

Optimal Outcome in Children with Autism

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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.

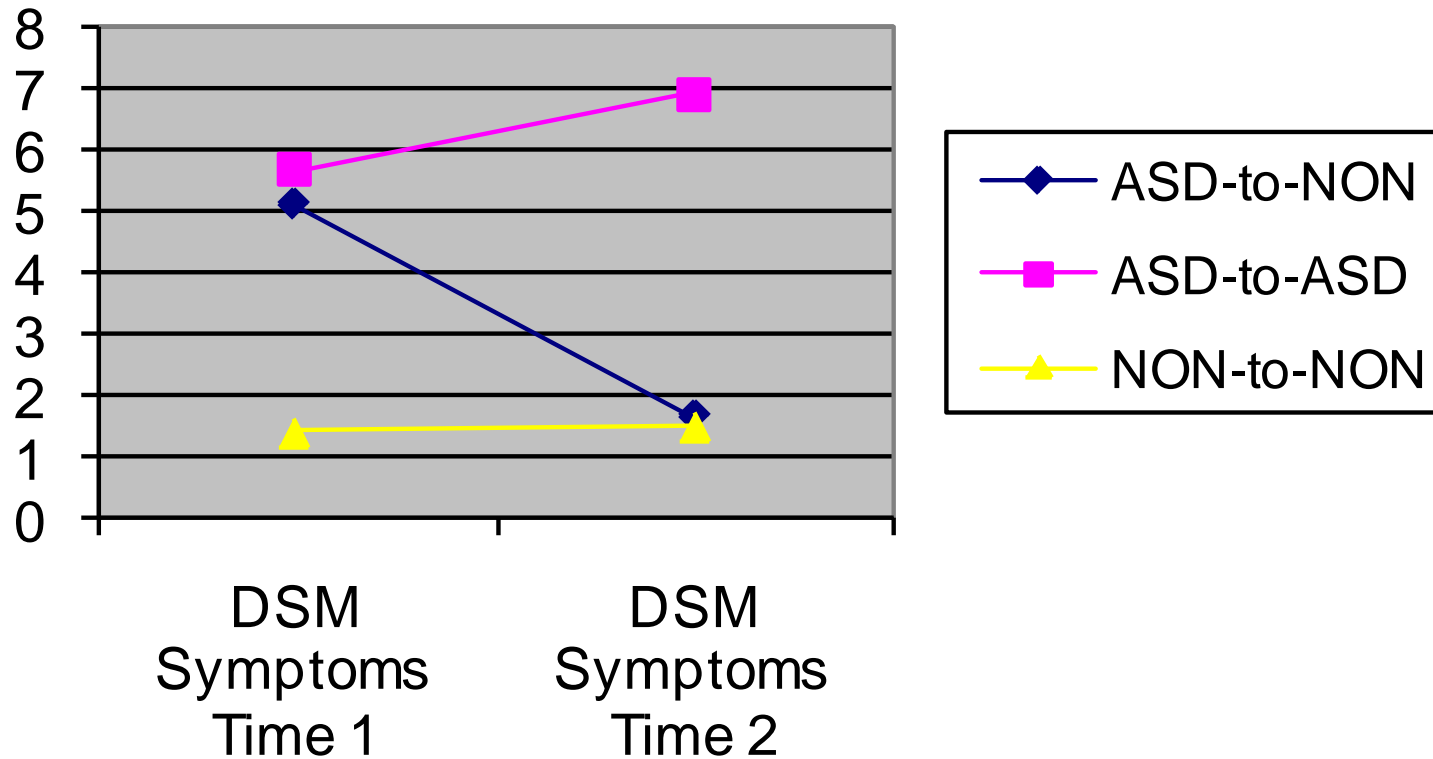
Purpose of our “optimal outcome” studies

