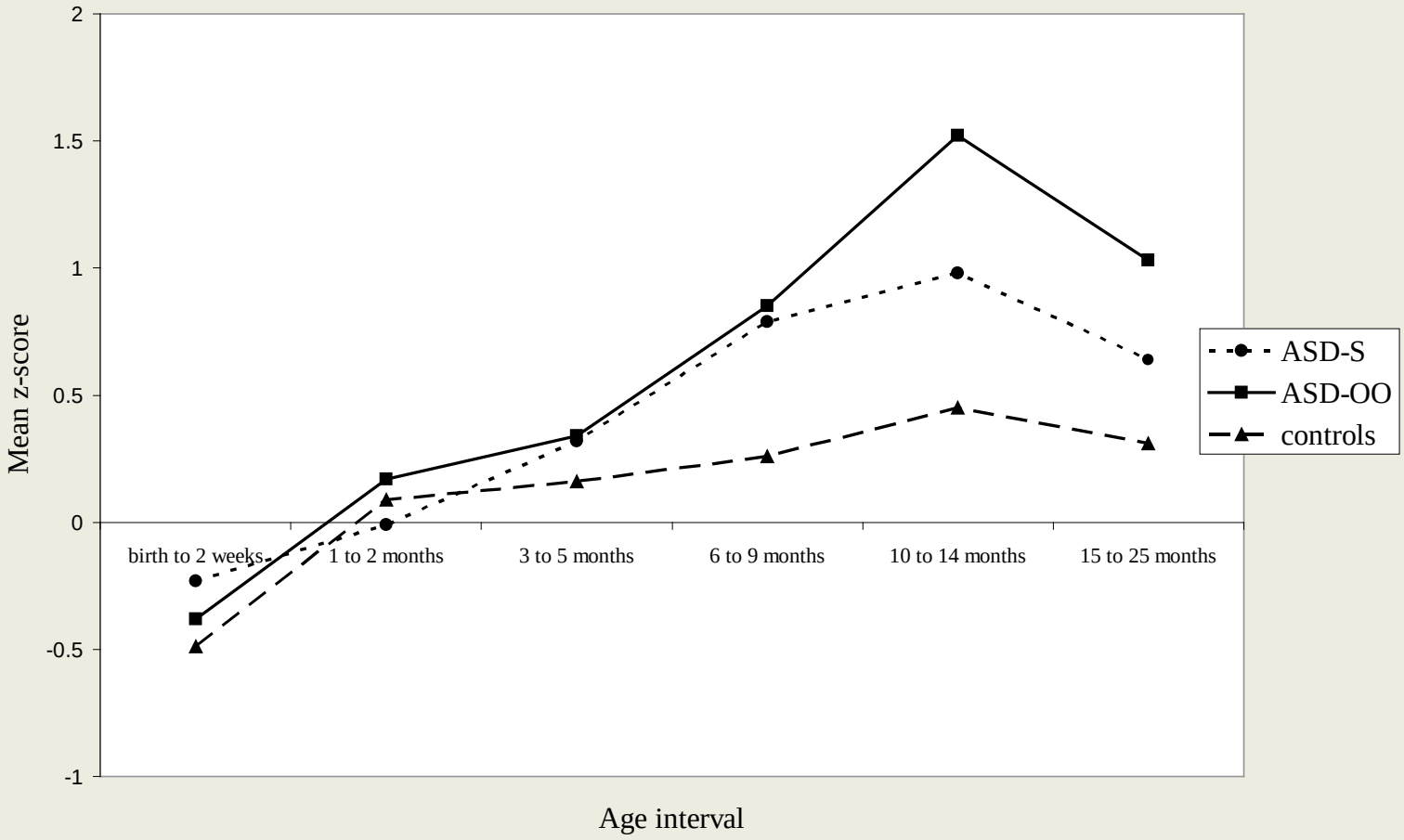
Can Head Circumference predict?

Mraz, K.D., Dixon, J., Dumont-Mathieu, T., Fein, D. (2009) Accelerated Head and Body Growth in Infants Later Diagnosed with Autism Spectrum Disorders: A Comparative Study of Optimal Outcome Children. Journal of Child Neurology

We predicted that the optimal outcome children would have more typical head circumference findings.

Mean HC z-score group differences

Figure 2. Mean HC z-scores for ASD-S, ASD-OO, and control groups



Current Study: Acknowledgements

- Funding: NIMH (NIH R01 MH076189)
- Collaborators:
  - Bob Schultz, Children's Hosp. of Philadelphia
  - Mike Stevens, Institute of Living, Hartford
  - Letty Naigles, Marianne Barton, Inge-Marie Eigsti, University of Connecticut
- Recruitment: Lynn Brennan, Harriet Levin
- Graduate students: Dr. Mike Rosenthal, Katherine Tyson, Eva Troyb, Alyssa Orinstein, Molly Helt

Inclusion criteria

- All subjects:
  - Verbal, nonverbal, and full-scale IQ standard scores greater than 77
  - No major psychopathology (e.g., active psychotic disorder) that would impede full participation
  - No severe visual or hearing impairments
  - No seizure disorder
  - No Fragile X syndrome
  - no significant head trauma with loss of consciousness

Inclusion criteria for OO s's

- Participants had a documented ASD diagnosis made by a physician or psychologist specializing in autism before the age of 5
- Early language delay (no words by 18 months or no phrases by 24 months)
- Report (without information on diagnosis, summary, and recommendations) was reviewed by clinician blind to group, mixed in with foils
- No current ASD as per ADOS and expert clinical judgment
- Vineland Communication and Socialization >77
- Full inclusion in regular education with no aide, no social skills services

Inclusion criteria for HFA

- participants had to meet criteria for ASD on the ADOS (both Social and Communication domains and total score) and according to best estimate clinical judgment.

Inclusion criteria for TD

- No ASD at any point in their development, by parent report
- No first-degree relative with an ASD diagnosis
- No current diagnostic criteria for an ASD on the ADOS, or by clinical judgment
- Vineland Communication and Socialization domains >77

