DOWN SYNDROME AND AUTISM SCREENING: DIAGNOSIS AND PREVALENCE RTOI WEBINAR

October 27, 2008

Presented by AUCD and supported by Cooperative Agreement from the National Center on Birth Defects and Developmental Disabilities (NCBDDDD) at Center for Disease Control and Prevention (CDC)
Webinar Agenda

I. Welcome & Introduction – Sue Lin, MS Project Director, AUCD-NCBDDD Cooperative Agreement

II. Presentation

- **Down Syndrome and Autism Screening: Diagnosis and Prevalence** – Susan Hyman, MD and Edwin van Wijngaarden, PhD (Strong Center for Developmental Disabilities, NY UCEDD); Cordelia Robinson, PhD and Susan Hepburn, PhD (JFK Partners, CO UCEDD)

III. Discussant

- Diana Schendel, PhD, NCBDDD, CDC

IV. Question and Answer
Overview: AUCD-NCBDDDD Cooperative Agreement

- Strengthen the nation's capacity to carry out public health and disability activities
- Foster collaborations among AUCD, its network (UCEDD, LEND, DDRC) members, and NCBDDDD
- Provide technical assistance to State Disability and Health Grantees
- Enhance the capacity of states and creating collaborative systems change in the early identification, assessment, service coordination for children with autism spectrum disorder and related disabilities through Act Early Regional Summits
- Strengthen expertise in the fields of birth defects and developmental disabilities through training of professionals in public health and related fields.
- Facilitate a wide range of research, education, and dissemination activities.
Research Topics of Interests (RTOI)

RTOI are specific research area of significance identified by scientists at NCBDDD, CDC. Past RTOI projects have focused on the following areas:

- Health Communication and Education
- Prevention of Secondary Conditions
- Healthcare Cost Analysis
- Quality of Life Studies
- Developmental Factors and Outcomes
- Health Promotion Interventions
- Co-Morbidity Prevalence Studies

Specific disabilities areas include: autism, Down syndrome, Duchenne muscular dystrophy, epilepsy, Fragile X syndrome, hearing loss, fetal alcohol syndrome, spina bifida, and Tourette syndrome.
Presenters and Discussant

Susan Hyman, MD
Edwin van Wijngaarden, PhD
Strong Center for Developmental Disabilities
University of Rochester Medical Center

Cordelia Robinson, PhD
Susan Hepburn, PhD
JFK Partners University of Colorado at Denver Health Sciences Center

Diana Schendel, PhD
NCBDDD, CDC
Webinar Guidelines

- All participants lines will be MUTED during the presentation
- Operator will facilitate the Q&A session
- Participants may submit questions online during presentation through Go To Webinar text box at any time

Sample webinar screen
A Population Based Study of the Prevalence of Autism Spectrum Disorders in Children with Down Syndrome

Cordelia Robinson, Ph.D, RN
Susan Hepburn, Ph.D
JFK Partners
University of Colorado Denver
School of Medicine
Why is it important to determine risk for comorbidity?

- Potential for understanding the neurobiology of autism, phenotypic symptoms of autism, in conjunction with phenotypic symptoms of Down syndrome
- Provision of appropriate services to children with both diagnoses
- Determine strategies for screening
- Better understanding of child and access to appropriate support mechanisms for families
Prevalence of Autism Symptoms in Children with Down Syndrome: Findings from Colorado
Aim 1

Conduct a population-based epidemiological study of the prevalence of ASD in children with Down syndrome
Recruitment Process

Colorado Dept. of Public Health and Environment (CDPHE) utilizes their birth registry monitoring program to mail invitation letters to families of children with Down syndrome who were:
- While mother resided in 1 of 10 Front Range Colorado counties

Mile High Down Syndrome Society publicizes the study and mails 228 invitation letters to member families

Families who respond are offered a screening test for social, communication, and behavioral difficulties, and the possibility of a follow-up diagnostic evaluation
Recruitment Through CDPHE Birth Registry
(Colorado Responds to Children with Special Needs)

