Comorbid Autism Spectrum Disorder (ASD) and Serious Mental Illness (SMI)

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Alcobra	X			
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Neuren	X			
Roche	X			
Seaside Therapeutics	X			
SyneuRX International	X			

Objectives

At the conclusion of this webinar the participant should be able to:

- Discuss DSM-5 criteria for and the prevalence of Autism Spectrum Disorder (ASD)
- Describe the prevalence of Psychiatric Disorders in individuals on the Autism Spectrum Disorder (ASD)
- Have a frame for differentiating between whether an individual's functional impairment stems from their mental illness or from their ASD
- Describe Current Evidence Based Interventions

Off-Label Use

Food and Drug Administration (FDA-US) approved treatments :

- Risperidone - children (5-16 years) with autism, use for irritability
- Aripiprazole - children (6-17 years) with autism, use for irritability

All other interventions constitute off-label use

DSM-5 Changes in Criteria for Autism Spectrum Disorders 299.00

- New Diagnosis: Autism Spectrum Disorder
  - Includes, and eliminates the distinctions between:
    - Autistic Disorder (Autism)
    - Asperger's Disorder (Asperger Syndrome)
    - Childhood Disintegrative Disorder
    - Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS)
  - "PDD" not used
- Rett's Disorder removed (would be specified under "Associated with known medical or genetic condition")

DSM-5 Autism Spectrum Disorder

- Criteria for ASD
  - Two clinical domains (instead of the 3 in DMS-IV)
    - A-Deficits in social communication and social interaction (blends social with communication)
    - B-Restricted, repetitive patterns of behavior (includes insistence on sameness)
  - Symptoms must be present in early childhood
  - Symptoms must impair functioning

Diversity in Autism Spectrum Disorders

- Intellectual level
- Communication level
- Behavioral level

PREVALENCE

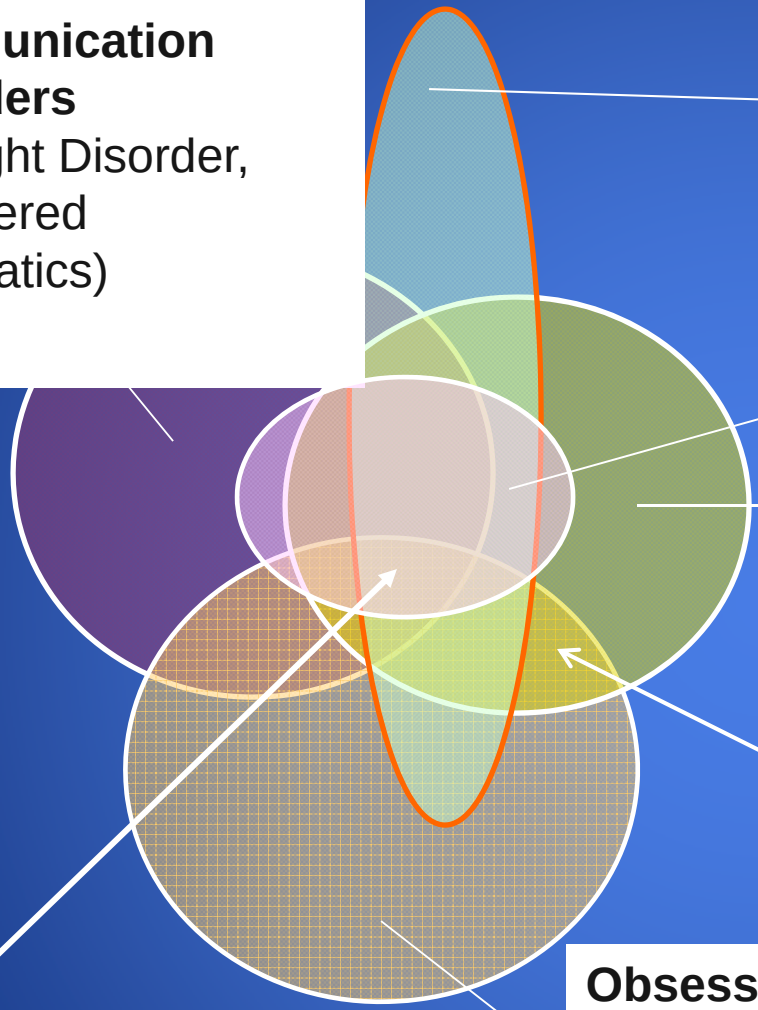
1975: 1/5000
1985: 1/2500
1995: 1/500
2000: 1/150
2004: 1/125
2006: 1/110
2008: 1/88
2010: 1/68