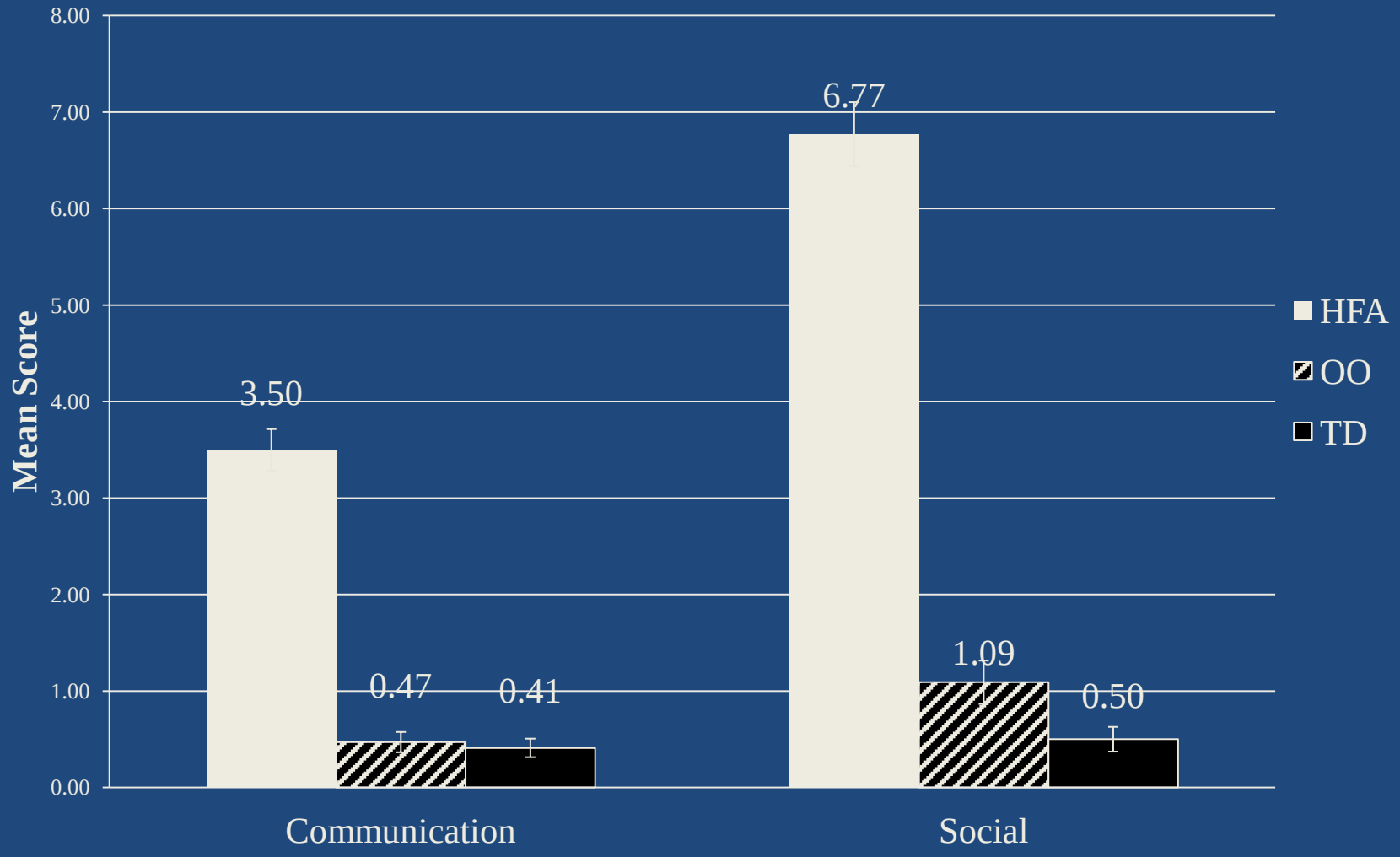
Domains of Data Collection

- Cognitive functioning
- Social functioning
- Executive functioning
- Language functioning
- Academic functioning
- Psychiatric functioning
- Intervention, medical, developmental history
- Structural and functional imaging
- 4 experimental tasks (top-down processing, categorical induction, tone discrimination, dual task performance)

Fein et al (2013) J. Child Psychol. and Psychiat.

	HFA (n=44)	OO (n=34)	TD (n=34)	*p*
Sex	**40 M; 4 F**	**27 M; 7 F**	**31 M; 3 F**	**.23**
Age	**13.9 (2.7)**	**12.8 (3.5)**	**13.9 (2.6)**	**.20**
VIQ	**105.4 (14.4)**	**112.7 (13.7)**	**112.0 (11.2)**	**.03**
NVIQ	**110.2 (12.8)**	**110.3 (15.1)**	**112.8 (11.3)**	**.64**

ADOS Algorithm Totals



Social Communication Questionnaire (Lifetime)

N=34 HFA	N=30 OO	N=32 TD	p	
22.65 (6.15)	17.10 (6.68)	1.50 (1.24)	<.001	HFA>OO >TD

ADI-R Lifetime

	HFA	OO	*F*	*p*
N	44	33		
Socialization	20.30 (5.33)	15.24 (6.43)	14.05	<.001
Communication	15.51 (5.07)	14.30 (4.73)	1.12	.29
Repetitive Behaviors	6.19 (2.30)	5.85 (2.33)	0.40	.53

Vineland Adaptive Behavior

	HFA	OO	TD	*p*
Commun.	**82.70 (13.86)**	**98.30 (12.66)**	**93.44 (9.12)**	**<.001**
Socializ.	**75.51 (16.02)**	**102.03 (8.44)**	**101.74 (8.56)**	**<.001**
Daily Living	**75.40 (14.26)**	**92.30 (15.88**	**88.76 (9.26)**	**<.001**

For all comparisons, OO, TD > HFA

Benton Face Recognition

	HFA	OO	TD	*p*
N	**40**	**33**	**34**	
Benton z-score	**z = -0.49 (1.25)**	**z = -0.02 (1.19)**	**z = 0.27 (0.79)**	**.01 TD>HFA**

Academic Skills (Troyb et al, in press, Autism: The International Journal)

- Measures of decoding, passage comprehension, written expression, and math problem solving
- All three groups performed in the average range on all subtests
- No significant differences between OO and TD groups. The HFA group scored significantly lower on reading comprehension and math problem solving.

Psychiatric Co-Morbidity

- Most common co-morbidities reported for ASD:
  - Anxiety (esp. specific and social phobias)
  - OCD
  - Tics
  - Depression
  - ADHD
  - ODD
- As much as 70% of ASD individuals have one co-morbid condition and 41% have 2 (Simons et al, 2008)

% with Current Psychiatric Disorders (Tyson et al IMFAR 2010)

	TD	HFA	Optimal outcome
Specific phobia	0	5	14
ADHD	0	40	21
Tics	0	20	7

Summary

- OO group show no obvious social, language or cognitive difference from TD group
- Predictors of OO are similar to predictors of good outcome in general (higher cognitive and motor functioning, milder social symptoms)
- High rates of repetitive behavior do not preclude OO
- OO group does not show head circumference growth different from persisting ASD
- Above average IQ in OO group
- Residual deficits or vulnerabilities in the OO group (anxiety, attention)

Some Open Questions

- What percent of ASD children can reach this outcome?
- Is behavioral intervention necessary to produce this outcome?
- Do the children with OO potential have a distinctive set of etiologies?
- Are the OO participants arriving at overt behavior through different means (fMRI may illuminate)

Possible Mechanisms of Loss of Symptoms and Diagnosis

- The early clinical picture represented a transient developmental delay
- Behavioral intervention bypasses intrinsic motivation
- Neurologically based deficit in social orienting is prevented from disrupting further neurological development (Mundy & Crosson)

- Pairing social contact with primary reinforcers results in social contact developing secondary reinforcing value (Dawson) (but how does the connection become autonomous?)
- Suppressing interfering behaviors, especially stimulatory and repetitive behaviors
- Forcing attention to the environment rather than the internal world
- Teaching alternative routes to the same skills (fMRI may illuminate)