<table>
<thead>
<tr>
<th>Total # children with Down syndrome (born to a study area resident between 1996 and 2003)</th>
<th>497</th>
</tr>
</thead>
<tbody>
<tr>
<td># of deaths</td>
<td>55</td>
</tr>
<tr>
<td># invitation letters sent</td>
<td>442</td>
</tr>
<tr>
<td># returned undeliverable</td>
<td>150</td>
</tr>
<tr>
<td># letters assumed delivered</td>
<td>292</td>
</tr>
<tr>
<td># enrolled/screened</td>
<td>124</td>
</tr>
</tbody>
</table>

Response rate = 124/292 = 42.5%
### Comparison of Responders and Non Responders

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Responders</th>
<th>Non Responders</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=124 (28%)</td>
<td>N=319 (72%)</td>
<td></td>
</tr>
<tr>
<td>Mother age at birth (yrs)</td>
<td>Mean 34</td>
<td>Mean 31</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Maternal education (yrs)</td>
<td>Mean 15</td>
<td>Mean 14</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>White non-Hispanic</td>
<td>%</td>
<td>%</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>White Hispanic</td>
<td>82</td>
<td>51</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Males</td>
<td>64</td>
<td>54</td>
<td>NS</td>
</tr>
<tr>
<td>1997 birth year</td>
<td>04</td>
<td>12</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>2002 birth year</td>
<td>27</td>
<td>14</td>
<td>P&lt;0.01</td>
</tr>
</tbody>
</table>
Procedures for Enrollment

- Interested family contacts project and is screened for study eligibility

- Eligible families participate in a telephone screening using either the M-CHAT or the SCQ (depending upon child’s age)

- All families whose child screens positively for risk of ASD are invited for a full evaluation

- A randomly selected sample of 2/3 of all families whose child screens negatively is invited for a full evaluation
## Characteristics of Participants in Screening (n=124)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age of child Range</td>
<td>73 months</td>
</tr>
<tr>
<td></td>
<td>31 - 142</td>
</tr>
<tr>
<td>Gender</td>
<td>65% male</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>70%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8%</td>
</tr>
<tr>
<td>African-American</td>
<td>5%</td>
</tr>
<tr>
<td>Biracial/Other</td>
<td>17%</td>
</tr>
<tr>
<td>Mother’s age at birth of child</td>
<td>34 years, 3 months</td>
</tr>
<tr>
<td>Mother’s education</td>
<td></td>
</tr>
<tr>
<td>&lt; High School:</td>
<td>3%</td>
</tr>
<tr>
<td>High School:</td>
<td>14%</td>
</tr>
<tr>
<td>College:</td>
<td>60%</td>
</tr>
<tr>
<td>Post-Grad:</td>
<td>23%</td>
</tr>
</tbody>
</table>
### Participant Flow: Screening $\rightarrow$ Evaluation (n=124)

<table>
<thead>
<tr>
<th></th>
<th>Screened Positive (n=53)</th>
<th>Screened Negative (n=71)</th>
<th>Total (n=124)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invited to full evaluation</td>
<td>53 (100%)</td>
<td>47 (66%)</td>
<td>100 (81%)</td>
</tr>
<tr>
<td>Consented to participate</td>
<td>45 (85%)</td>
<td>33 (70%)</td>
<td>78 (78%)</td>
</tr>
<tr>
<td>Completed evaluation</td>
<td>45 (85%)</td>
<td>32 (68%)</td>
<td>77 (77%)</td>
</tr>
</tbody>
</table>
## Evaluation Battery

<table>
<thead>
<tr>
<th>Category</th>
<th>Measurement Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developmental functioning</td>
<td>Mullen Scales of Early Learning</td>
</tr>
<tr>
<td></td>
<td>Differential Ability Scales</td>
</tr>
<tr>
<td></td>
<td>Vineland Scales of Adaptive Behavior</td>
</tr>
<tr>
<td>Autism symptoms</td>
<td>Autism Diagnostic Observation Schedule</td>
</tr>
<tr>
<td></td>
<td>Autism Diagnostic Interview-Revised</td>
</tr>
<tr>
<td>Temperament and behavior</td>
<td>Carey Scales of Temperament</td>
</tr>
<tr>
<td></td>
<td>Developmental Behavior Checklist</td>
</tr>
<tr>
<td>Executive function</td>
<td>Behavior Rating Inventory of Executive Function (Preschool version)</td>
</tr>
<tr>
<td>Sensory issues</td>
<td>Short Sensory Profile</td>
</tr>
</tbody>
</table>
A *developmental perspective* is applied in considering symptom endorsement. Only impairments in social and communicative behavior that are below expectations for developmental functioning are considered as relevant symptoms.