Prevalence and Extent of the Challenge

- Highly heritable yet etiology is elusive in 80% of cases
- **75%** of children with an ASD require treatment for emotional, physical or behavioral problems
- One of the most challenging disorders for families and providers

Psychiatric Comorbidities

Communication Disorders
(Thought Disorder, Disordered Pragmatics)



Attention Deficit Hyperactivity
(Executive Dysfunction, Hyperactivity, Impulsivity, Inattention)

Mood Disorders
(Mood Dysregulation, Anxiety, Depression, Mania)

Anxiety Disorders
(Social Interaction/"Empathy": ?Shyness/Social Phobia, Disinterest/Schizoid, "Hostile Intent"/Schizotypal)

Asperger's

Autism

Obsessive Compulsive Disorder
(Restricted interests
Rigid behavior
Stereotypic behavior
Compulsions)

What Challenges Does the Community ASD Population Have?

(Lecavalier, 2006)

- Easily Frustrated (60%)
- Inattention (50%)
- Hyperactivity (40%)
- Temper tantrums (30%)
- Irritability (20%)
- Fearful/Anxious (13%)
- Harming self (11%)
- Destroying property (11%)
- Physical fighting (5%)

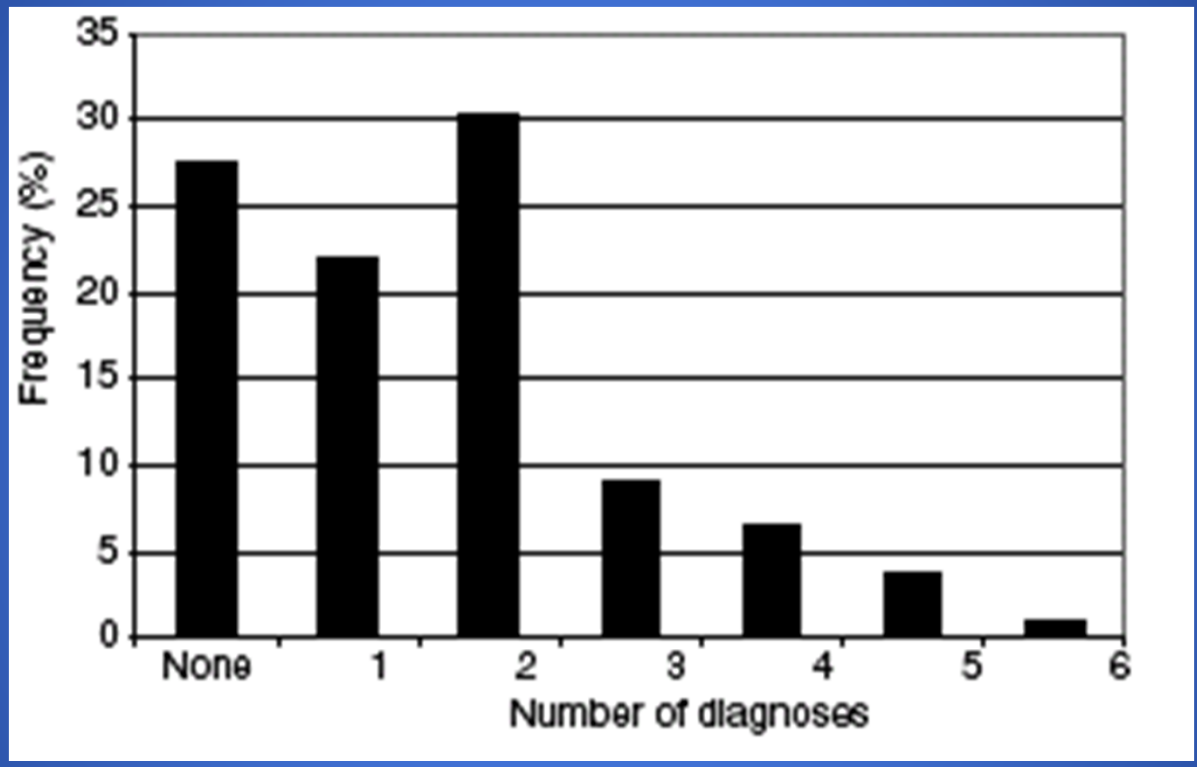
Most Common Chief Complaint on Inpatient Admission