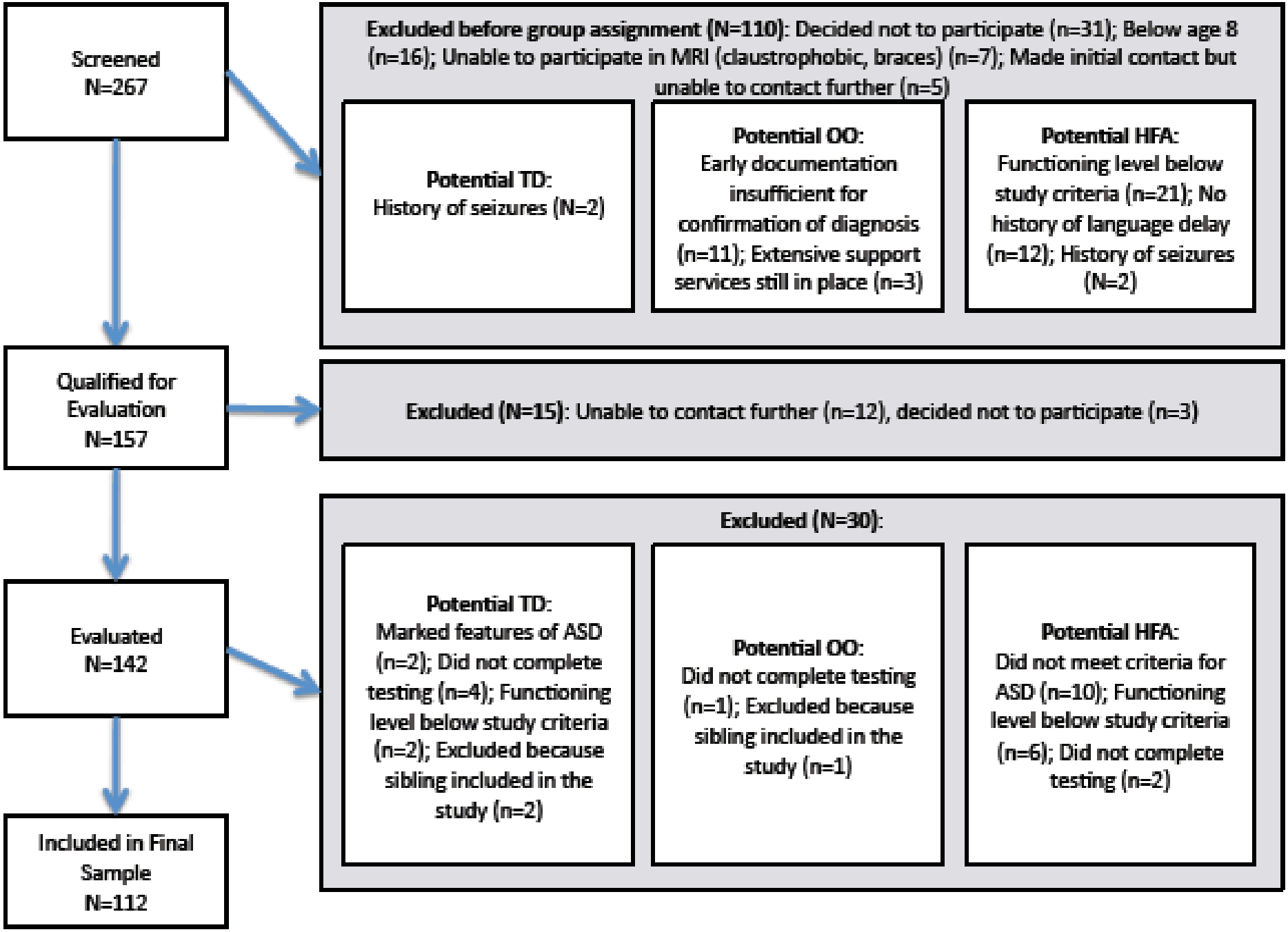
Future Directions

- Increase geographic and demographic diversity
- Adult outcome
- Biological differences between ASD-stable and Optimal Outcome individuals:
  - Genetic findings
  - Family history
  - Early growth parameters
  - Imaging findings
- Long term follow-up of children we diagnosed at age 2 to estimate % Optimal Outcome and identify predictors
- Follow children moving into OO to track reduction in symptoms
- Intervention histories

Setting the record straight…

- Children do not generally ‘grow out of’ autism
- These findings are not an argument for less early detection and intervention, but for more

Thank you


Screened
N=267
Excluded before group assignment (N=110): Decided not to participate (n=31); Below age 8 (n=16); Unable to participate in MRI (claustrophobic, braces) (n=7); Made initial contact but unable to contact further (n=5)
Potential TD:
History of seizures (N=2)
Potential OO:
Early documentation insufficient for confirmation of diagnosis (n=11); Extensive support services still in place (n=3)
Potential HFA:
Functioning level below study criteria (n=21); No history of language delay (n=12); History of seizures (N=2)
Qualified for Evaluation
N=157
Excluded (N=15): Unable to contact further (n=12), decided not to participate (n=3)
Evaluated
N=142
Excluded (N=30):
Potential TD:
Marked features of ASD (n=2); Did not complete testing (n=4); Functioning level below study criteria (n=2); Excluded because sibling included in the study (n=2)
Potential OO:
Did not complete testing (n=1); Excluded because sibling included in the study (n=1)
Potential HFA:
Did not meet criteria for ASD (n=10); Functioning level below study criteria (n=6); Did not complete testing (n=2)
Included in Final Sample
N=112

Predictors of Better Outcome

- higher initial IQ
- better receptive language
- imitation
- better motor skills*
- better pretend play
- less repetitive behavior
- milder overall severity
- better overall adaptive skills
- earlier diagnosis
- earlier treatment
- diagnosis of PDD-NOS rather than Autistic Disorder

Background

- Piven et al (1996) followed 38 high-IQ individuals with ASD from age 5 to age 13-28
- Majority showed improvement in social behavior and communication, but only half in repetitive behaviors
- 5 lost the ASD diagnosis, but all had persistent significant impairments in social interaction and/or repetitive behavior

- Turner and Stone (2007) followed 48 children diagnosed at age 2 to follow-up at age 4.
- 18 children lost the diagnosis
  - milder social symptoms
  - higher cognitive functioning
  - were younger at initial diagnosis
  - tended to have persisting language problems

Specific Phobias

- HFA: crowds, babies, dogs,
- OO: dark, stink bugs, ants and bees, loud noises, crowds, elevators, ketchup, germs, dogs, crying, boats/water, heights
- TD: dogs, forests, snakes

Interpretations of the autistic to ADHD clinical picture

- Comorbid ASD/ADHD; autism resolves, leaving the ADHD clinical picture
- The children are a severe subtype of ADHD that presents as autism in the early years
- Attention impairment is part of ASD; when social, behavioral, and communication impairments subside, attention impairments remain

Mechanisms of Co-Morbidity

- Reactive disorder because of stress
- Overlapping symptoms with different causes
- Common underlying pathophysiology
- Misdiagnosis (avoidant anxious children may meet ADOS criteria for ASD)
- Subtypes of ASD that include other symptoms

Meeting of the IACC

Study of Health Outcomes in Children with Autism and their Families

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HEALTH CARE AND HUMAN SERVICES POLICY, RESEARCH, AND CONSULTING - WITH REAL-WORLD PERSPECTIVE.

Study of Health Outcomes in Children with Autism and Their Families

Presentation for Interagency Autism Coordinating Committee

January 29, 2013

Discussion Outline

- **Project Overview**
- **Key Findings**
- **Questions**

Project Overview

Research Team

- The Lewin Group
- OptumInsight
- OptumHealth
- Drexel University

Objective

Use existing administrative data to further our understanding about Autism Spectrum Disorders (ASD), including:

- diagnosis,
- risk factors,
- health outcomes of children with ASD and their family members,
- health care use by children with ASD and their family members.

Deliverables

- 5 reports
- 3 manuscripts
- Dataset delivered to National Database for Autism Research (NDAR)

What are Administrative Claims Data?