Two experienced clinicians participated in the child’s evaluation in more than 50% of cases.

Clinicians *independently* reviewed all available data and completed a symptom checklist based on DSM-IV-TR, with each symptom referenced to specific ADOS and ADI-R items.

Clinicians determined a final clinical diagnosis based on case definitions.
Reliability Procedures for Diagnoses

- Interobserver reliability conducted on more than 40% of ADOS administrations and 20% of ADI interviews

- Kappa coefficients on individual DSM-IV symptoms ranged from 0.40 ("play with peers appropriate to developmental level") to 0.82 ("stereotyped and repetitive language"). Ten of 12 symptoms had kappa coefficients above 0.70

- Agreement on diagnostic status was assessed on 44 cases, kappa = 0.70, p > .001

- Disagreements (n=6) resolved through consensus discussion with 3 or more clinicians
Case Definitions

Autistic Disorder =

- (1) child obtains a score at or above the spectrum cutoff on either the ADOS or ADI/R

  \textit{AND}

- (2) an experienced clinician conducts a thorough case review and endorses 6 or more DSM-IV-TR symptoms (at least 2 social, 1 communication, and 1 restricted behavior)

  \textit{AND}

- (3) the child’s social and communicative impairments were evident prior to age 3
Case Definitions

Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS)

(1) child obtains a score at or above the spectrum cutoff on either the ADOS or ADI/R

AND

(2) an experienced clinician conducts a thorough case review and endorses fewer than 6 DSM-IV-TR symptoms, with
- At least 1, but not more than 2 social symptoms
- At least 1 communication symptom
- At least 1 restricted symptom

AND

(3) Impairments were evident prior to age 3.
Data Analysis

All prevalence estimates are weighted to account for the sampling fraction (i.e., 2/3) used to select screen negative children.

95% confidence intervals are calculated, taking differential sampling into account.
## Findings from Evaluations

<table>
<thead>
<tr>
<th>Disorder</th>
<th>N</th>
<th>Weighted % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autistic Disorder</td>
<td>6</td>
<td>6.5 (1.0, 12.0)</td>
</tr>
<tr>
<td>PDD-NOS</td>
<td>10</td>
<td>11.8 (4.6, 19.0)</td>
</tr>
<tr>
<td>Total ASD</td>
<td>16</td>
<td>18.3 (9.7, 26.9)</td>
</tr>
</tbody>
</table>
Prevalence of ASD in Children with Down syndrome

<table>
<thead>
<tr>
<th>Enrolled children with Down Syndrome</th>
<th>18.3% (9.7%, 26.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated minimum prevalence of Down syndrome + ASD *</td>
<td>4.1% (2.3%, 6.0%)</td>
</tr>
<tr>
<td>8 yr old children in 2 Denver metro counties (ADDM)</td>
<td>0.6% (0.5%, 0.8%)</td>
</tr>
</tbody>
</table>

*(Denominator is total birth cohort of DS; assumes children we identified as having ASD comprised all dual-diagnosis children in the cohort.)*
Prevalence of ASD in Children with Down syndrome

Minimum estimate is 7 times the prevalence in general population of 8 year old children.
Aim 2

Evaluate the appropriateness of screening tools for autism (M-CHAT, SCQ) with children with Down syndrome by examining sensitivity and specificity.
Results of Screening

M-CHAT
(N=85)

--
(Not at risk)
(N=46)
54%

+
(At risk for ASD)
(N=39)
46%

SCQ
(N = 39)

--
(Not at risk)
(N=25)
64%

+
(At risk for ASD)
(N=14)
36%
## Comparison of all Screening Results and Evaluation Results