- 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

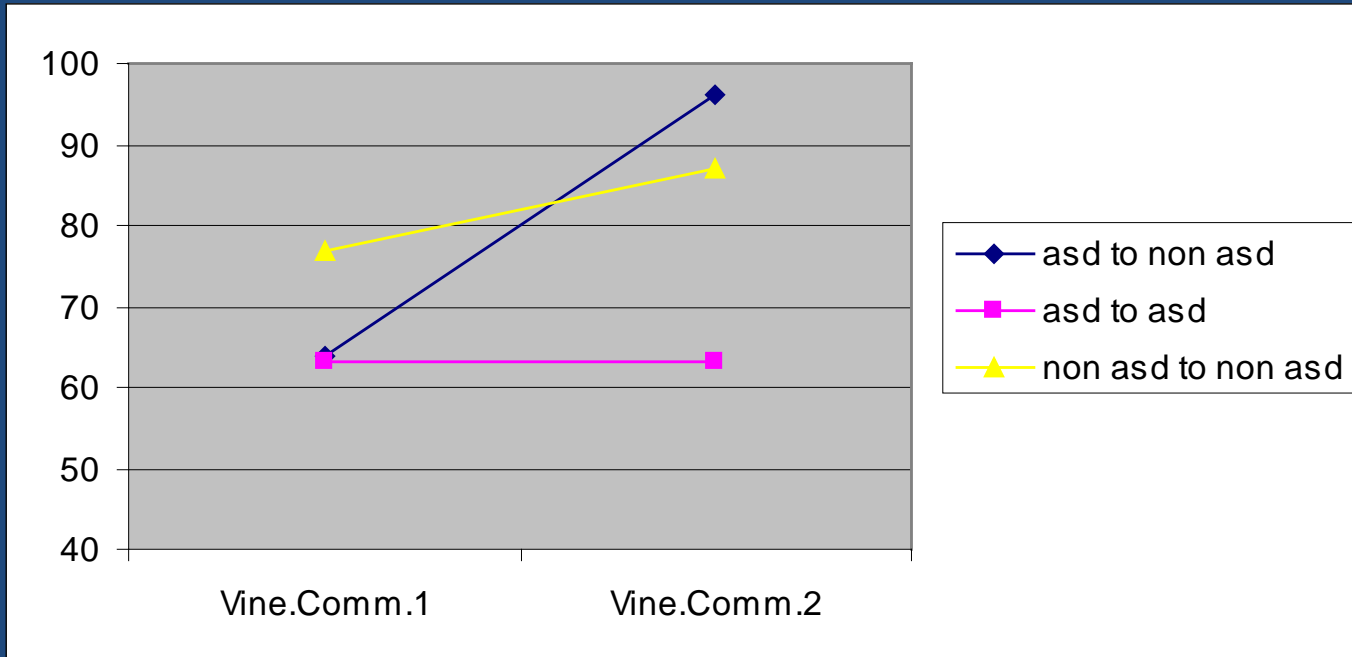
Background

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