- Data submitted by providers (e.g., doctors, hospitals, etc.) to payers (e.g., health insurance companies) for payment of services
- Procedures/services not covered by health plan (e.g., ABA, speech therapy offered at school) are not included
- Usually does not include all of the clinical information related to an individual

Study Sample Information

Data Set Attribute	Description
Timeframe to be used in study	2001-2009
Medical information	Diagnosis code(s), procedure code(s), some provider characteristics (e.g., specialty), cost/payment (health plan and beneficiary responsibility)
Pharmacy information	Drug, dosage, length of script in days, minimal information on prescriber
Mental & behavioral health information	Similar information to medical claims for individuals with behavioral health coverage (ASD covered at least partially)
Sociodemographic (income and race)	Not available in claims data but our data is linked to outside source of data about income and race, but missing in 40-50% of sample.
Family linkage	Logic included in our programming to identify likely parent and siblings with the same insurance
Representation	Dataset is geographically diverse across the US and fairly representative of the population

Study Sample Size

Sample Description	Sample Size (ASD)*	Comparison Group (no ASD)
Children	46,236	138,876
Parents of children	80,164	232,229
Siblings of children	57,056	195,868

*Presence of one or more claims with an ICD-9 for Asperger's, Autism, or PDD-NOS

- Approximately 80% of the children with ASD were male
- Just over half of the sample was between 2-10 years of age
- Race/ethnicity was not available for ~ half of the children, but for those where it was available over 75% were white

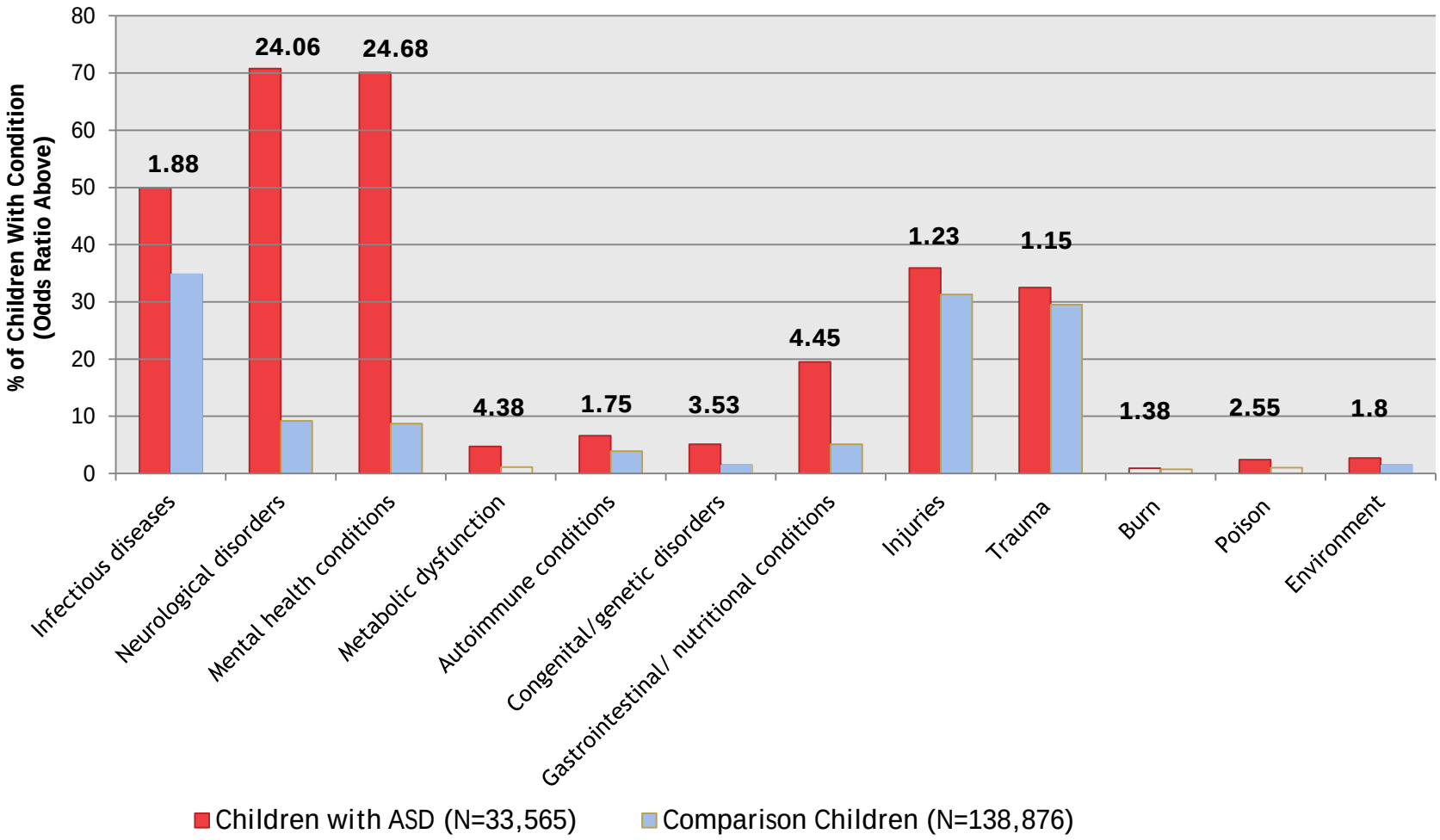
A Chart Review informed our identification of children with ASD using claims data

- Using ~430 medical charts, we assessed the extent to which a claim with an ASD diagnosis was confirmed by clinical information in the physician's chart
  - If a child had one claim with an ASD diagnosis, the Positive Predictive Value (PPV)=74.2%
  - If a child had two or more claims with an ASD diagnosis, the PPV increased to 87.4%
  - Thus, the rest of our analysis only included children with 2 or more ASD diagnosis codes in claims as having ASD (n=33,565).