<table>
<thead>
<tr>
<th>Risk Identified in Screening</th>
<th>Clinical Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>YES:</strong> ASD (N=45)</td>
<td><strong>NO:</strong> ASD</td>
</tr>
<tr>
<td>YES: ASD</td>
<td>Wt% = 31.1%</td>
</tr>
<tr>
<td>Sensitivity: 82.4%</td>
<td>Wt% = 68.9%</td>
</tr>
<tr>
<td>(False positive)</td>
<td></td>
</tr>
<tr>
<td>NO: ASD</td>
<td>Wt% = 6.2%</td>
</tr>
<tr>
<td>(False negative)</td>
<td>Wt% = 93.8%</td>
</tr>
</tbody>
</table>

N=77
Summary for each Tool

<table>
<thead>
<tr>
<th></th>
<th>M-CHAT</th>
<th>SCQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>Specificity</td>
<td>57%</td>
<td>67%</td>
</tr>
<tr>
<td>False Positive</td>
<td>74%</td>
<td>55%</td>
</tr>
<tr>
<td>False Negative</td>
<td>8%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Both tests over-identified children as at risk for autism
Recommendations Regarding use of Screening Tools for Children with Down syndrome

Develop different scoring algorithms which capture the essential aspects of autism that are qualitatively distinct from developmental delays in social and communicative behavior, such as:

– Sharing affect
– Responding and initiating joint attention
– Imitation
– Social orienting
– Using nonverbal behaviors to demonstrate communicative intention
Aim 3

Examine child characteristics associated with social and communication impairments in children with Down syndrome.

- Cognitive functioning
- Problem behavior
- Executive functioning
Measures

- Cognitive/Developmental functioning
  - Mullen Scales of Early Learning
  - Differential Ability Scales

- Problem Behavior
  - Developmental Behavior Checklist

- Executive function
  - Behavior Rating Inventory of Executive Function (BRIEF)
Is the co-occurrence of ASD in Down syndrome related to cognitive functioning?

Cognitive impairment by diagnostic group (n=65)

<table>
<thead>
<tr>
<th>Weighted % of participants</th>
<th>Down syndrome</th>
<th>Down syndrome+ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild 70-55</td>
<td>48.1</td>
<td>14.3</td>
</tr>
<tr>
<td>Moderate 54-40</td>
<td>30.8</td>
<td>21.4</td>
</tr>
<tr>
<td>Severe &lt;40</td>
<td>21.2</td>
<td>64.3</td>
</tr>
</tbody>
</table>

p=<.007
Findings

Children with Down syndrome and ASD had significantly lower developmental quotients than those without co-occurring ASD

Mean for the Down syndrome+ASD group = 37
Mean for Down syndrome without ASD = 50
(p = <.001)
Findings

However, not all children with severe cognitive impairments presented with autism symptoms and

Not all children with autism symptoms were severely impaired
Is the co-occurrence related to specific forms of problem behavior?

Developmental Behavior Checklist (n = 64)

- Down syndrome (n=49)
- Down syndrome+ASD (n=16)


Weighted Mean

- Disruptive: p = .037
- Self-Abs.: p = .001

30
Findings

- Children with Down syndrome and ASD were reported to exhibit more self-absorbed behaviors and poorer social relating than other children with Down syndrome.

- There were no differences in disruptive or externalizing behaviors.

- Information concerning self-absorbed behaviors could be useful in screening.
Is the co-occurrence related to problems in executive function?

**Domain Scores on the BRIEF by Diagnostic Group (n = 58)**

- **Inhibition**: 
  - Down syndrome (n=42)
  - Down syndrome+ASD (n=16)
  - p < .01

- **Shifting**: 
  - Down syndrome (n=42)
  - Down syndrome+ASD (n=16)
  - p < .01

- **Emot Control**: 
  - Down syndrome (n=42)
  - Down syndrome+ASD (n=16)
  - p < .01

- **Flexibility**: 
  - Down syndrome (n=42)
  - Down syndrome+ASD (n=16)
  - p < .01

- **Metacognition**: 
  - Down syndrome (n=42)
  - Down syndrome+ASD (n=16)

- **Working Memory**: 
  - Down syndrome (n=42)
  - Down syndrome+ASD (n=16)

- **Planning/Organ.**: 
  - Down syndrome (n=42)
  - Down syndrome+ASD (n=16)
Findings

Children with Down syndrome and ASD were more impaired in shifting attention, maintaining emotional control, and being flexible in problem-solving than other children with Down syndrome.