- Aggression 28%
- Self Injurious Behavior 23%
- Property Destruction 17%
- Tantrums 16%
- Decreased Functioning 8%
- Sexualized Behavior 4%
- Elopement 4%

Rates of Psychiatric Disorders in Samples of Individuals with Autism Spectrum Disorders

- Rates vary widely across studies- diagnostic overshadowing
- Sample selection
- Methods for case ascertainment
  - Chart reviews or counting from existing databases
  - Informant based
  - Direct patient evaluation
- Critical source of problems relate to symptom identification- operationalizing
- Rating Scales Validated in ASD population

Comorbid Psychiatric Disorders in Autistic Children



Frequency of the number of comorbid lifetime DMS-IV psychiatric diagnoses per autistic child

Top 3: Specific Phobia (43%), OCD (37%), and ADHD (31%)

Leyfer O, Folstein S et al. *J Autism Dev Disord* (2006) 36:849-861

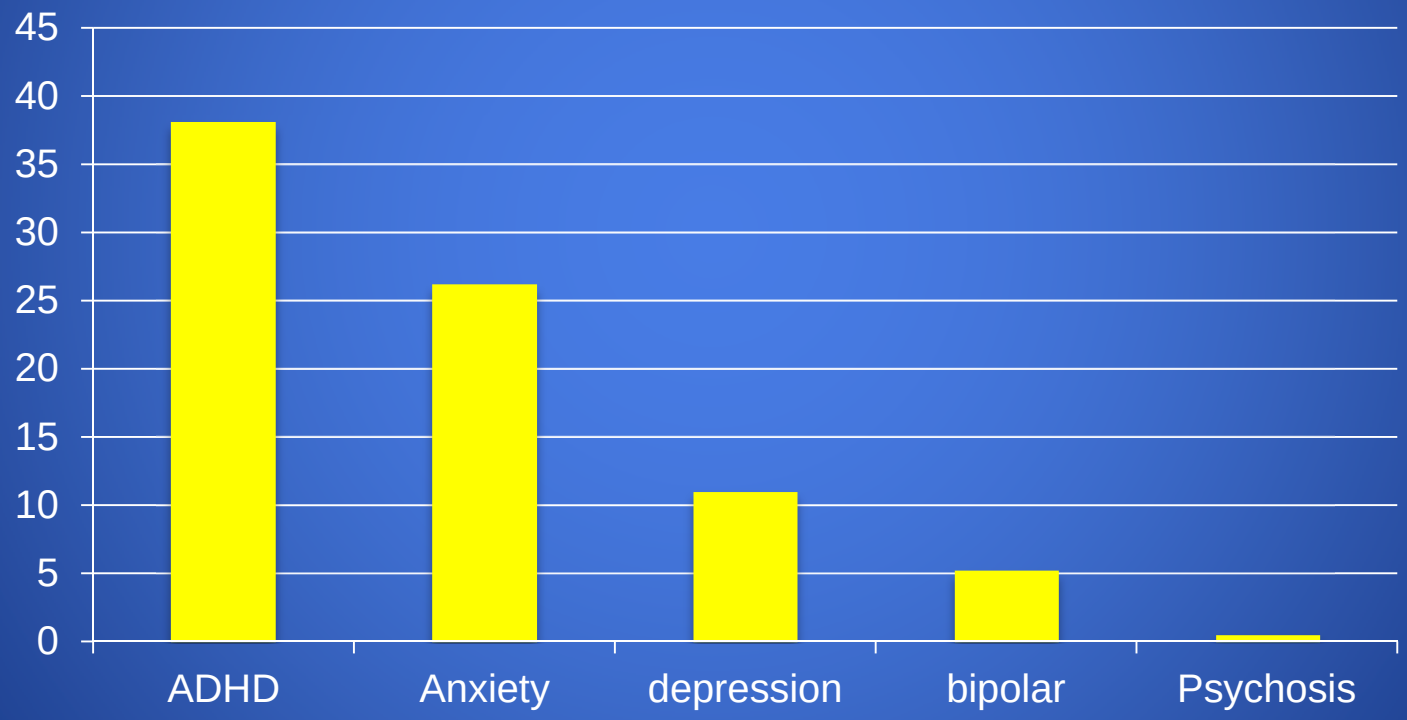
Comorbid Psychiatric Diagnoses Given by Community Providers Per Parent Survey