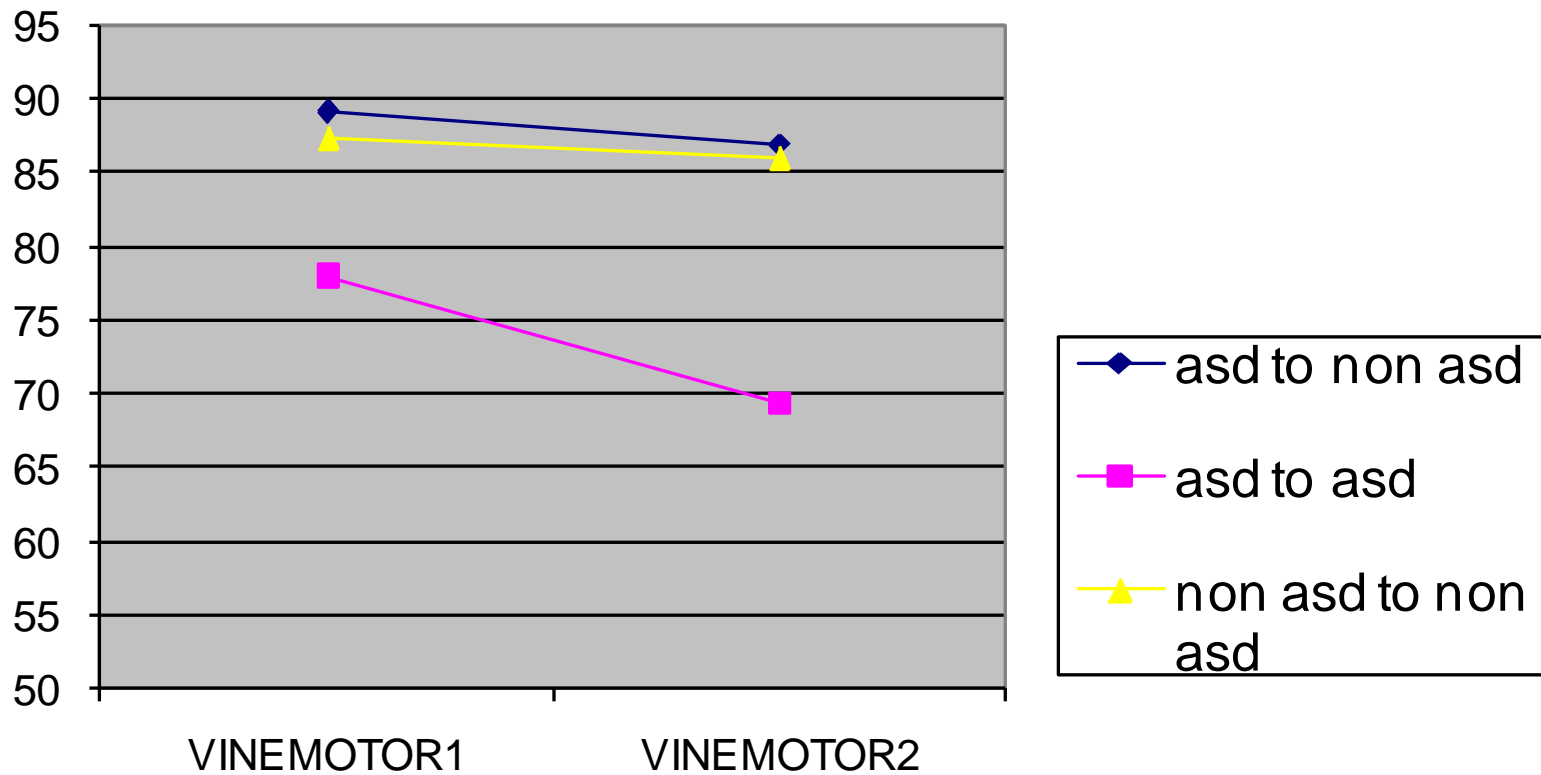
DSM-Symptoms



Vineland Communication



Vineland Motor



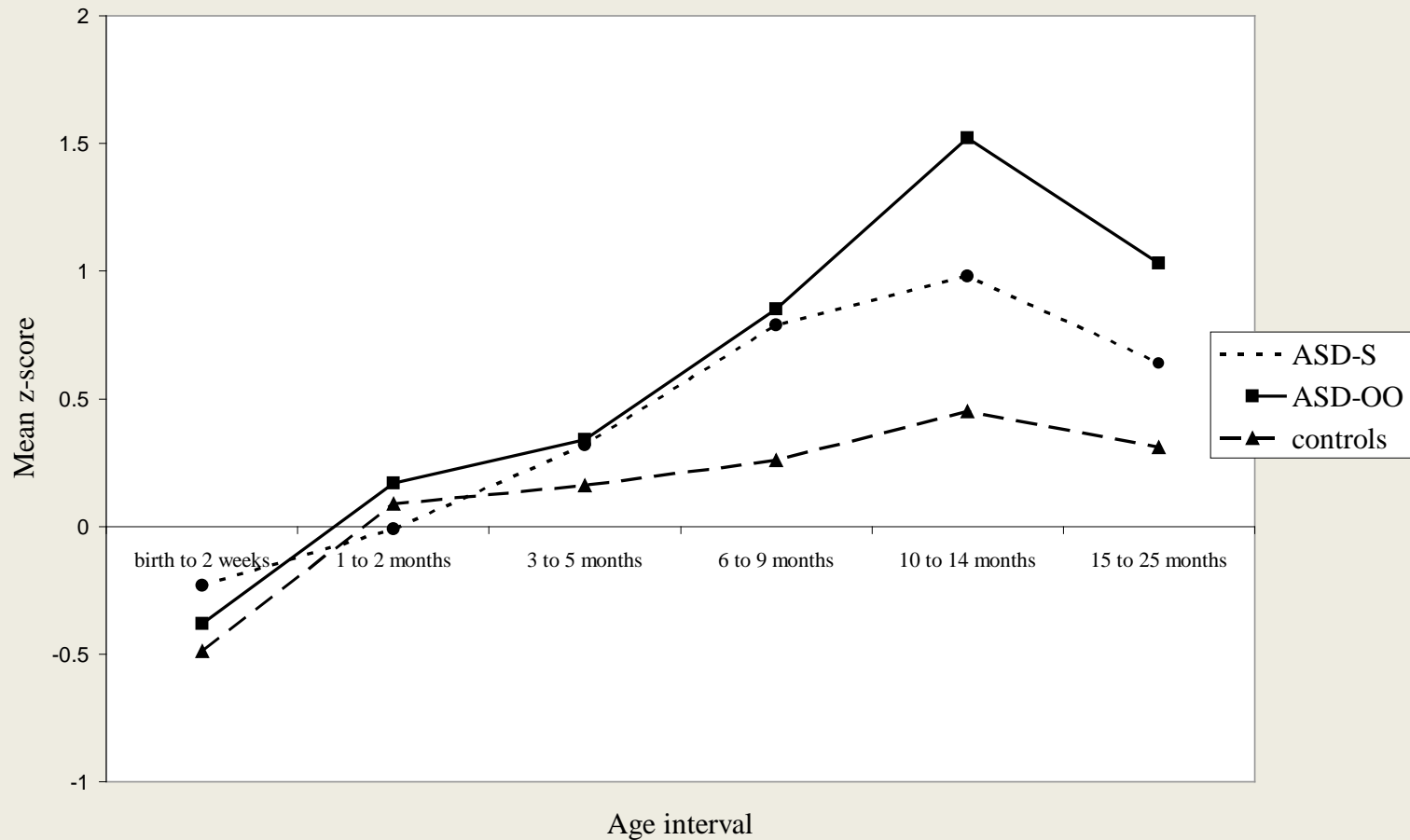
Can Head Circumference predict?