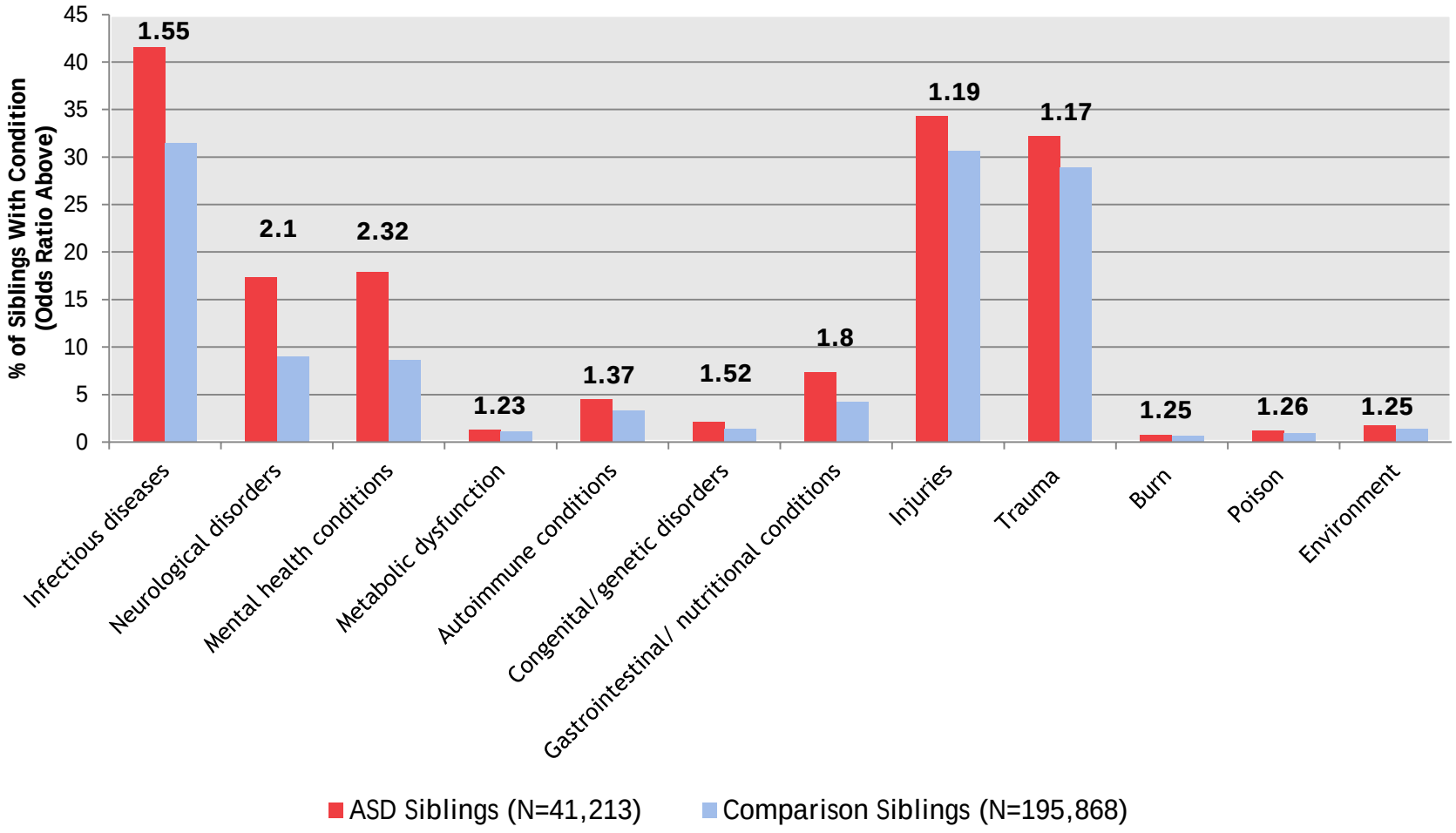
Discussion Outline

- Project Overview
- **Key Findings**
- Questions

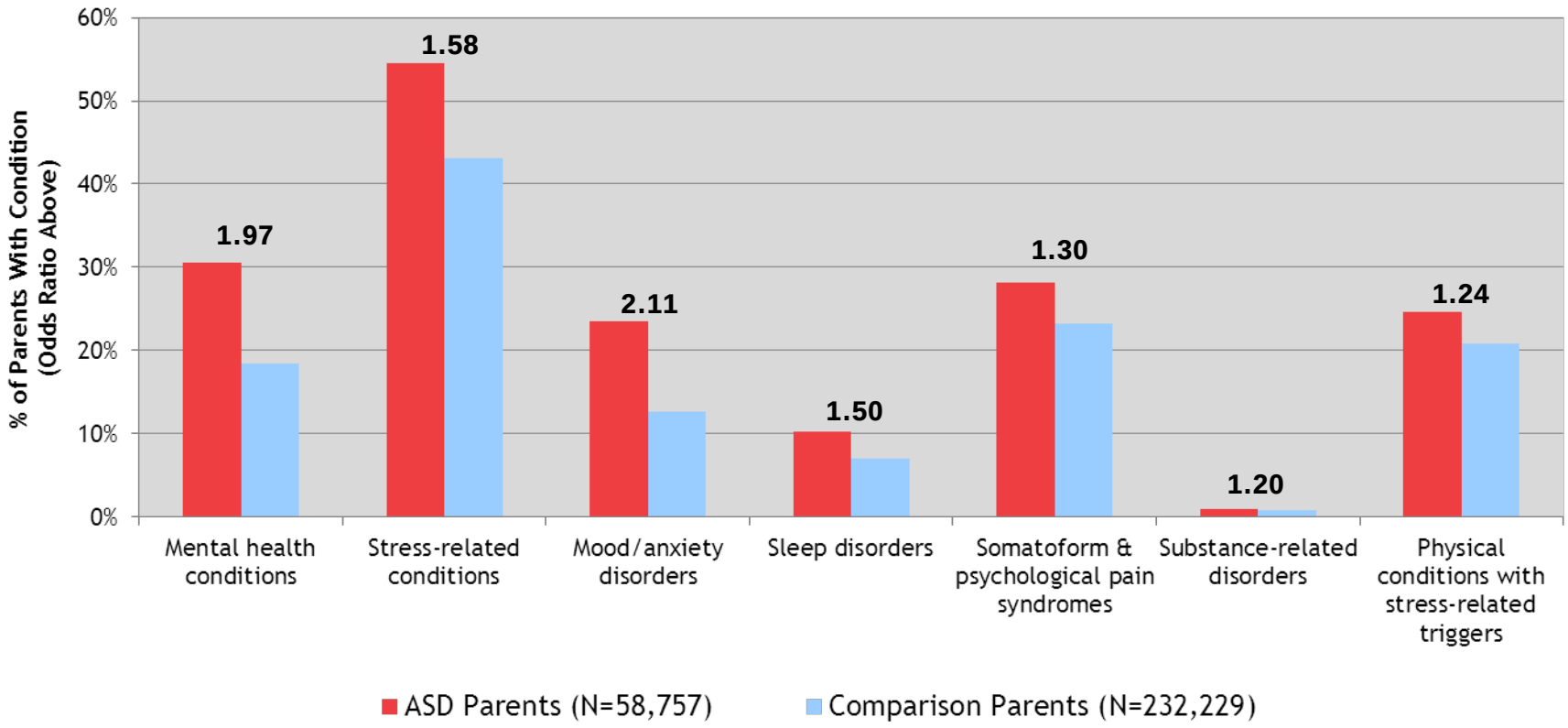
Health Outcomes:
ASD vs. Comparison Children



Health Outcomes:
ASD Siblings vs. Comparison Siblings



Health Outcomes:
ASD Parents vs. Comparison Parents



Gastrointestinal Disorders among children with and without ASD

Research Topics

We studied:

1. The occurrence of gastrointestinal conditions in children with ASD compared to those without, and
2. How the occurrence of GI conditions changed after the ASD diagnosis compared to before the ASD diagnosis.

Results

We found that:

1. Children with ASD were much more likely to have a GI condition than children without ASD (OR = 3.94).
2. The odds for having a GI condition were higher in the 12 month period after the ASD diagnosis than the 12 months before (OR= 1.39).

Parental stress-related conditions

Research Topics

We studied:

1. The occurrence of stress-related conditions in parents of children with ASD compared to parents of children without ASD, and
2. The occurrence of stress-related conditions in parents following his/her child's initial ASD diagnosis compared to before the diagnosis.

Results

We found that:

1. Parents of children with ASD had higher odds of having a stress-related condition than parents of children without ASD (OR=1.48).
2. Among parents of children newly diagnosed with ASD, the odds of having a stress-related condition were higher in the 12 month period after the child's diagnosis (OR=1.32) than in the 12 month period before.

Health Care Use: ASD and Comparison Children

- Children with ASD had an average of 21 total health care visits (office and outpatient) annually, as compared to 5 visits for children without ASD
  - Children with ASD had an average of 11 total behavioral health visits (subset of total health care visits), compared to less than 1 for children without ASD
- Children with ASD were prescribed, on average, ~3 unique medications annually, compared to ~2 unique medications for children without ASD

Adherence to MMR Vaccination

Research Topics

We studied:

1. The relationship between diagnosis of ASD in a child and MMR vaccination rates among younger siblings (12-24 month old group)

Results

We found that:

1. Younger siblings of children with ASD were less likely to be vaccinated with the first MMR than their older siblings with ASD (69.2% vs. 82.2%)
2. Younger siblings of children with ASD were less likely to be vaccinated with MMR than younger siblings of children without ASD (69.2% vs. 84.9%).

Topics Pending Publication

Research Topics

1. Injury Among Children With Autism Spectrum Disorders
2. Psychotropic Medication Use and Polypharmacy in Children with Autism Spectrum Disorders

Results

The results to these research questions are currently under consideration for publication.