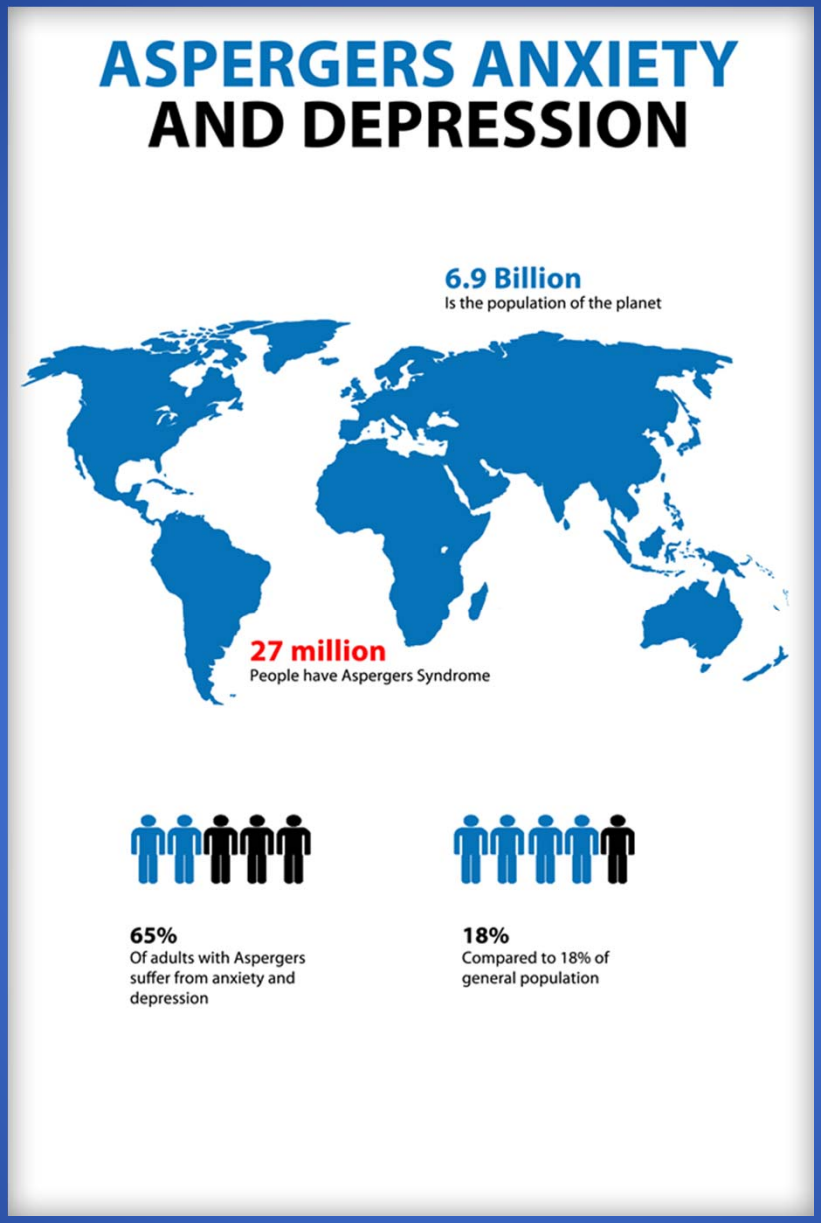
(Rosenberg et al, 2011)