There were no differences in working memory, planning, or inhibition, which have been previously demonstrated to be areas of relative difficulty for persons with Down syndrome.

Differences in executive function may be related to overall cognitive ability or may be indicative of more extensive frontal lobe impairment in children with Down syndrome and ASD.

Future studies that include a larger sample and more comprehensive measures of executive functioning are needed to address this question effectively.
Video examples
In Conclusion

These are the first epidemiologic studies demonstrating an increased rate of ASD in children with Down syndrome.

Clinical application of DSM IV criteria remains important in making an ASD diagnosis in people with Down syndrome with critical review of the information provided by the ADI-R and ADOS.

There appear to be group differences in cognitive functioning, overall problem behavior, self-absorbed behaviors, cognitive flexibility and emotional control between children with Down syndrome who do and not have ASD.

The behavioral phenotype of co-occurring Down syndrome and ASD may be unique and screening procedures need to be refined to emphasize areas of relative difference.
Acknowledgement

Funding from AUCD-RTOI: RTOI 2005-1/2-07 and RTOI 2005-1/2-06
This project is funded wholly or in part by the Centers for Disease Control and Prevention (CDC), National Center on Birth Defects and Developmental Disabilities (NCBDDDD) under Cooperative Agreement U59/CCU321285 to the Association of University Centers on Disabilities (AUCD). The content of this material does not necessarily reflect the views and policies of CDC, NCBDDDD. No official support or endorsement by the CDC, NCBDDDD is intended nor should be inferred.
Colorado Co-investigators

• University of Colorado Denver
  – Carolyn DiGuiseppi, M.D., Ph.D.
  – Nancy Raitano Lee, Ph.D.
  – Amy Philofsky, Ph.D.
  – Audrey Blakeley-Smith, Ph.D.
  – Katy Ridge
  – Kristina Kaperich, MPH
  – Jonathan M. Davis

• Colorado Department of Public Health and Environment
  • - Lisa Miller, MD
  • - Margaret Ruttenber

• Colorado State University
  • Deborah Fidler, Ph.D.
  • Ashley Cole

• Mile High Down Syndrome Association
  • Sarah Hartway
  • Linda Barth
Medical and Behavioral Characteristics of Children with Down Syndrome in New York State

Susan L. Hyman
Edwin van Wijngaarden
Caroline I. Magyar
Stephen B. Sulkes
Emily Kuschner

Nancy Roizen
Charlotte Druschel
Elaine Hill
Sharon Nagel
Lisa Rodgers
Alison Diehl
Specific Aims

1. To determine the prevalence of ASD in children with Down syndrome in a large, diverse population

2. Examine the medical and behavioral characteristics of children with Down syndrome with/without ASD

3. Evaluate the methods used to screen for and diagnose ASD in children with Down syndrome
Recruitment Strategy

• New York Congenital Malformation Registry
  – One of the largest Congenital Malformation Registries in the US
  – Reporting required by regulation for chromosomal or persistent metabolic disorder or congenital structural defect
  – Restricted recruitment to NY State outside of NY City

• Clinical Services for Children with Down Syndrome at the University of Rochester

• Family Support Organizations in New York State
1453 Children with DS (age 3-13 yrs) born and living in NYS identified by NCMR

Level 1: Medical History, MCHAT, SCQ (n=438) + PDD-MRS (n= 382)

Level 2: ADI-R, Vineland, RBS-R (n=217) Screen positive and next screen negative

Level 3: ADOS, Leiter, EOWPVT, PPVT (n=76) ADI-R positive and ADI-R negative
## Demographics of Participants