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

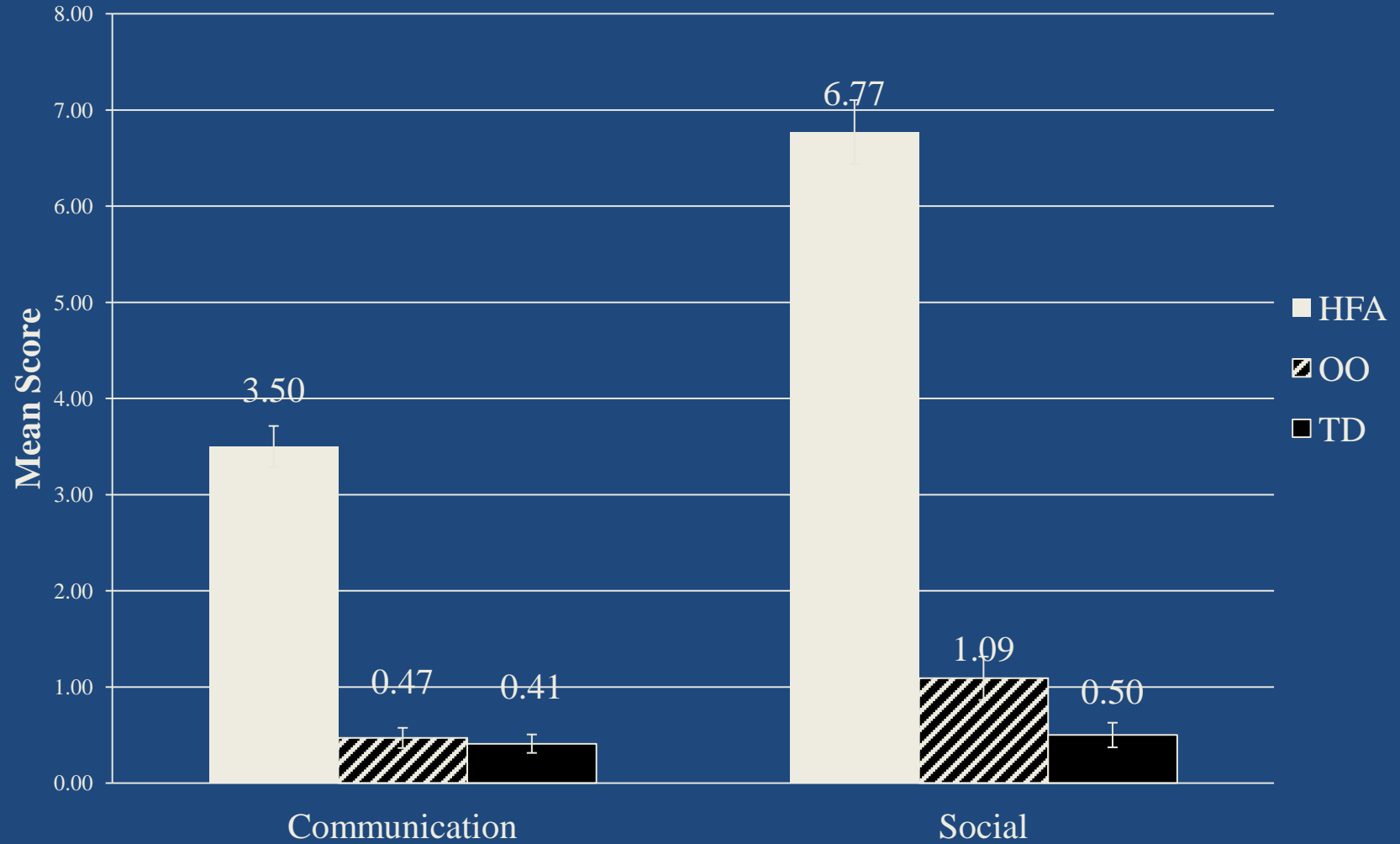
Domains of Data Collection

- 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) | <i>p</i> |
|-------------|-------------------------|-------------------------|-------------------------|------------|
| 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 | <i>F</i> | <i>p</i> |
|-----------------------------|-------------------------|-------------------------|-----------------|-----------------|
| 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 | <i>p</i> |
|---------------------|--------------------------------|--------------------------------|--------------------------------|-----------------|
| 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 | <i>p</i> |
|---------------------------|--|--|---|--------------------------------|
| 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)