- National on line registry established in 2006 - “Interactive Autism Network”
- Parent report
- 4,343 participants between ages 5-18 years
- Allowed for the assessment of community assigned comorbid diagnoses in ASD (rather than research assigned)
- Examined factors associated with comorbidity (e.g. age, gender type and severity of ASD)

Comorbid Psychiatric Diagnoses Given by Community Providers Per Parent Survey

(Rosenberg et al, 2011)





http://www.aspergerstestsite.com/714/asperger-anxiety/#.UxeAIs70E4c

Signs of Depression for ASD

- Deviation of autistic symptoms from baseline
  - Intensification or decrease
- Atypical affective changes
  - Increased aggression
  - Increased irritability
  - Increased agitation
  - Labile moods
  - Preoccupation with themes of death

ASD and Bipolar Disorder

- 27% (14/52) of youth with ASD also had BD or 12% of all children in the overall sample who had BD (Wozniak et al, 1997).
- Youth with ASD +family history of BD compared to those without a FH of BD had extremes of affect, cyclicity, intense obsessive interests, neurovegetative symptoms, and regression (Herzberg, 1996;Delong, 1994)

ASD and Bipolar Disorder

- Symptoms of Bipolar disorder may be masked by symptoms associated with ASD
- Baseline behaviors may become more intense or exaggerated during manic or depressive episodes
- The key is to look for a distinct change from baseline and for episodes (Frazier et al, 2002)

Autistic Features in Childhood-Onset Schizophrenia (COS)

- Up to 55% of COS patients have prepsychotic developmental disorders with similarities to autism
  - Language delays
  - Motor development abnormalities (including transient motor stereotypies)
  - Deficits in communication and social relatedness
- NIMH study of COS – 28% have comorbid COS and Autism Spectrum Disorder (ASD)

Diagnostic Confusion – Where Does it Come from?