Utility of Claims Data for ASD Risk Factor Research

- We assessed whether claims data could be useful in future research to examine risk factors for ASD:
  - Early life risk factors in children
  - Maternal risk factors during pregnancy and prior to conception
  - Paternal risk factors prior to conception
  - Included risk factors that would be captured in claims such as: preterm birth, chronic maternal health conditions prior to pregnancy or during pregnancy (e.g., asthma and depression), medication use, anesthesia use, infertility treatment, and early immunizations
- Estimated sample size of mother-child pairs and father-child pairs for each risk factor and comparison groups

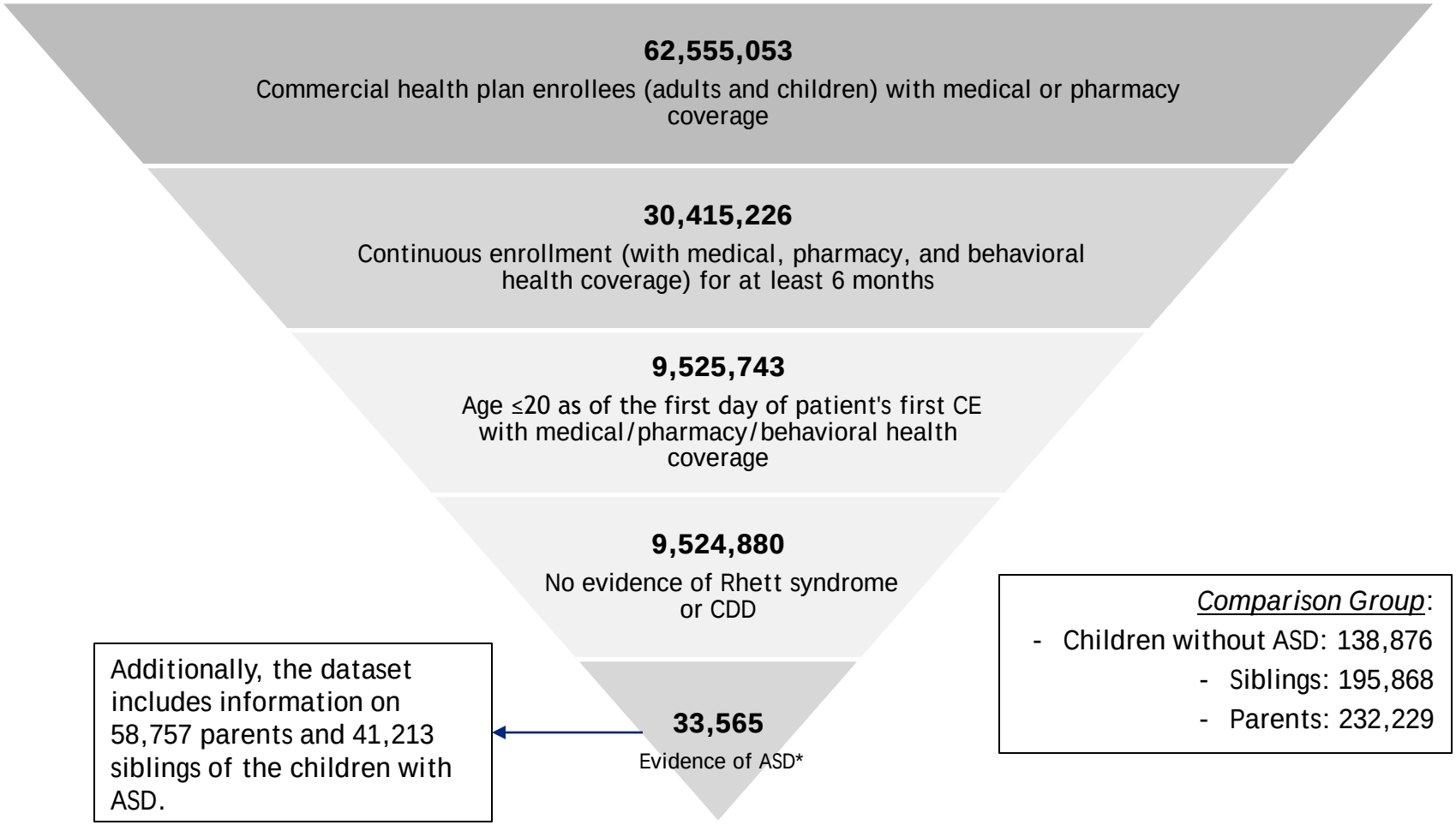
Strengths and Limitations

- Strengths
  - Large dataset that is generally representative of the US population
  - Constructed a cohort of children highly probable to have ASD, which is larger than many comparable studies on ASD
  - Data spans a ten-year period
  - Were able to link children with ASD to their family members and examine the impact of ASD on sibling and parental health
- Limitations
  - Administrative claims data are generated for payment purposes, so diagnoses that do not impact payment are likely under-reported (e.g. obesity)
  - Severity of ASD not well captured in data (e.g. Mental retardation and non-verbal status likely under-reported)
  - Surveillance bias may have impacted our results (though our analysis suggested it was not a significant factor)

Question and Answer Session

QUESTIONS?

Study collected information on a large sample of children with ASD



*presence of two or more claims with an ICD-9 for Asperger's, Autism, or PDD-NOS

Sample Sizes for Risk Factor Research

	ASD	Comparison
	N (%)	N (%)
Mothers identified via FAMID and appropriate age relative to child with ASD (or comparison child)	**31,329**	**119,143**
Mothers identified via validated methods (e.g., enrolled at birth of child between 2001 - 2009)	2,176 (6.9%)	10,703 (8.9%)
Fathers identified via FAMID and appropriate age relative to child with ASD (or comparison child)	**30,191**	**119,143**
Enrolled at conception (+/- 7 days)	1,513 (5.0%)	7,204 (6.0%)
Children	**33,565**	**138,876**
Enrolled birth to 24 months	1,767 (5.2%)	4,876 (3.5%)

Meeting of the IACC

Afternoon Agenda (cont'd)

2:30 **National Children's Study Update**
Alan Guttmacher, M.D.
Eunice Kennedy Shriver National Institute of Child Health and Human Development and Member, IACC

2:50 PM **Break**

Meeting of the IACC

National Children's Study Update

These slides do not reflect decisions of the IACC and are for discussion purposes only.

THE NATIONAL CHILDREN'S STUDY

Alan E. Guttmacher, M.D.

Director

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

January 29, 2013

Overall Goal of the NCS

- To improve the health and well-being of children and to identify antecedents of healthy adulthood
  - By examining the multiple effects of environmental influences and biological factors on the growth, health, and development of ~100,000 children across the U.S., following them from before birth until age 21 years

IMPROVING THE HEALTH OF AMERICA'S CHILDREN

THE NATIONAL CHILDREN'S STUDY

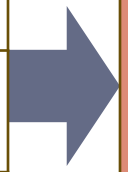
HEALTH GROWTH ENVIRONMENT

- Largest and most ambitious U.S. long-term study of child health and development ever
- Longitudinal study of biological and broadly defined environmental factors, such as:
  - Air; water; soil; dust; noise; diet; social and cultural setting; access to health care, socio-economic status, and learning; etc.