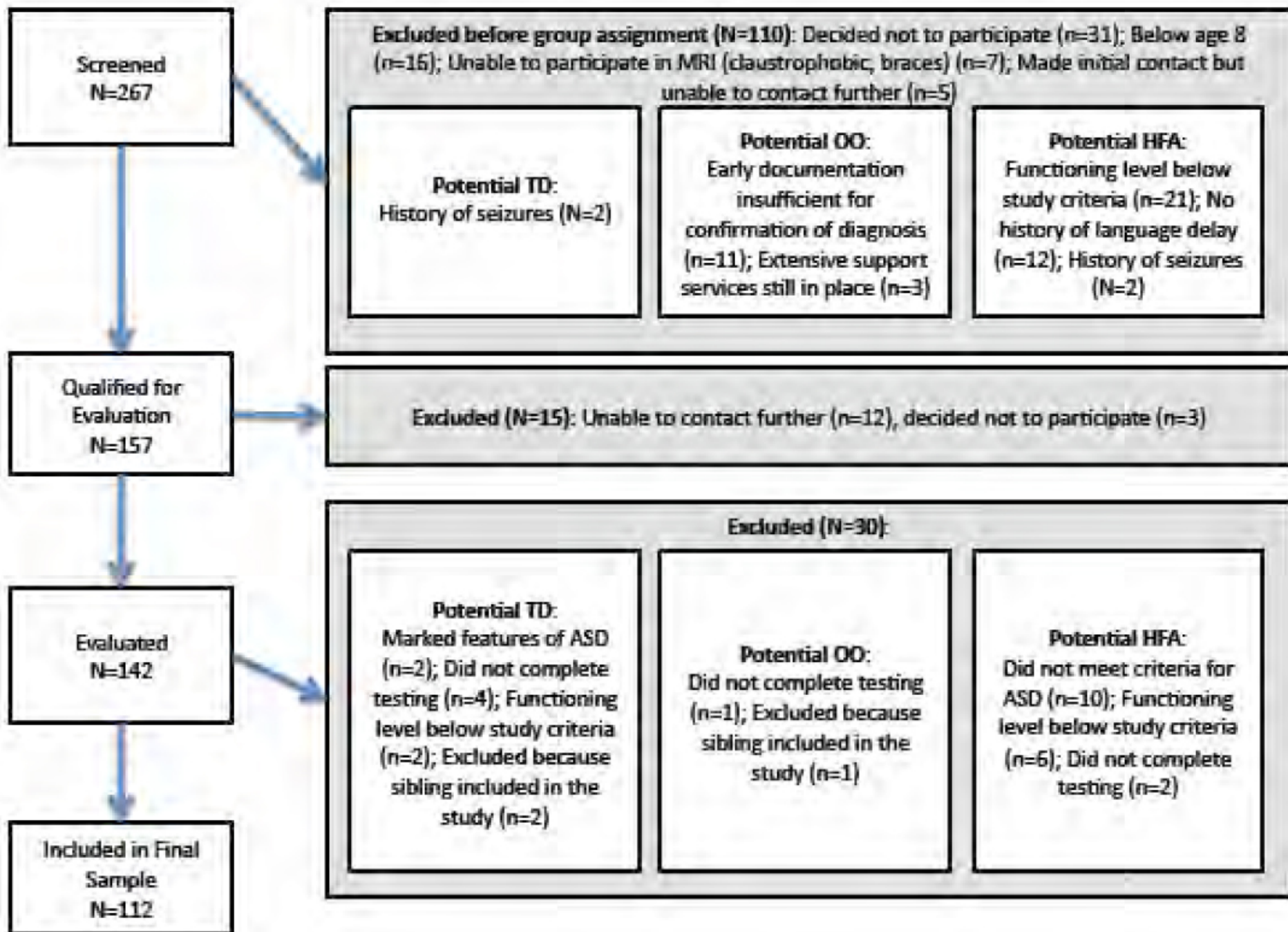
Future Directions

- 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



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