Autism ↔ Schizophrenia

Impairment in nonverbal communication ↔ Social withdrawal

Lack of social or emotional reciprocity ↔ Affective Flattening

Stereotyped use of language ↔ Disorganized speech

Lack of varied, spontaneous play ↔ Disorganized behavior

Abnormal preoccupation with stereotyped interests ↔ Delusions

Stereotyped motor mannerisms ↔ Disorganized/catatonic behaviors

General impairments in social communication ↔ Negative symptoms

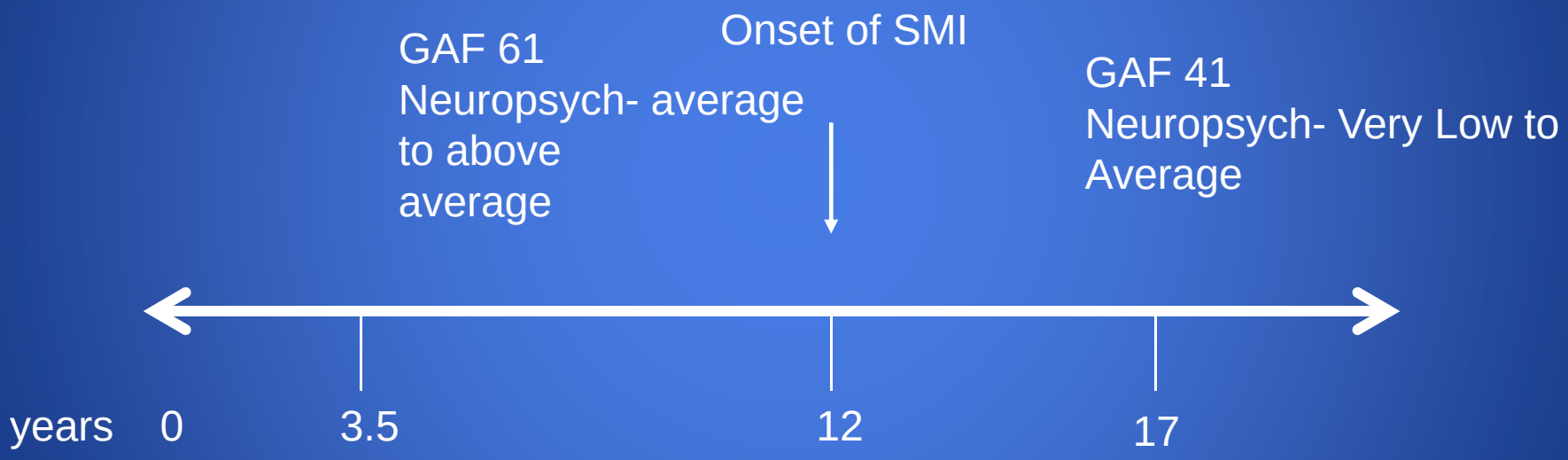
PSYCHOSIS

Starling, F & Dossetor,D (Pervasive Developmental Disorders and Psychosis. (2009) Current Psychiatry Reports 2009, 11:190–196

- Thought disorder and bizarre behavior – unreliable due to the fact that they are also core PDD symptoms.
- Delusions -more reliable but cautiously useful as "unusual world view" and idiosyncratic obsessions also seen commonly in ASDs (AS)
- auditory hallucinations should be differentiated from self-talk or pseudohallucinations
- Delusions and Hallucinations= hallmark of psychosis

Determining Etiology of Dysfunction

Time line



INTERVENTIONS

General Intervention Aims

- Reduce unsafe behaviors
- Improve self-regulation skills
- Increase positive social interactions
- Increase parent/guardian management skills
- Acquire adequate community supports to sustain post-discharge for inpatients

Treatment of Autism Spectrum Disorders

- Multi-Modal Approach
  - Behavioral
  - Educational
  - Pharmacological
- Target Appropriate Developmental Stage
  - Early Assessment and Intervention
  - Ongoing Therapy

“Mainstay” Treatments:

- Autism Spectrum Disorder specific, interaction-based therapy
  - Applied Behavioral Analysis (ABA)
  - SCERTS (Social, communication, emotional regulation, transactional support)
  - Many others
- Speech/language therapy
- Social skills group (“Lunch Bunch,” other)

Common Additional Treatments

- Occupational Therapy
  - Overall level of adaptive functioning
  - Fine motor skills
  - Sensory processing (integration)
- Physical Therapy
- Cognitive Behavioral Therapy
- Behavioral Interventions (sleep, self-help skills)
- Life Skills
- Other
  - Activities (swimming, music group, massage)
  - Animal (therapeutic horseback riding, service dogs)

Psychopharmacology Evaluation

- Inventory of Symptoms
- Detailed Developmental History
- Medical History
- Detailed History about Changes in Environment
- Ask about use of vitamins, supplements or oral chelating agents

Diagnostic Interviews and Tools Used to Measure Outcomes of Treatment

- Autism Comorbidity Interview Present and Lifetime Version (ACI-PL)
- Clinical Global Impressions Scale
- Aberrant Behavior Checklist
- Children's Psychiatric Rating Scale
- Children's Yale-Brown Obsessive Compulsive Scale Modified for Pervasive Developmental Disorder

Target of Medication

- Core Features of Autism
  - Impaired social interaction and communication
  - Repetitive behavior/ restricted interests
- Specific Behavioral Problems
  - Aggression, Irritability, Self-injury
  - Hyperactivity
  - Anxiety (stereotypy/repetitive behaviors)
  - Sleep

There are currently no medications that are FDA approved for treating core features of ASDs.