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male 52.7%</td>
</tr>
<tr>
<td>Age at Enrollment</td>
<td>9 years, 63% ages 3-10 yrs</td>
</tr>
<tr>
<td>Race</td>
<td>92.5% Caucasian, 3.9% African American</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>4.8% Hispanic</td>
</tr>
<tr>
<td>Parental Education</td>
<td>72.2% College or more, 10.5% High School or less</td>
</tr>
<tr>
<td>Mother’s Age at Birth</td>
<td>33.5 years</td>
</tr>
</tbody>
</table>
### Level 1: Medical History

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>% Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Disease</td>
<td>55.2</td>
</tr>
<tr>
<td>Vision Problems</td>
<td>56.8</td>
</tr>
<tr>
<td>Hearing Problems</td>
<td>39.3</td>
</tr>
<tr>
<td>Thyroid Disease</td>
<td>27.1</td>
</tr>
<tr>
<td>Celiac Disease</td>
<td>5.2</td>
</tr>
<tr>
<td>Alopecia</td>
<td>4.8</td>
</tr>
<tr>
<td>Seizures</td>
<td>6.8</td>
</tr>
<tr>
<td>Asthma/Reactive Airway Disease</td>
<td>31.8</td>
</tr>
</tbody>
</table>
Regression of Milestones and Down Syndrome

- Loss of language and other milestones on ADI-R (10.9% of 174)
  - 1/3 lost language alone, ½ lost other skills alone
  - 11/19 with loss of milestones had + ADI-R
- Loss of milestones is accompanied by history of medical illness
  - Seizures, heart surgery, leukemia
- Loss of language milestones is reported at a later age than that reported in ASD
  - Language 44 m (SD=19)
  - Other skills 27 m (SD=25)
Level 1: Screening Data Suggests that Symptoms of ASD are Common in DS

<table>
<thead>
<tr>
<th>Test</th>
<th>Total</th>
<th>Subjects 3 - 10 yrs</th>
<th>Subjects 10-14 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCHAT</td>
<td>48.0%</td>
<td>44.6%</td>
<td>53.9%</td>
</tr>
<tr>
<td>SCQ</td>
<td>29.7%</td>
<td>25%</td>
<td>37.6%</td>
</tr>
<tr>
<td>PDD-MRS</td>
<td>29.1%</td>
<td>27.9%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Any Screen</td>
<td>56.7%</td>
<td>51.7%</td>
<td>65.3%</td>
</tr>
</tbody>
</table>
Level 2: ADI-R Current vs. Diagnostic Algorithm

Note: Half of this sample are Screen Positive

<table>
<thead>
<tr>
<th></th>
<th>Total (n=216)</th>
<th>Subjects 3-10 yrs (n=137)</th>
<th>Subjects 10-14 yrs (n=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADI-R Diagnostic Algorithm</td>
<td>40.7%</td>
<td>35.8%</td>
<td>49.4%</td>
</tr>
<tr>
<td>ADI-R Current Algorithm</td>
<td>16.7%</td>
<td>19%</td>
<td>12.7%</td>
</tr>
</tbody>
</table>
Level 3: ADOS Positive Scores may Capture Symptoms not seen as ASD Previously

Note: Half had positive ADI-R

<table>
<thead>
<tr>
<th></th>
<th>Total (n=76)</th>
<th>Subjects 3-10 yrs (n=54)</th>
<th>Subjects 10-14 yrs (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADOS</strong></td>
<td>46.1%</td>
<td>40.7%</td>
<td>59.1%</td>
</tr>
<tr>
<td><strong>Consensus Clinical Diagnosis</strong></td>
<td>44.9%</td>
<td>41.8%</td>
<td>52.2%</td>
</tr>
</tbody>
</table>
Level 3: Sensitivity and Specificity

- ADI-R and ADOS were both positive in 23/76 cases
- Compared to Expert Clinical Diagnosis:
  - ADI-R (Dx): Sensitivity 73.5, Specificity 71.4
  - ADI-R (Current): Sensitivity 38.2, Specificity 90.5
  - ADOS: Sensitivity 88.2, Specificity 88.1
Interpretation of the Data

Sensitivity, Specificity, and Response Rate
Study Design

- Study entire target population
- Probability sampling
- Non-probability sampling
Example: SCQ Screening (1)

60 out of 200 children screened positive on SCQ: 30%

Sensitivity = 57% and specificity = 93% (using ADI-R as gold standard)
Example: SCQ Screening (2)