- Data resource with linked environmental and biological samples, not a conventional "study"
- "Exemplar hypotheses," but not designed to answer specific hypotheses only
- All data generated will be quickly and freely available to all researchers, whether or not they are funded through the NCS

NCS: Examples of Exposures and Health Outcomes

Exposures	Examples
Physical Environment	Housing quality, neighborhood
Chemical Exposures	Pesticides, phthalates, heavy metals, BPA
Biologic Environment	Infectious agents, endotoxins, diet
Genetics	Interaction between genes and environment
Psychosocial milieu	Family structure, socio-economic status, parenting style, social networks, exposure to media and violence



Health Outcomes	Examples
Pregnancy Outcomes	Prematurity, birth defects
Neurodevelopment & Behavior	Autism, learning disabilities, schizophrenia, conduct and behavior problems
Injury	Head trauma, injuries requiring hospitalizations
Asthma	Asthma incidence and exacerbation
Obesity & Physical Development	Obesity, diabetes, altered puberty

NCS: Components

- Major components:
  - **Vanguard Study**: ~4,000 children; started 2009; 40 diverse sites; designed to inform Main Study science, logistics, and costs
  - **Main Study**: ~100,000 children; runs ~4 years behind Vanguard Study; planned start in 2013
  - **Formative Research**: Short term studies, often methods development, to inform Vanguard and Main Studies; will also inform many non-NCS research efforts

NCS Main Study: Sample Size

- Of 100,000 children, an estimated
  - 30,000 will be overweight (17,000 obese)
  - 12,000 will be born preterm (before 37 weeks)
  - 5,000 will have learning disorders
  - 5,000 will have asthma
  - 1,000-3,000 will have autism spectrum disorders
  - 320 will develop childhood cancers
  - 125 will have Down syndrome
  - 50 will have Fragile X syndrome

Main Study Design Principles

- Anchored in a national probability sample
- Recruitment through health care providers
  - Birth cohort: via selected hospitals and birthing centers
  - Prenatal cohort: via community based prenatal providers and clinics that refer to the selected hospitals and birthing centers
- Sample size of 100,000
  - Birth and prenatal cohorts to total about 90,000
  - Additional convenience cohorts to total up to 10,000 for preconception and additional targeted populations

In Case You Should Ask

Q: “If kids have autism, when will you find out?”

A: Using screening instruments currently planned for NCS study visits (including the Ages and Stages questionnaire and the Modified Checklist for Autism in Toddlers) the lowest age would be ~18 months. We also plan to have access to medical records to learn about any other assessments that might allow earlier diagnosis.

(The NCS has a return of results policy for medically actionable findings and will work with parents and primary care providers to share outcomes.)

In Case You Should Ask

Q: “Would you consider other instruments, testing, etc., for kids at elevated risk for autism?”

A: Yes! And, NCS has already invested in formative research to see if autism screening sensitivity and specificity for all children can be improved. A current multisite study on autism assessment tools will conclude later this year. It compares a battery of three brief novel assessments (a video-guided parent self-report; a parent interview, and a direct observation) that can be implemented by NCS field staff to “gold standard” ASD case confirmation (an Autism Diagnostic Observation Schedule by a research-reliable assessor and a DSM-based diagnostic assessment by a qualified clinician).

NCS: Summary

- Longitudinal data on ~100,000 children from before birth to age 21
- With linked biological and environmental (broadly defined) exposure samples

- An unparalleled resource to understand childhood health, growth, and development

Meeting of the IACC

Break

Meeting of the IACC

Afternoon Agenda (cont'd)

3:05 **IACC Business**

Thomas Insel, M.D.
Director, NIMH, and Chair, IACC

Susan A. Daniels, Ph.D.
Acting Director, OARC and Executive Secretary, IACC

- 2012 Strategic Plan Update
- 2013 Strategic Plan Update Process
- 2012 Summary of Advances
- 2011-2012 Portfolio Analysis
- Other Activities

Meeting of the IACC

IACC Business

Thomas Insel, M.D.
Director, National Institute of Mental Health and Chair, IACC

Susan A. Daniels, Ph.D.
Acting Director, Office of Autism Research Coordination and
Executive Secretary, IACC

Responsibilities under CAA

- Coordinate HHS activities
- Advise HHS Secretary Sebelius
- Establish autism research priorities
  - **IACC Strategic Plan for ASD Research**
- Communicate advances in the field
  - **IACC Summary of Advances in ASD Research**
- Monitor Federal activities and research trends
  - **IACC ASD Research Portfolio Analysis Report**
- Serve as a forum for public discussion

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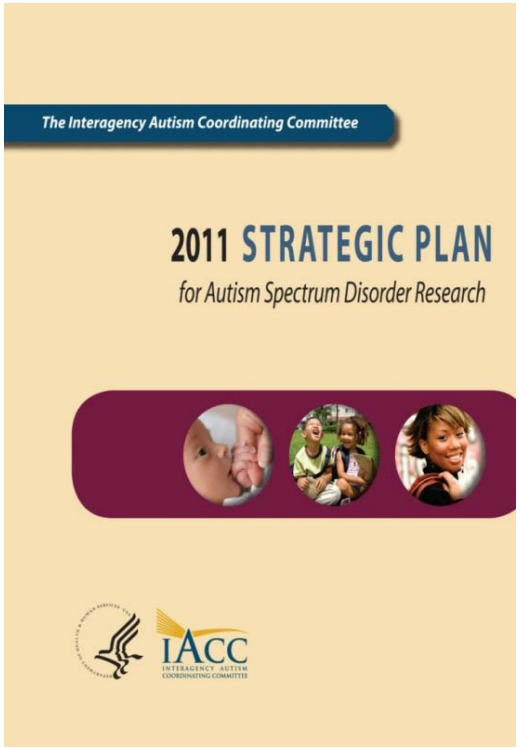
Strategic Plan for ASD Research



The IACC does not fund research, but encourages federal agencies and private organizations that fund ASD research to use the Strategic Plan in charting the course for new research

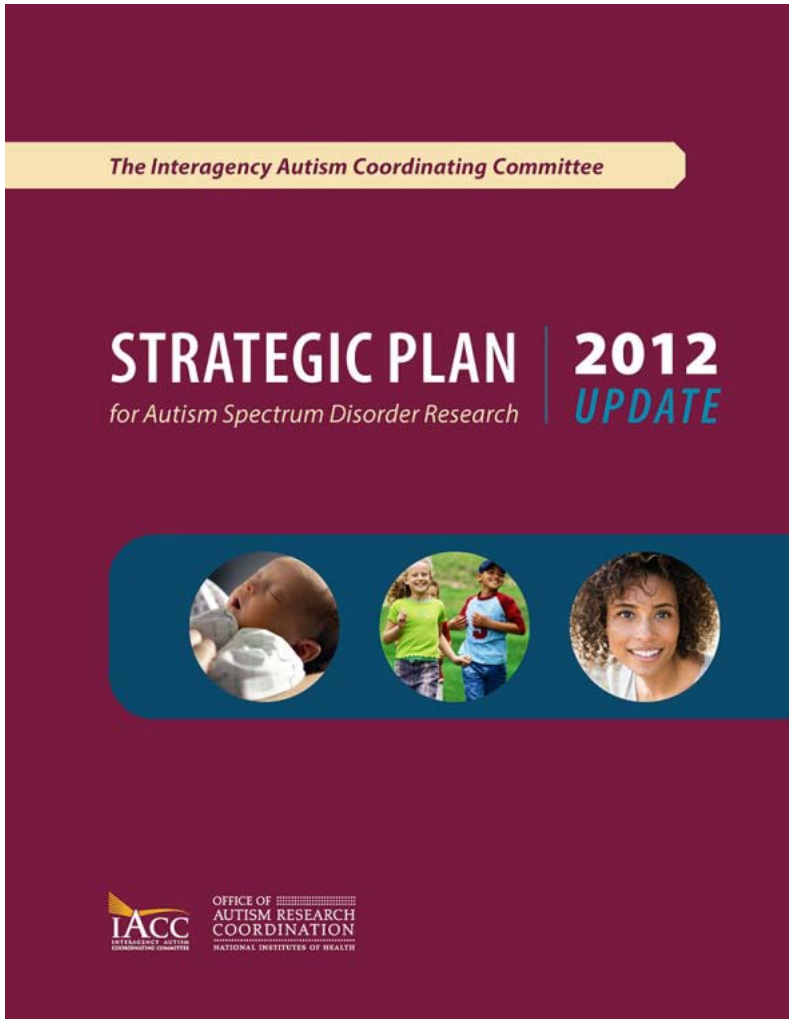
Purpose:

- Focus, coordinate, and accelerate high quality research
- Answer the urgent questions of families and individuals affected by ASD

2011 Strategic Plan:

- 78 research objectives
- New objectives in 2011 included nonverbal ASD, health promotion and safety

New! **IACC Strategic Plan – 2012 Update**



Update on progress made in 2011 and 2012

Answers the questions:

- "What do we know?"

  Summary of progress in each of the 7 critical Question areas of the IACC Strategic Plan

- "What do we need?"

  Describes remaining gaps, emerging issues and new opportunities

2013 Strategic Plan Update

- What kind of product?
- What process to use?
- Timeline?

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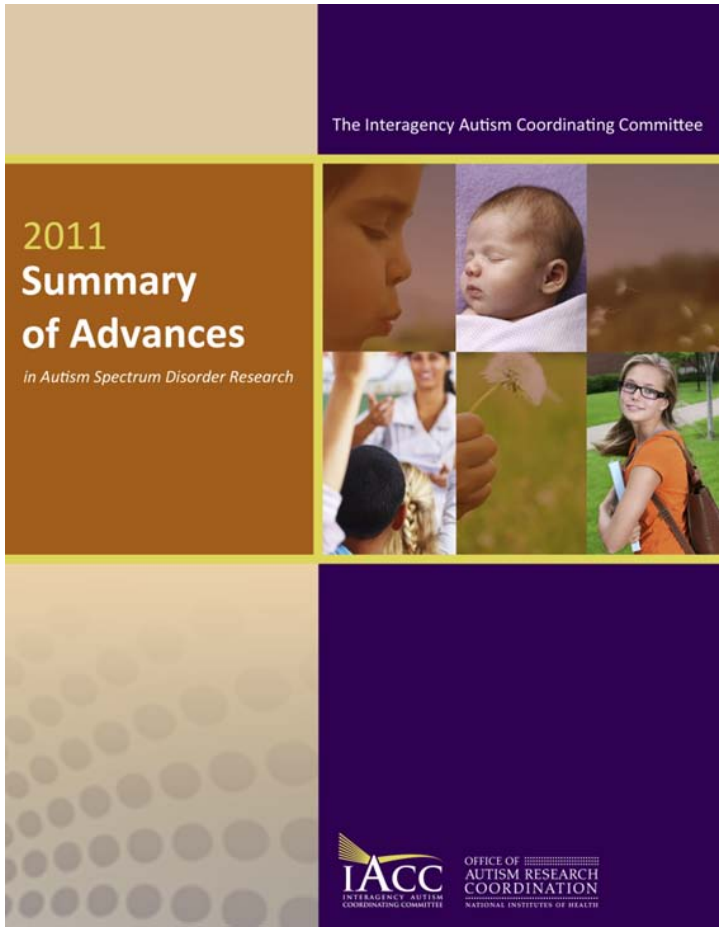
IACC Summary of Advances



- Conducted on a yearly basis
- Lay-friendly summaries of the 20 most significant advances in ASD biomedical and services research
- Publications included are selected by the IACC
- New insights into ASD:
  - Prevalence
  - Diagnosis
  - Biology
  - Risk factors
  - Interventions
  - Lifespan issues

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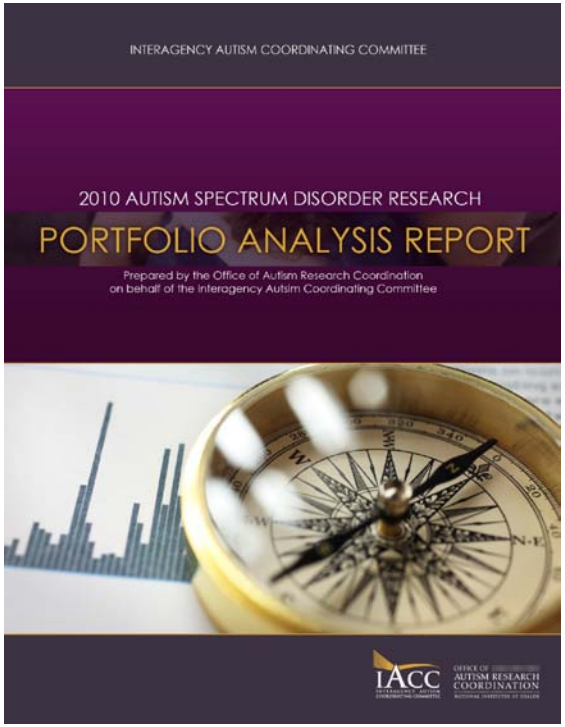
IACC ASD Research Portfolio Analysis



- Assists the IACC in fulfilling the CAA requirement to monitor Federal activities related to Autism Spectrum Disorder (ASD)
- Provides comprehensive analysis of the ASD research portfolio across both Federal agencies and private organizations
- Informs the IACC and stakeholders about the funding landscape and current directions in ASD research
- Helps the IACC monitor progress in fulfilling the objectives of the IACC Strategic Plan
- Highlights gaps and opportunities to guide future activities

CAA Report to Congress

- 2011 report coordinated by OARC on behalf of the HHS Office of the Secretary
- Content included:
  - Information on HHS and Department of Education agencies and programs related to autism research and services
  - Agency budget figures
  - Progress on:
    - Prevalence
    - Age of diagnosis and intervention
    - Adult services

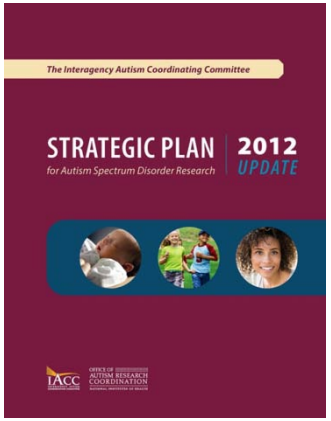
Next report due September 2013

Other Activities?

Other Activities that can contribute to the IACC's fulfillment of roles and responsibilities:

- **Interagency coordination**
- **Communicating/public forum regarding changes in the field or emerging issues**
- **Advising**

IACC
INTERAGENCY AUTISM
COORDINATING COMMITTEE



IACC
INTERAGENCY AUTISM
COORDINATING COMMITTEE

All IACC publications and more information about the IACC are available at: www.iacc.hhs.gov

For comments, questions,
listserv access and requests, e-mail:
iaccpublicinquiries@mail.nih.gov

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Meeting of the IACC

Afternoon Agenda (cont'd)

4:15 PM	**Public Comment Discussion Period**
4:45	**Wrap-Up**
5:00	**Adjournment**

Upcoming IACC Full Committee Meetings:

April 9, 2013

July 9, 2013

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Meeting of the IACC

Public Comment Discussion

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Meeting of the IACC

Wrap-Up

Meeting of the IACC

Adjournment