Evidence for Medications to Treat Irritability, Aggression and Self Injury

Drug	Indicated Age	Labeled Indication	Dosing Studied	Evidence
Aripiprazole	6+	Irritability	5-15 (8.6 mg)	A
Risperidone	5+	Irritability	0.5-3.5 mg (1.8mg)	A
Methylphenidate	None	None	0.125 to 0.5 mg/kg/day	A
Divalproex	None	None	20 mg/kg	B
Buspirone (n=22)	None	None	15- 45 mg	D

Evidence for Medications to Treat Hyperactivity

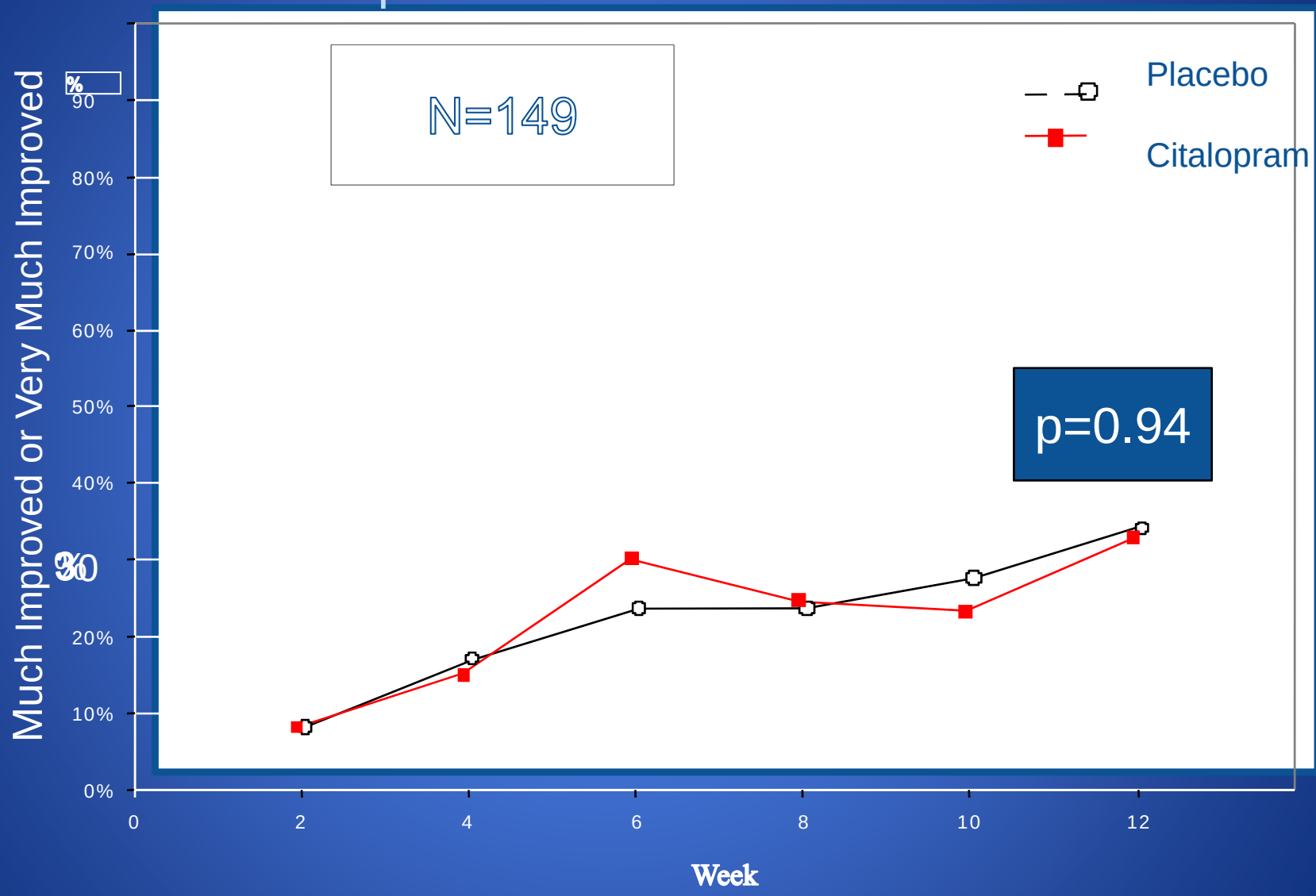
Drug	FDA Indicated Age	Labeled Indication	Dosing Studied	Evidence
Methylphenidate	None	None	0.125 to 0.5 mg/kg per dose	A
Atomoxetine	None	None	1.2 mg/kg	B
Clonidine	None	None	0.15-0.2 mg	C
Guanfacine	None	None	1-3 mg (TID)	B