14 out of 60 children screening positive on SCQ do not have ASD
Example: SCQ Screening (3)

46 children screening negative on SCQ do have ASD
True prevalence: 92 of 200 children have ASD (46%)
Non-Response Bias

- Computing response rates

\[
\text{Response Rate} = \frac{\text{number of completions}}{\text{number in sample}}
\]

\[
\text{Response Rate} = \frac{\text{number of completions}}{\text{number in sample} - (\text{noneligible} + \text{nonreachable})}
\]

- Non-response bias
  - Response rate
  - Factors that differ between non-responders vs. responders
  - Association of these factors with ASD
However, no conclusive evidence in our data that education, race or ethnicity is related to ASD diagnosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Consents (%)</th>
<th>Refusals (%)</th>
<th>Not Eligible/Located %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mother Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean, SD)$^a$</td>
<td>33.3 (6.2)</td>
<td>32.7 (6.7)</td>
<td>31.0 (7.6)</td>
</tr>
<tr>
<td>Education (years)$^b$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>4.5</td>
<td>12.8</td>
<td>19.3</td>
</tr>
<tr>
<td>12</td>
<td>24.2</td>
<td>33.2</td>
<td>30.4</td>
</tr>
<tr>
<td>13-15</td>
<td>24.2</td>
<td>24.5</td>
<td>21.4</td>
</tr>
<tr>
<td>16+</td>
<td>45.5</td>
<td>27.1</td>
<td>25.5</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.7</td>
<td>2.4</td>
<td>3.4</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>4.3</td>
<td>9.3</td>
<td>18.0</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>95.7</td>
<td>90.7</td>
<td>82.0</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>95.2</td>
<td>89.6</td>
<td>78.9</td>
</tr>
<tr>
<td>Black</td>
<td>2.6</td>
<td>7.5</td>
<td>15.2</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>1.2</td>
<td>2.1</td>
<td>5.0</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>1.0</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Father Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father’s Age (mean, SD)$^a$</td>
<td>35.0 (6.3)</td>
<td>34.8 (7.2)</td>
<td>32.9 (7.1)</td>
</tr>
<tr>
<td>Father’s Education (years)$^b$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>3.8</td>
<td>8.0</td>
<td>10.2</td>
</tr>
<tr>
<td>12</td>
<td>27.3</td>
<td>33.3</td>
<td>26.4</td>
</tr>
<tr>
<td>13-15</td>
<td>24.2</td>
<td>18.3</td>
<td>15.8</td>
</tr>
<tr>
<td>16+</td>
<td>37.6</td>
<td>27.9</td>
<td>27.6</td>
</tr>
<tr>
<td>Unknown</td>
<td>7.2</td>
<td>12.6</td>
<td>19.9</td>
</tr>
</tbody>
</table>
**Research Question**

**Target Population**

Generalizability fairly secure:

Same ASD prevalence exists among children with DS from highly educated, white U.S. families residing in New York State

Generalizability less secure

- Less educated, other racial or ethnic groups
- Other states, countries
- Future populations

**Truth in Universe**

**Infer**

**Actual Plan**

**Study Subjects**

Prevalence of ASD observed in a sample of 438 children with DS born and residing in New York State

**Findings in the Study**
Summary and Conclusions

• Children with Down Syndrome are at high risk for symptoms of autism.
• Expert clinical assessment with attention to the confounds of developmental level and sensory impairments is necessary for children with Down Syndrome.
• Screening for autism in children with Down Syndrome should not be limited to 18 and 24 months as recommended by the AAP.
• Further research is needed to examine diagnostic methods for ASD in children with Intellectual Disabilities.
This project is funded wholly or in part by the Centers for Disease Control and Prevention (CDC), National Center on Birth Defects and Developmental Disabilities (NCBDDD) under Cooperative Agreement U59/CCU321285 to the Association of University Centers on Disabilities (AUCD). The content of this material does not necessarily reflect the views and policies of CDC, NCBDDD. No official support or endorsement by the CDC, NCBDDD is intended nor should be inferred.
And our thanks to the families and children throughout New York who shared their time and experience