ASD Core Symptoms and Targeted Interventions

- Repetitive Behaviors
  - Selective Serotonin Reuptake Inhibitors
    - (Fluvoxamine and fluoxetine studied in adults)
  - Atypical antipsychotics – secondary outcome of irritability studies -improved CY-BOCS scores for repetitive behaviors
  - Divalproex – benefit seen in very small randomized controlled trial of 13 individuals with ASD
  - Limit therapy to those who display anxiety distress associated with repetitive behaviors or when behaviors are severe

Benvenuto et al, Brain & Development 35, 119-127, 2013; Kaplan and McCracken, Pediatr Clin North Amer 59: 175-187, 2012; Dove et al, Pediatrics 130, 717-726, 2012)

Response in Double Blind Placebo Controlled Trial of Citalopram in Youth with ASDs



Much Improved or Very Much Improved on (CGI-I) over 12-Week

Evidence-based Treatments for Depression/Anxiety and Sleep for those on the Spectrum

(Kaplan and McCracken, Pediatr Clin North Amer 59: 175-187, 2012)

- Depression and Anxiety
  - Limited guidance in literature
  - Support for use of selective serotonin reuptake inhibitors in adults with ASD
  - High rate of activation and somatic complaints in children
- Sleep Disorders
  - Use Medications only when psychosocial treatments fail
  - Lack of FDA-approved treatments
  - Several recent small randomized controlled trials of melatonin have had encouraging results
    - Up to 6 mg/day
    - no significant side effects

Glutamate/GABA related Treatments in ASD

- Lemonnier et al 2012 – Randomized Controlled Trial of bumetanide – chloride channel antagonist that reinforces GABA activity
  - 60 children (age 3-11) with autism or Asperger's
  - 1 mg daily for 3 months
  - Significant reduction in Childhood Autism Rating Scale scores
  - Significant improvement vs placebo on CGI-I
  - Non-significant reduction in ADOS scores – significant when analysis excludes the most severely affected patients

Combined Treatment

- Parent Training (PT) and Risperidone
  - PT plus med showed modest benefit over medication alone after 24 weeks
  - One year follow up- advantage of combined treatment attenuated by more than half at follow up

Scahill et al Jaacap 51; 136-146, 2012; Arnold et al. Jaacap 51; 1173-1184, 2012

Clinical Pearls for Prescribing in ASD

- Start with agents that have better adverse effect profiles before moving to atypicals
- The old axiom is still true: START LOW, GO SLOW
- Effects are maximized at lower doses than used in typically developing children
- Often medications are less tolerated than in typically developing individuals

Key Take Home Points

- DSM-5, ASD one category - Two core domains with specifiers
- Autism is a complex disorder
- Important to Assess for Psychiatric Comorbid Conditions
- Provided a frame for determining the route of an individuals functional impairment (ASD vs SMI)
- Covered Evidence Based Interventions

American Academy of Pediatrics Toolkit

- *Autism: Caring for Children With Autism Spectrum Disorders: A Resource Toolkit for Clinicians*
- Contents
  - CD
    - Physician fact sheets
    - Family handouts
    - Supporting documents
  - Printed materials
    - Poster (CDC "Act Early" campaign)
    - Brochure samples
- www.aap.org/publiced/autismtoolkit.cfm

Thank You!